Comparison of Magnetoencephalographic Spikes with and without Concurrent Electroencephalographic Spikes in Extratemporal Epilepsy

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Department of Neurology, Gil Medical Center, Gachon Medical School, Inchon, Korea,
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Park, H.M., Nakasato, N., Iwasaki, M., Shamoto, H., Tominaga, T. and Yoshimoto, T. Comparison of Magnetoencephalographic Spikes with and without Concurrent Electroencephalographic Spikes in Extratemporal Epilepsy. Tohoku J. Exp. Med., 2004, 203 (3), 165-174 — Interictal spikes in patients with epilepsy may be detected by either electroencephalography (EEG) (E-spikes) or magnetoencephalography (MEG) (M-spikes), or both MEG and EEG (E/M-spikes). Localization and amplitude were compared between E/M-spikes and M-spikes in 7 adult patients with extratemporal epilepsy to evaluate the clinical significance of MEG spikes. MEG and EEG were simultaneously measured using a helmet-shaped MEG system with planar-type gradiometers and scalp electrodes of the international 10-20 system. Sources of E/M-spikes and M-spikes were estimated by an equivalent current dipole (ECD) model for MEG at peak latency. Each subject showed 9 to 20 (mean 13.4) E/M-spikes and 9 to 31 (mean 16.3) M-spikes. No subjects showed significant differences in the ECD locations between E/M- and M-spikes. ECD moments of the E/M-spikes were significantly larger in 2 patients and not significantly different in the other 5 patients. The similar localizations of E/M-spikes and M-spikes suggest that combination of MEG and EEG is useful to detect more interictal spikes in patients with extratemporal epilepsy. The smaller tendency of ECD amplitude of the M-spikes than E/M-spikes suggests that scalp EEG may overlook small tangential spikes due to background brain noise. Localization value of M-spikes is clinically equivalent to that of E/M-spikes.

magnetoencephalography; electroencephalography; epilepsy; interictal spike; equivalent current dipole

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Magnetoencephalography (MEG) and electroencephalography (EEG) provide higher time resolutions than other clinical neuroimaging techniques. Theoretically, scalp EEG detects both tangential and radial components of a current source in a spherical volume conductor, whereas MEG detects only the tangential components (Cohen and Cuffin 1983; Hämäläinen et al. 1993). However, MEG has detected a large number of epileptic discharges without concurrent activity in conventional scalp EEG in patients with temporal lobe (Knowlton et al. 1997; Iwasaki et al. 2002b; Zijlmans et al. 2002; Iwasaki et al. 2003; Lin et al. 2003) and extratemporal lobe (Knowlton et al. 1997; Park et al. 2002; Yoshinaga et al. 2002) epilepsy. Therefore, the sensitivity of MEG and EEG for the detection of epileptic discharges does not depend only on source orientation.

Simultaneous MEG and subdural EEG demonstrated that synchronized epileptic activity involving the lateral neocortex extending over an area of 3 to 4 cm$^2$ was necessary to produce a detectable MEG signal at the scalp (Baumgartner et al. 1992; Mikuni et al. 1997; Oishi et al. 2002). In contrast, scalp EEG can only detect epileptic activity in an area of at least 6 or 10 cm$^2$ (Cooper et al. 1965). Thus, MEG may require a smaller area of epileptic cortex to produce detectable signals than scalp EEG. However, such comparison of detectability may be limited because subdural EEG preferentially detects the radial current from the gyral cortex, so the contribution of the tangential current from the sulcal cortex may be underestimated. Comparison of EEG and MEG spikes may be complicated in the mesial temporal lobe and other “deep” epilepsy locations because the initial spike activity may be overlooked by scalp EEG and/or MEG simply due to the large distance between the sources and sensors.

The present study compared the location and strength of the equivalent current dipole (ECD) for MEG spikes which were associated and not associated with concurrent EEG spikes in patients with extratemporal lateral convexity epilepsy to enable simple comparison of the detectability between MEG and EEG, and to investigate why some spikes are detected by MEG but not by EEG and whether the source location differs.

**MATERIALS AND METHODS**

**Patients**

This study included 7 adult patients, 3 males and 4 females aged 15 to 44 years, with localization related epilepsy. Epileptogenicity in the lateral convexity was confirmed by observation of structural lesions by magnetic resonance (MR) imaging in 5 patients (two with frontal lobe lesions, one with a parietal lobe lesion, and two with hemimegalencephaly) and focal seizure onset by electrocorticography (ECoG) via chronic implantation of subdural grid electrodes in two patients. The clinical profiles are presented in Table 1. Informed consent for this study was obtained from all patients.

