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Localization of Abnormal Discharges Causing Insular Epilepsy by Magnetoencephalography

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The insula, one of the five cerebral lobes of the brain, is located deep within the brain and lies mainly beneath the temporal lobe. Insular epilepsy can be easily confused and misdiagnosed as temporal lobe epilepsy (TLE) because of the similar clinical symptoms and scalp electroencephalography (EEG) findings due to the insula location and neuronal connections with the temporal lobe. Magnetoencephalography (MEG) has higher sensitivity and spatial resolution than scalp EEG, and thus can often identify epileptic discharges not revealed by scalp EEG. Simultaneous scalp EEG and MEG were performed to detect and localize epileptic discharges in two patients known to have insular epilepsy associated with cavernous angioma in the insula. Epileptic discharges were detected as abnormal spikes in the EEG and MEG findings. In Patient 1, the sources of all MEG spikes detected simultaneously by EEG and MEG (E/M-spikes) were localized in the anterior temporal lobe, similar to TLE. In contrast, the sources of all MEG spikes detected only by MEG (M-spikes) were adjacent to the insular lesion. In Patient 2, the sources of all MEG spikes detected simultaneously by EEG and MEG (E/M-spikes) were localized in the anterior temporal lobe. These findings indicate that MEG allows us to detect insular activity that is undetectable by scalp EEG. In conclusion, simultaneous EEG and MEG are helpful for detecting spikes and obtaining additional information about the epileptic origin and propagation in patients with insular epilepsy.

Keywords: electroencephalography; insular epilepsy; magnetoencephalography; spike; temporal lobe epilepsy
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The insula, one of the five cerebral lobes of the brain, is located deep within the brain and lies mainly beneath the temporal lobe (Penfield and Faulk 1955). Scalp electroencephalography (EEG) is relatively insensitive to detect neuronal activity in the insula because of this deep location, so insular epilepsy is rarely reported (Fiol et al. 1988; Cukiert et al. 1998). Furthermore, the insular cortex has multiple connections with the adjacent cerebral cortex, especially with the temporal lobe (Penfield and Faulk 1955; Augustine 1996), so that insular epilepsy shares similar clinical features with temporal lobe epilepsy (TLE), including nausea, abnormal throat sensation, epigastric discomfort, chewing, and lip smacking (Fiol et al. 1988; Roper et al. 1993; Cukiert et al. 1998; Isnard et at. 2000; Ostrowsky et al. 2000). Scalp EEG localizes the epileptic discharges of both TLE and insular epilepsy in the anterior temporal lobe. Therefore, insular epilepsy may be misdiagnosed as TLE, unless a structural lesion is identified within the insula (Roper et al. 1993; Cukiert et al. 1998) or epileptic discharge is detected within the insula by invasive EEG monitoring using intracranial electrodes (Roper et al. 1993; Isnard et al. 2000).

Magnetoencephalography (MEG) is a noninvasive neurophysiologic technique to detect the magnetic fields generated by electric currents in the brain, and has been frequently used to localize the epileptic discharges in patients with focal epilepsy (Stefan et al. 1992; Nakasato et al. 1994; Knowlton et al. 1997; Jin et al. 2007), but not in patients with insular epilepsy.

We performed MEG in two patients with insular epilepsy, and show that MEG has the potential to identify focal epileptic discharges localized in the insula against the background of extensive propagated activity in the temporal lobe.

Methods

Patient profiles

Patient 1: A 29-year-old right-handed male suffered his first generalized tonic clonic seizure at the age of 22 years, followed by recurrent complex partial seizures consisting of motionless staring and loss of consciousness occurring three to four times per month. Neurological examination found no abnormalities. Magnetic reso-

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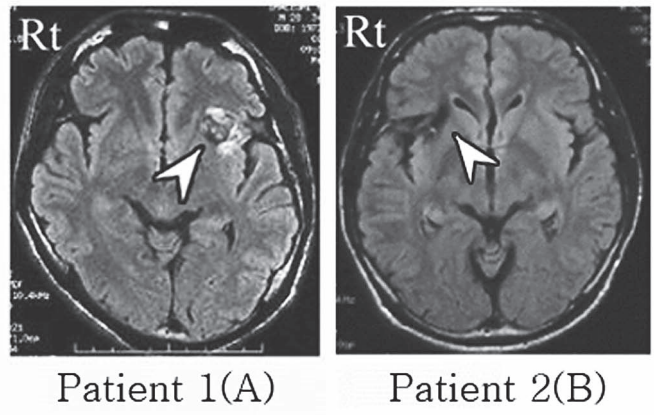

Fig. 1. Fluid-attenuated inversion recovery magnetic resonance images of Patients 1 and 2. Cavernous angioma is located in the left (Patient 1, A) and right (Patient 2, B) anterior insulae (white arrowheads).

nance (MR) imaging showed a cavernous angioma in the left insula (Fig. 1A). Scalp EEG demonstrated epileptic discharges in the left frontotemporal region. Long-term video EEG monitoring identified complex partial seizures with the typical TLE pattern of scalp EEG characterized by rhythmic 5 to 7 Hz ranged theta activity in the left anterior temporal area. The patient became seizure-free following the initiation of combined carbamazepine and lamotrigine medication.

