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Analysis of ictal magnetoencephalography using gradient magnetic-field topography (GMFT) in patients with neocortical epilepsy

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HIGHLIGHTS

- Gradient magnetic-field topography (GMFT) is useful for ictal magnetoencephalography (MEG).
- GMFT delineates the area of ictal MEG onset (ictal GMFT) at the gyral-unit level.
- The ictal GMFT area is concordant with the ictal onset zone of intracranial electroencephalography.

ABSTRACT

Objective: We aimed to validate the usefulness of gradient magnetic-field topography (GMFT) for analysis of ictal magnetoencephalography (MEG) in patients with neocortical epilepsy.
Methods: We identified 13 patients presenting with an ictal event during preoperative MEG. We applied equivalent current dipole (ECD) estimation and GMFT to detect and localize the ictal MEG onset, and compared these methods with the ictal onset zone (IOZ) derived from chronic intracranial electroencephalography. The surgical resection areas and outcomes were also evaluated.
Results: GMFT detected and localized the ictal MEG onset in all patients, whereas ECD estimation showed localized ECDs in only 2. The delineation of GMFT was concordant with the IOZ at the gyral-unit level in 10 of 12 patients (83.3%). The detectability and precision of delineation of ictal MEG activity by GMFT were significantly superior to those of ECD ($p < 0.05$ and $p < 0.01$, respectively). Complete resection of the IOZ in the concordant group provided seizure freedom in 3 patients, whereas seizures remained in 9 patients who had incomplete resections.
Conclusions: Because of its higher spatial resolution, GMFT of ictal MEG is superior to conventional ECD estimation in patients with neocortical epilepsy.
Significance: Ictal MEG study is a useful tool to estimate the seizure onset in patients with neocortical epilepsy.

1. Introduction

Magnetoencephalography (MEG) is a powerful tool for noninvasive preoperative evaluation of intractable epilepsy. MEG provides information of the spatial distribution of epileptic foci, which corresponds well to the surgical results (Otsubo et al., 2001; Pataraia et al., 2004; Oishi et al., 2006; Knowlton et al., 2006). Analysis with the equivalent current dipole (ECD) method has been conventionally applied for interictal spikes in preoperative MEG. However, ictal events are only occasionally captured during MEG recording. Since Stefan et al. (1992) reported their analysis of ictal magnetoencephalographic activity, several reports have been published on the usefulness of ictal MEG (Shiraishi et al., 2001; Eliashiv et al., 2002; Oishi et al., 2002; Tilz et al., 2002; Assaf et al., 2003; Tanaka et al., 2004; Yoshinaga et al., 2004; Medvedovsky et al., 2012). Although these studies using ECD succeeded in localizing ictal magnetoencephalographic activity, ECD analysis of ictal MEG has been controversial due to the low signal-to-noise ratio (SNR) during ictal activity (Tanaka et al., 2004; Tanaka et al., 2009; Yagyu et al., 2010). Because ECD estimation requires enough SNR for statistically appropriate confidence, the application of ECD

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for ictal onset activity with low SNR is unreliable. Although reports on several spatial filters to localize the source of ictal onset have recently been published (Tanaka et al., 2009; Yagyu et al., 2010; Fujiwara et al., 2012), there are no adequate methods to validate their estimated results statistically.

Gradient magnetic-field topography (GMFT) was developed to represent the spatio-temporal dynamics of brain surface activity (Hashizume et al., 2007). Unlike ECD estimation or other spatial filters, with GMFT there is no need to solve the biomagnetic inverse problem. Moreover, because GMFT is less influenced by the SNR, it can delineate brain activity even at the early phase of epileptic spikes, which is usually not suitable for appropriate ECD localization (Shirozu et al., 2010). The spatio-temporal accuracy was proved by comparison between GMFT and cortical voltage activity simultaneously recorded with intracranial electroencephalography (EEG) (Shirozu et al., 2016). The aim of this study was to validate the usefulness of GMFT for analysis of ictal MEG. We hypothesized that GMFT is superior to ECD for analysis of ictal neuromagnetic dynamics, even during early ictal activity.

2. Methods

2.1. Patients

We retrospectively reviewed 13 patients (10 males and 3 females; 5–45 years old) with intractable neocortical epilepsy who had ictal events during preoperative MEG. All of them had undergone epilepsy surgery, including cortical resection and/or multiple subpial transection, between 2000 and 2012. Twelve of the 13 patients underwent implantations of intracranial electrodes and chronic intracranial EEG monitoring (CiEEG) to determine the epileptogenic foci and resection areas. At their last follow-up examination, the patients' seizure outcomes were evaluated using Engel's classification system (Engel et al., 1993).