**MEG and EEG recording**

Spontaneous interictal EEG and MEG were simultaneously measured in a magnetically shielded room for about 30 minutes in the drowsiness to light sleep states. EEG used 28 channel electrodes including anterior temporal electrodes placed on the scalp according to the international 10-20 system. MEG was measured by whole head neuromagnetometer systems with 122 or 204 channels (Neuromag Ltd., Helsinki, Finland). The MEG sensors consisted of rectangular pairs of planar gradiometers aligned in a helmet-shaped dewar vessel, into which the patient’s head was inserted during the measurement. The details of this system are described elsewhere (Ahonen et al. 1993). EEG and MEG data were sampled at 400 Hz and band-pass filtered between 0.03 to 130 Hz. The total recording was divided into 5 or 6 sets and stored in a hard disk for later offline analysis. The head coordination system was acquired before each set to minimize the error in coordinate integration between MEG and MR imaging.
All patients underwent three-dimensional MR imaging after MEG recording. Three fiducial markers were attached at the nasion and bilateral preauricular points, identical to those used in MEG. T1-weighted MR imaging was obtained using a Signa Advantage (GE Medical System, 1.5 Tesla). The MR images consisted of 124 sequential sagittal slices of 1.5 mm thickness, with 256×256 points on a field of view of 240×240 mm. After reconstructing the three-dimensional images, the fiducial points were identified to transform the MR imaging coordinate system to the MEG coordinate system. For source modeling, the MR imaging head shape data were used to determine the best-fit single sphere for each subject’s head.

**Spike sampling**

EEG and MEG data were reviewed separately and 50 spikes were identified. If less than 50 spikes were identified, all data sets were checked.

EEG data were digitally filtered with a bandpass of 0.5 to 45 Hz. EEG spikes were identified by a standard method with bipolar and referential montages. The time and distribution of every identified EEG spike was listed.

MEG data were digitally filtered with a bandpass of 2 to 45 Hz. MEG spikes were identified by visual inspection on plot as a spike with clear morphology and amplitude above background activity. Every identified MEG spike was listed on the plot. Then, every identified MEG spike on plot was checked for dipole pattern by isofield map and the source was estimated by a single dipole model. MEG spikes were accepted for the present study with an isofield map consistent with a physiologically reasonable dipole source localization.

We defined E/M-spikes as spikes appearing on both EEG and MEG simultaneously (peak time difference less than 100 milliseconds), E-spikes as spikes appearing only on EEG, and

**MR imaging**

All patients underwent three-dimensional MR imaging after MEG recording. Three fiducial markers were attached at the nasion and bilateral preauricular points, identical to those used in MEG. T1-weighted MR imaging was obtained using a Signa Advantage (GE Medical System, 1.5 Tesla). The MR images consisted of 124 sequential sagittal slices of 1.5 mm thickness, with 256×256 points on a field of view of 240×240 mm. After reconstructing the three-dimensional images, the fiducial points were identified to transform the MR imaging coordinate system to the MEG coordinate system. For source modeling, the MR imaging head shape data were used to determine the best-fit single sphere for each subject’s head.

**Table 1. The list of 7 cases with extratemporal lateral convexity epilepsy**

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (year)</th>
<th>Epileptogenic hemi-sphere</th>
<th>Seizure type</th>
<th>MRI lesion</th>
<th>Intercitial spike localization</th>
<th>Surgical intervention</th>
<th>Class of seizure outcome (Engel 1987)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>19</td>
<td>R</td>
<td>SPS</td>
<td>none</td>
<td>C4 B' F R Rol</td>
<td>R Rol resection</td>
<td>I</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>26</td>
<td>R</td>
<td>SPS to F sGTC</td>
<td></td>
<td>C4-P4 R F -</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>30</td>
<td>L</td>
<td>SPS to Hemi</td>
<td>P</td>
<td>F3-C3 L F -</td>
<td>L P resection</td>
<td>III</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>44</td>
<td>L</td>
<td>SPS to P CPS</td>
<td>none</td>
<td>P3 L P P</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>15</td>
<td>L</td>
<td>SPS to CPS</td>
<td></td>
<td>F3-F7 L F -</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>27</td>
<td>L</td>
<td>SPS to Hemi</td>
<td>sGTC</td>
<td>F3-C3 L F -</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>22</td>
<td>R</td>
<td>SPS F</td>
<td></td>
<td>C4-F4 R F R Rol</td>
<td>R Rol resection &amp; MST</td>
<td>III</td>
</tr>
</tbody>
</table>