Patient 2: A 33-year-old right-handed male had suffered simple partial seizures since the age of 28 years, manifesting as epigastric discomfort with nausea and chest tightness occurring one to two times per week. Neurological examination found no abnormalities. MR imaging showed a cavernous angioma in the right insula (Fig. 1B). Scalp EEG identified epileptic discharges in the right anterior temporal area. The patient became seizure-free following the initiation of carbamazepine medication.

Both patients underwent only standard medical procedures approved in Japan, including both EEG and MEG, with written informed consent. No experimental intervention was performed.

MEG and EEG

MEG and EEG were simultaneously performed in a shielded room to detect spontaneous epileptic discharges. An MEG system covering the whole head was used with 204 (Patient 1) and 122 (Patient 2) channels (Neuromag Ltd., Helsinki, Finland). EEG was measured with 28 channel electrodes including anterior temporal electrodes according to the usual international 10-20 system guidance. Measurements were continued for 30 minutes in the awake and sleep states for each patient. EEG and MEG spikes were selected by visual inspection of the simultaneous EEG and MEG data. EEG spikes were identified by well-known standard methods with bipolar and referential montages. MEG spikes were identified as clear dipole patterns of magnetic fields on an isofield contour map, and localized in the brain by estimation of the equivalent current dipole (ECD) with the head-fitting model, a standard method for MEG. The estimated dipole was represented with position, orientation, and moment values, and superimposed on the three-dimensional T1-weighted MR images (1.5 tesla; GE Medical System, Milwaukee, WI, USA) for spike localization. We defined M-spikes or E-spikes as spikes appearing in only the MEG or EEG recordings, respectively. E/M-spikes were defined as spikes appearing simultaneously in both the MEG and EEG.

Results

Patient 1: Combined MEG and EEG detected a total of 16 spikes including 11 E/M-spikes and 5 M-spikes. Scalp EEG showed that all spikes had left frontotemporal distribution, whereas MEG demonstrated that the E/M-spikes were localized in the left anterior temporal lobe with posterior orientation in a small and tight clustering. MEG showed the M-spikes were scattered around the perilesional insular area with either upward or downward orientation (Fig. 2), and these M-spikes had smaller ECD moment than the E/M-spikes (Fig. 3).

Patient 2: Combined MEG and EEG detected a total of 110 E/M-spikes but no M- or E-spikes. Scalp EEG showed that all spikes had right frontotemporal distribution, whereas MEG demonstrated the E/M-spikes were localized in the right anterior temporal lobe with either posterior-downward or anterior-upward orientations (Fig. 4).

Discussion

Combined MEG and EEG showed that the most common type of spike was the E/M-spikes in our two patients with insular epilepsy. Scalp EEG showed the E/M-spikes had frontotemporal distribution and MEG demonstrated the E/M-spikes localized in anterior temporal lobe. This spike type, also known to be common in TLE (Iwasaki et al. 2002), may represent temporal lobe activity propagated from the insula. The insular cortex is known to have dense neuronal connections to the temporal cortex (Penfield and Faulk 1955; Augustine 1996; Isnard et al. 2000; Ostrowsky et al. 2000). Consequently, insular epilepsy and TLE are likely to have common clinical features as well as similar scalp EEG distribution and MEG localization of E/M-spikes.