2.2. Surgical strategy

All patients underwent routine preoperative examinations, including evaluation of seizure semiology, neuropsychological tests, routine EEGs, long-term video EEGs, magnetic resonance imaging (MRI), single-photon emission computed tomography, and MEGs. After a comprehensive discussion at the Epilepsy Center of Nishi-Niigata Chuo National Hospital, Japan, the patients were advised of the indication for surgery as well as the necessity for CiEEG. The resection areas were determined by the presumed epileptogenic zones derived from the CiEEG results, including the ictal onset zone (IOZ) and the area with early propagation of ictal activity. The IOZ was determined as the area where the ictal discharges started. The ictal discharges included the following activities: low-voltage fast activity, spike bursts, and rhythmic spikes. One patient (Case 8), who had not received CiEEG, underwent surgery on the basis of the results of preoperative evaluation.

All patients or their parents provided written, informed consent before each surgical treatment.

2.3. MEG recording

MEG was performed using a 306-channel (204 channels of planar gradiometers and 102 channels of magnetometers), whole-head type neuromagnetometer (Neuromag system; Elekta-Neuromag Oy, Helsinki, Finland) at a sampling rate of 600.615 Hz and with a band-pass filter of 0.1–200 Hz. Although the routine recording time consisted of 4–6 series of 5-min epochs, the total recording time varied for each patient due to interruption by an ictal event or prolongation for capture of ictal events. Notification of ictal events was obtained by on-line visual detection of ictal waveforms and by observation of patients using a monitoring camera inside the magnetically shielded room. During recording, the state of each patient differed, as follows: awake with eye-closing, sleep deprivation, and drug-induced sleep (oral pentobarbital administration or low-dose thiopental drip infusion).

2.4. MEG analysis by ECD

For ECD analysis, we used dipole-fit software (x-fit; Elekta-Neuromag Oy, Helsinki, Finland). ECDs were calculated with a band-pass filter of 3–45 Hz. For analysis of interictal spikes, ECDs were fitted at the peak of the spikes. The pattern of interictal ECD distribution was divided into 3: tight cluster, broad cluster, and scatter. The tight cluster pattern showed the interictal ECD densely located within 1 gyrus. The broad cluster pattern had a dense distribution of interictal ECDs in 2 or more gyri. The scatter pattern showed sparse distribution of ECDs in the same lobe or hemisphere.

For ictal ECD analysis, several time points during an extended period of ictal onset were selected, because the actual ictal onset often could not be identified by visual inspection. For the same reason, we did not select sensors for dipole fitting, and we ignored the goodness-of-fit (GOF). The ictal ECD was defined by a typical dipole pattern isocontour map that showed a clear influx and efflux pattern. The distribution pattern of the ictal ECD was classified into 3 categories: localized, scatter, and failed. The localized pattern denoted ictal ECDs located within 1 or 2 gyri, and the scatter pattern showed ictal ECDs that were detected but not localized. The ictal and interictal ECDs were then superimposed onto the patient's individual MRI.

2.5. Ictal MEG analysis by GMFT

The data from the 204 channels of the planar gradiometers were used for GMFT analysis, which was calculated using MATLAB-based free software (hns_meg; http://meg.aalip.jp). The rationale for GMFT and its process of generation have been described elsewhere (Hashizume et al., 2007; Shirozu et al., 2010; Shirozu et al., 2016). In our study, we used a band-pass filter of 10–50 Hz for GMFT analysis. Areas exceeding 200 femto-tesla (fT)/cm were determined to be activated areas, which were distinguishable from background activity. This threshold was determined by the fact that the gradient magnetic-field of biomagnetic background activity is usually observed to be 50–200 fT/cm.

First, ictal MEG discharges were identified visually from the ictal events described above, in which we scanned the ictal waveforms with time segments of 5–10 s. The ictal MEG discharges started with spike bursts or repetitive spikes, which were followed by background changes, evolving fast activity, spike bursts or rhythmic spikes. GMFT was applied to these time segments and calculated with intervals of 50 ms (ms) at the first step. Then, the first activated period was recognized as the ictal onset, which was cross-referenced to the MEG waveforms. At the second step, 200 ms including the presumed ictal onset period was progressed to further detailed analysis with intervals of 2 ms, and finally, the ictal onset area (ictal GMFT) where the activated GMFT area actually appeared first was determined (Fig. 1). A linear interpolation method was employed in a 2-ms step evaluation, in which MEG recordings were resampled from 600.615 Hz to 1000.0 Hz. Because GMFT visualizes the maximum power at evenly spaced samples over a specified interval, there is no deterioration of the data of frequency of epileptic activity.

In this study, the results of GMFT analysis of ictal MEG were not considered during the preoperative evaluation.