SPS, simple partial seizure; CPS, complex partial seizure; sGTC, secondarily generalized tonic clonic seizure; L, left; R, right; B, bilateral; F, frontal; P, parietal; Rol, rolandic; Hemi, hemisphere; *propagation from right to left; MST, multiple subpial transection.
M-spikes as spikes appearing on only MEG. The time difference between EEG and MEG spike peaks was measured for the E/M spikes.

The source of the MEG spike peak was estimated by a single dipole model for the E/M- and M-spikes. The ECD location in the lateral (X), anterior (Y) and superior (Z) directions from the midpoint of the bilateral preauricular points and ECD moment were compared between the E/M- and M-spikes for each patient. Student’s t-test was used for statistical analysis and the criterion for statistical significance was \( p < 0.05 \).

**RESULTS**

**Spike detection**

The total number of MEG spikes ranged from 18 to 49 (mean 29.7) in each patient, consisting of 9 to 20 (mean 13.4) M/E-spikes and 9 to 31 (mean 16.3) M-spikes. Fig. 1 and 2 present typical examples of spikes.

**Time lag of the spike peaks**

The absolute time lag between the EEG and MEG spike peaks in E/M-spikes was 0.2 to 17.4 (mean 6.1) milliseconds.

**Location of the spike ECD**

No significant difference was found in ECD localization between the E/M-spikes and M-spikes in any patient (Fig. 3). The mean differences for X, Y, and Z were 2.1, 3.0, and 3.0 mm, respectively.

**Moment of the spike ECD**

The moments of the E/M-spikes were statistically larger than those of the M-spikes in two cases (Case 1 and 2) and slightly larger in four cases but there were no statistical significance (Case 3,4,5, and 6) (Fig. 3). In contrast, only one patient (Case 7) had a larger moment for the M-spike than the E/M-spike but there was no statistical significance.

**DISCUSSION**

This study compared the clinical information provided by the M-spike and the E/M-spike in patients with lateral convexity epilepsy and found that the ECD of M-spikes and E/M-spikes showed no localization difference but M-spikes tended to have a smaller moment.

The present study included patients with lateral convexity epilepsy to compare spike ECD parameters as in our previous study of spike detectability between EEG and MEG (Park et al. 2002). Comparison of detectability is easier for lateral convexity epilepsy than mesial or basal temporal epilepsy in which deeper sources may be overlooked by the limited sensor array configurations of scalp EEG and MEG systems. In the present study, all analyzed spikes originated from the relatively superficial cortex with adequate coverage from the scalp EEG and MEG sensors. Both EEG and MEG have higher sensitivity for superficial sources than for deep sources (Cohen and Cuffin 1983; Hämäläinen et al. 1993; Nakasato et al. 1994; Knowlton et al. 1997; Stefan et al. 2000).

The EEG and MEG systems used in the present study had different head coverage densities. MEG was measured by a whole head system with 204 sensors, whereas EEG was measured by the 28 channels of the international 10-20 system. A higher density of EEG electrodes might pick up more spikes (Laarne et al. 2000; Lantz et al. 2003) and increase the ratio of EEG spikes. However, the present study was designed to compare ECD parameters between E/M-spikes and M-spikes, not the spike detectability between EEG and MEG. The international 10-20 electrode system is typical for current routine clinical simultaneous measurement of EEG and MEG (Stefan et al. 1992; Iwasaki et al. 2002a; Park et al. 2002; Yoshinaga et al. 2002; Zijlmans et al. 2002; Lin et al. 2003).