However, MEG detected M-spikes with different ECD localization, orientation, and moment compared to the E/M-spikes in our Patient 1. We suggest that the M-spikes represent more restricted focal epileptic discharges in the peri-lesional insular cortex. The ECDs of M-spikes may be

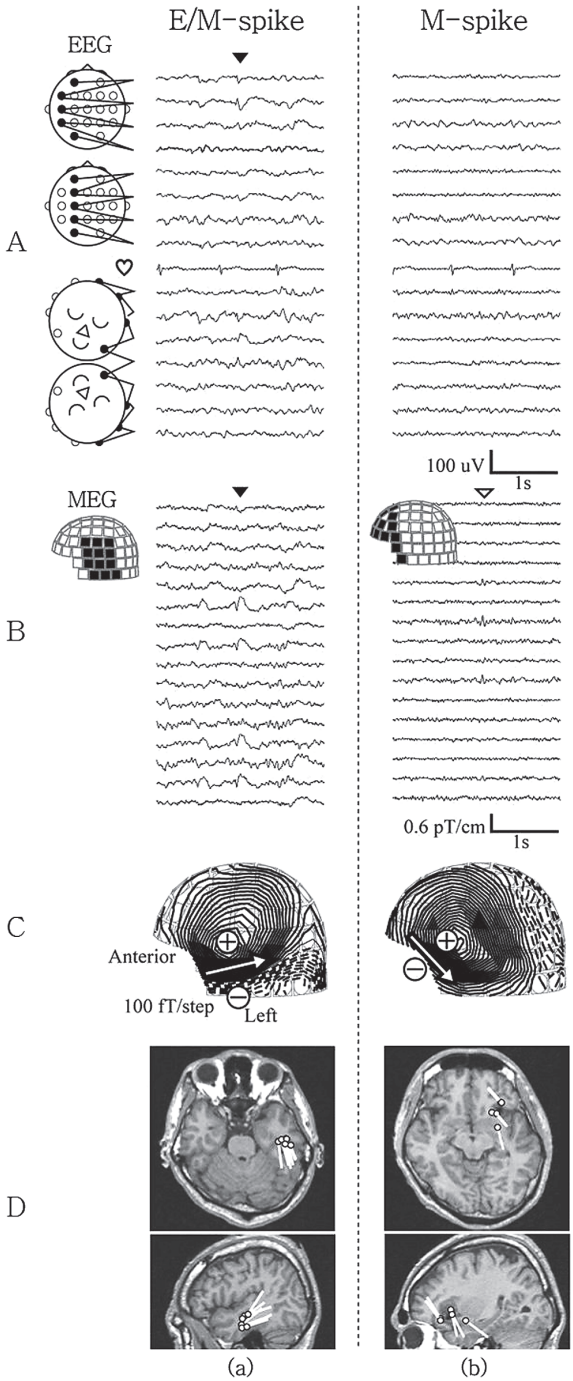

Fig. 2. Simultaneous recording of scalp EEG and MEG in Patient 1. (A, B) Epileptic discharges are detected on both EEG and MEG recordings (E/M-spike, black arrowheads) or on the MEG recording only (M-spike, white arrowhead). (C) Isofield contour maps of both the E/M-spikes and M-spikes showing a clear dipole pattern over the left frontotemporal area. (D) Equivalent current dipoles (ECDs) of the E/M- and M-spikes superimposed on the T1-weighted magnetic resonance images. Circles indicate the ECD position and bars indicate the ECD orientation. Note that the ECDs of the E/M-spikes show anterior temporal lobe localization (a), which is also typical of temporal lobe epilepsy. In contrast, the ECDs of the M-spikes are localized in the peri-lesional insular cortex (b).

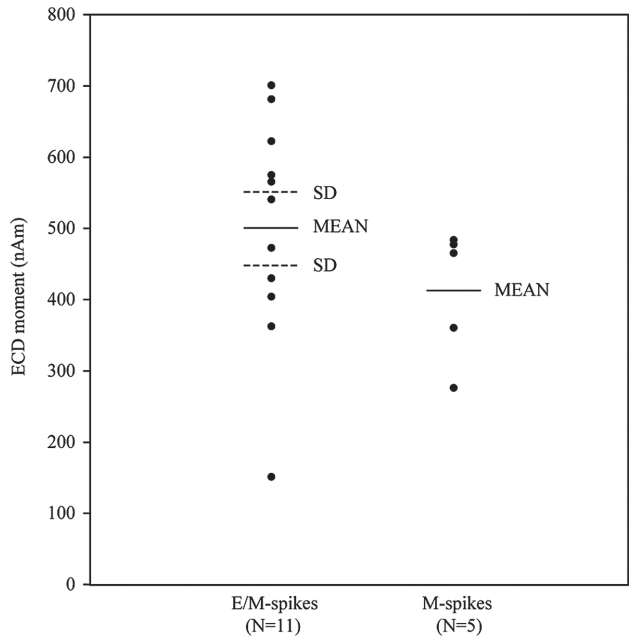

Fig. 3. ECD moments of all MEG spikes in Patient 1. Horizontal bars indicate the mean ECD moment value with standard deviation (S.D.). The M-spikes tended to have smaller ECD moment than the E/M-spikes.

