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Minimum norm estimates in MEG can delineate the onset of interictal epileptic discharges: A comparison with ECoG findings ☆

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ABSTRACT

The analysis of epileptic discharges in magnetoencephalography with minimum norm estimates (MNE) is expected to provide more precise localization of epileptic discharges compared with electroencephalographic estimations. However, the clinical feasibility of MNE remains unclear. In this study, we aimed to elucidate the onset and propagation patterns of interictal spikes using MNE. Seven patients with intractable epilepsy whose epileptogenicity was assumed to exist in the convexity of the cerebral cortex were studied. For MNE and electrocorticography (ECoG), we characterized the propagation patterns of interictal epileptic discharges according to the area in which they originated and where they extended; we then examined whether the propagation patterns observed in MNE were identified by ECoG. We also examined the relationship between the positions of spikes estimated by the equivalent current dipole (ECD) method and MNE. Among the seven patients, nine propagation patterns of epileptic discharges were observed by MNE, all of which were also identified by ECoG. In seven patterns, the epileptic activity propagated around the initial portion. However, in two patterns, the center of activities moved according to propagation with maintained activity of the initial portion. The locations of spikes identified by the ECD method were within the areas estimated by MNE when the epileptic activity propagated. However, the ECD method failed to detect onset activities identified by MNE in three of nine patterns. Thus, MNE is more useful as a means of presurgical evaluation for epilepsy than the ECD method because it can delineate the onset of epileptic activities as shown in ECoG.

1. Introduction

For the treatment of localization-related epilepsy, and especially epilepsy surgery, it is essential to accurately estimate the location of the epileptogenic zone. One of the most reliable ways is by electrocorticography (ECoG), using grid electrodes located directly on the cerebral cortices. Because ECoG is an invasive examination, the locations of the electrodes used for ECoG are deliberately determined based on information from less invasive tests including scalp electroencephalography (EEG), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT) and positron emission tomography (PET). Magnetoencephalography (MEG) is one of the least invasive methods for measuring brain function. MEG measures the magnetic fields generated from cerebral electrical activity. Unlike EEG recordings, magnetic fields are not influenced by the volume conductors of the head such as the skin, skull and cerebrospinal fluid. Thus, MEG has better spatial resolution than EEG. Because of these characteristics, MEG has been applied to the study of epilepsy (Minassian et al., 1999; Ishibashi et al., 2002; Morioka et al., 1999; Nakasato et al., 1994; Oishi et al., 2002; Sutherling et al., 1987, 2001) and is now widely used in presurgical evaluations (Knowlton, 2006; Lau et al., 2008).

At present, the most common method for analysis of magnetic epileptic discharges is the equivalent current dipole (ECD) estimation method. This method is useful when the current source is localized enough to be calculated with few ECDs. However, most epileptic discharges rapidly extend to several brain areas such that the ECD method often fails to show how widely the current sources are distributed. Minimum norm estimates (MNE) is one method for localizing the source area (Hämäläinen and Ilmoniemi, 1994). Combined with noise normalization of dynamic

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statistical parametric mapping (dSPM), MNE provides the spatiotemporal distribution of current sources over the cortical surface using images derived from MRI (Dale et al., 2000; Molins et al., 2008). Several studies have demonstrated that MNE can provide more information about current sources than the ECD method in the evaluation of epileptic discharges (Shiraishi et al., 2005; Tanaka et al., 2009). A recent study of MNE and ECoG has shown that MNE accurately models the time course of frontotemporal spikes as observed in ECoG (Tanaka et al., 2010). These reports suggest that MNE can delineate patterns of epileptic discharges with a similar distribution to the actual ones. However, it has not been sufficiently established whether the distribution patterns observed in MNE are comparable to those of ECoG, which is the gold standard for evaluation of the epileptogenic zone.

The purpose of this study was to assess the feasibility of MNE analysis as a tool for evaluating epileptic discharges. Accordingly, we compared the findings of MNE analysis with those of ECoG and ECD analysis. If this non-invasive method can provide similar information to ECoG, MNE analysis could be a powerful tool for presurgical evaluation.

2. Materials and methods

2.1. Subjects

Five female and two male patients with medically intractable epilepsy, aged 16–35 years old (mean age: 26.0 years), were studied (Table 1). Their epileptogenic zones were assumed to be located on the convexity of the cerebral cortex as per the findings of scalp EEG, head MRI, and functional brain imaging such as I-123 iomazenil SPECT and 18-fluorodeoxyglucose PET. To detect the precise epileptogenic zone, all patients underwent ECoG using electrodes located in the convexity of the cerebral cortex. In two cases, subdural electrodes were also placed on the mesial temporal lobe. In all patients, ECoG recording was preceded by MEG. The operative procedures were selected based on the results of these examinations. All recordings and surgical operations were performed at Kyushu University Hospital. Post-operative seizure outcome was graded according to the Engel classification (Engel et al., 1993). We obtained informed consent from each patient for this study.