The present study found no statistical difference in the ECD localization of MEG spikes between the M-spikes and E/M-spikes, which emphasizes the clinical accuracy and utility of MEG. The present and previous reports (Iwasaki et al. 2002b; Park et al. 2002; Zijlmans et al. 2002; Lin et al. 2003) show that M-spikes are...
Fig. 1. Examples of interictal spikes in Case 1. (Left) Interictal spike discharges are detected by only MEG (M) or both EEG and MEG (E/M). (Right Top) Isofield contour maps of both M- and E/M-spike peaks show a clear dipole pattern over the right central area. Arrow lengths indicate the relative moment of the spike dipoles. (Right Bottom) Equivalent current dipoles (ECD) of the E- and E/M- spikes superimposed on the T1-weighted MR images. Circles indicate the ECD position and bars indicate the ECD orientation and moment. Note that the E/M- spike has significantly larger ECD moment than the M-spikes but the localizations are very similar (Fig. 3).
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often found more frequently and even exclusively in some patients. This study shows that the ECD location detected only by MEG is clinically equivalent to that detected by both MEG and EEG.

Paroxysmal cortical activation is not a simple event and source detection by MEG must be influenced by many factors, including dipole orientation, depth of source, spatial extension, and brain conductivity (Sutherling et al. 1988). MEG can be expected to have higher sensitivity than EEG. An active cortical area of 6 cm$^2$ is necessary to produce detectable signals in scalp EEG (Cooper et al. 1965) compared to 3 to 4 cm$^2$ for MEG (Mikuni et al. 1997; Oishi et al. 2002; Shigeto et al. 2002). In the present study, M-spikes generally had smaller ECD moments than E/M-spikes, except in one patient (Case 7). These results suggest that the source of the tangential current is generally smaller in M-spikes than in E/M-spikes. In other words, the small spike activity of the tangential current can be detected by MEG but not by scalp EEG. Although tangential current is theoretically detectable by scalp EEG, background brain noise may obscure the focal epileptic activity. Exceptionally in Case 7, the E/M-spikes had smaller ECD moments than the M-spikes, although the difference was not statistically significant. In this case, the radial component of the spike current might be dominant compared to the tangential component.

Fig. 2. Examples of interictal spikes in Case 7.

*(Top)* Interictal spike discharges are detected by only MEG (M) or both EEG and MEG (E/M). *(Middle)* Isofield contour maps of both M- and E/M-spike peaks show a clear dipole pattern over the right frontal area. Arrow lengths indicate the relative moment of the spike dipoles. *(Bottom)* Equivalent current dipoles (ECD) of the E- and E/M-spikes superimposed on the T1-weighted MR images. Circles indicate ECD position and bars indicate ECD orientation and moment. There was no significant difference in ECD moment between the E/M- and M-spikes (Fig. 3).
Fig. 3. Location and moment of equivalent current dipoles (ECD) of spikes detected by only MEG (M-spike) relative to those found by EEG and MEG (E/M-spike). X, Y and Z coordinates indicate lateral, anterior and superior position, respectively. Total numbers of E/M-spikes (closed squares) and M-spikes (open squares) are 20 and 20 in Case 1 (A); 18 and 31 in Case 2 (B); 9 and 9 in Cases 3 (C) and 4 (D); 14 and 20 in Case 5 (E); 14 and 16 in Case 6 (F); and 10 and 9 in Case 7 (F) respectively. No significant difference was found in ECD positions in each patient. ECD moments of M-spikes were significantly smaller than the E/M-spikes in Cases 1 and 2, non-significantly smaller in Cases 3 through 6 and non-significantly larger in Case 7.
Based on the present and previous studies, we propose a schema to explain the detection sensitivity of MEG and EEG spikes (Fig. 4). The factors affecting the sensitivity of EEG and MEG are simplified here to source orientation, source extension, and the effect of background brain noise. Radial current to the scalp can be measured by EEG but not by MEG (E-spike). Oblique current to the scalp can be measured by both EEG and MEG (E/M-spike). Tangential current to the scalp can be measured by both EEG and MEG under ideal conditions of no background brain noise. However, due to the smearing effect by inhomogeneous head conductivity, some of the tangential spikes may be overlooked by scalp EEG. Since MEG is far less influenced by inhomogeneous head conductivity, higher spatial resolution and thus higher sensitivity for tangential spikes can be expected. Tangential spikes can be detected by scalp EEG if the source is large enough to overcome the background brain noise. This may be why the ECD moment of the E/M-spikes was sometimes larger than that of the M-spikes in the present study as well as in a previous report (Lin et al. 2003).

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References


Stefan, H., Schneider, S., Feistel, H., Pavlik, G.,