scattered due to poor signal-to-noise ratios, and the orientation could be random if such restricted focal activity has multiple sources around the insular lesion. Scalp EEG cannot detect M-spike activity because the amplitude is too small to overcome the background brain noise resulting from the poor spatial resolution of scalp EEG (Park et al. 2004). The larger ECD moments of the E/M-spikes may reflect more extended sources compared to the M-spikes. Therefore, both the localization and orientation of the E/M-spikes are likely to be consistent for propagated activity, as observed in both Patients 1 and 2. Any small focus of activity in the insular cortex may be easily obscured by the background brain activity from the overlapping cortex. These considerations would explain why fewer M-spikes than E/M-spikes were detected in Patient 1 and why none were found in Patient 2. Therefore, we were surprised that MEG could detect the insular activity in Patient 1. Clearly, the insular activity can be detected against the background brain noise. Theoretically, MEG may fail to detect insular activity because MEG detects only tangential current to the scalp, whereas current generated from the insular cortex will be oriented radially to the scalp, since the insular cortex is roughly parallel to the scalp. However, presumably MEG detected the tangential current produced by the insular cortex possibly distorted by the structural lesion (Park et al. 2002).

Previously, M-spikes were considered to have similar localization to E/M-spikes in patients with TLE or extratemporal epilepsy (Park et al. 2002, 2004). However, the present findings in our Patient 1 suggest that the M-spikes

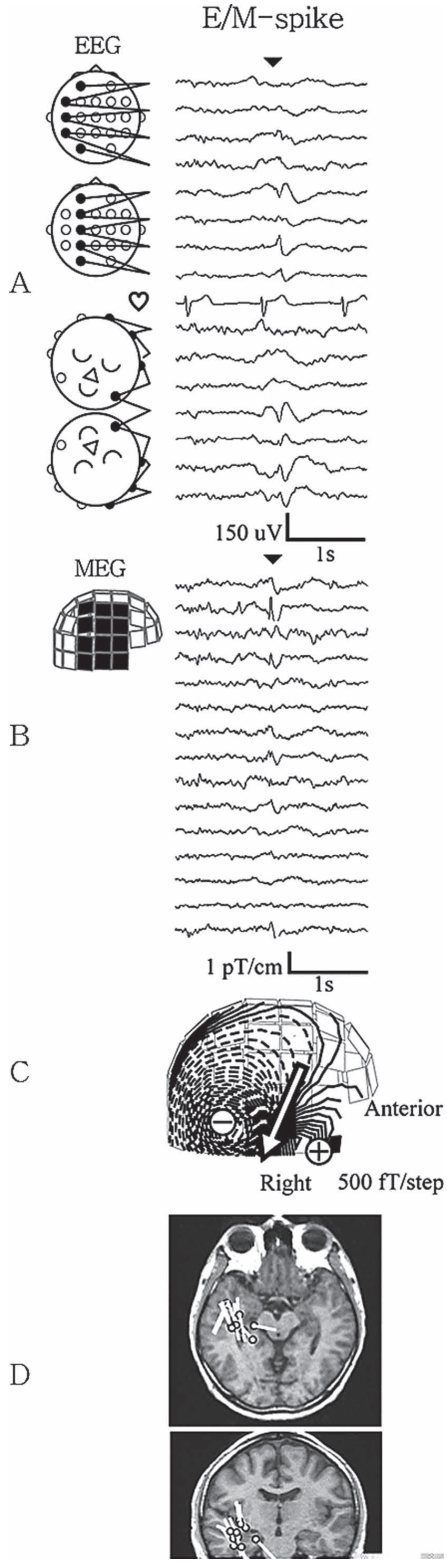

Fig. 4. Simultaneous recording of scalp EEG and MEG in Patient 2. (A, B) Epileptic discharges are detected on both EEG and MEG recordings (E/M-spike, black arrowheads). (C) Isofield contour map of the E/M-spikes showing a clear dipole pattern over the right temporal area. (D) ECDs of the E/M-spikes superimposed on the T1-weighted magnetic resonance images showing anterior temporal lobe localization.

may be earlier and more localized, and so may provide important localization information about the epileptic origin. We propose that the E/M-spikes represent only the extensively propagated activity in the temporal lobe but not the localized focal activity in the insula. Therefore, the detection of M-spikes has potential for the differential diagnosis of insular epilepsy. Such specific identification of the epileptic origin is very important to prevent erroneous diagnosis and incorrect treatment in patients with epilepsy, especially in patients with insular epilepsy caused by nonlesional or very subtle small lesional origins.

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Conflict of Interest

All authors have no conflict of interest in this study.

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