2.2. MRI

MRI was performed using a 3.0-T high-resolution MRI scanner (Achieva, Philips N.V, Eindhoven, the Netherlands) for diagnostic purposes and for supporting the analysis and interpretation of the MEG data (TE, 60 ms; TR, 100 ms; voxel size, $1.5 \times 1.5 \times 1.5$ mm^3).

2.3. MEG with simultaneous EEG recordings

MEG was performed preoperatively using a 306-channel (204 planar gradiometers and 102 magnetometers) whole-head system (Elekta-Neuromag, Helsinki, Finland) within a magnetically shielded room. The sampling rate was 1000 Hz with a band-pass of 0.03–200 Hz. EEG (Elekta-Neuromag, Helsinki, Finland) was performed simultaneously for visual screening of epileptic discharges using 19 scalp electrodes (International 10–20 system), with the same sampling rate and filter settings as used for MEG. We measured auditory-evoked fields (AEF) and somatosensory-evoked fields (SEF) before spontaneous recordings. One spontaneous recording session was approximately 3–5 min, and these were repeated 5–7 times. MEG and EEG were performed for a total of about 60 min in each patient.

2.4. MEG source analysis

The acquired MEG data were digitally filtered using a band pass filter of 3–30 Hz for offline analysis. By visual inspection, we manually selected the segments containing 30–40 recording points around spikes. Source estimation for the spikes was performed using two methods: ECD and MNE. The location of the ECD was calculated using dipole-fit software (source modeling, Neuromag Ltd., Helsinki, Finland) employing a single dipole model with a single sphere head model, because these are most wide spread usage for analyzing epileptic discharges. Dipoles were calculated for each time sample (about 100 ms) containing a MEG spike. Based on an index of fitness level, the goodness of fit (GOF) was evaluated for each ECD. The estimated ECDs were superimposed on each patient's cortical surface MR image to visualize the anatomic location. If the dipole was estimated to be outside the cerebrum, the dipole was defined as absent.

For each MEG spike analyzed with the ECD method, the spatiotemporal source distribution was calculated using MNE. The precise procedure for performing MNE has been described elsewhere (Hämäläinen and Ilmoniemi, 1994; Shiraishi et al., 2005; Tanaka et al., 2009). Briefly, each patient's cortical surface is reconstructed from high-resolution T1-weighted MR images using FreeSurfer software (Dale et al., 1999; Fischl et al., 1999). For the source space, we always employ the parameter setting "–ico 6" on the mne_ setup_source space command. The forward solution, which models the signal pattern generated by a unit dipole at each location on the cortical surface, is calculated using a boundary element method (BEM) (Hämäläinen and Sarvas, 1989; Oostendorp and Van Oosterom, 1989). An inverse solution is then calculated from the forward solution for MEG (Hämäläinen and Ilmoniemi, 1994; Dale and Sereno, 1993). Thus, the activation at each cortical location is estimated at each time point of the activity, and is simultaneously

Table 1
Clinical and demographic data.

Case	Age/sex	EEG focus	MRI lesion	Estimated epileptogenic zone	Operated area	Histology	Resection of initial portion	Outc
1	29/F	L_T	No lesion	L_mT,_LlatT	L_SAT L_latT_res L_latT_MST	Gliosis	Pat 1–1; + Pat 1–2; − (MST) Pat 1–3; +	IIIa
2	33/F	R_T	R_F; FCD, R_F; CA R_T; HS	R_mT, R_latT	R_SAT R_latT_res	HS	Pat 2; +	IIa
3	35/F	L_T	No lesion	L_latT	L_SAT L_latT_MST	Gliosis	Pat 3; − (MST)	IIIa
4	16/F	R_T	R_T; FCD	R_latT	R_latT_res	FCD, IIA	Pat 4; −	Ia
5	34/M	R_F	R_F; FCD	R_F	R_F_res	FCD, IIB	Pat 5; +	Ia
6	18/M	R_T	R_P; DNT	R_P	R_P_res	DNT	Pat 6; +	Ia
7	17/F	R_T	No lesion	R_F	R_F_res	FCD, IIB	Pat 7; +	Ia

L; left, R; right, T; temporal, F; frontal; P; parietal; mT; mesial temporal, latT; lateral temporal, FCD; focal cortical dysplasia, CA; cavernous angioma, HS; hippocampal sclerosis, DNT; dysembryoplastic neuroepithelial tumor, SAT; standard anterior temporal lobectomy, res; resection, MST: multiple subpial transection, IIA; FCD type IIA, IIB; FCD type IIB, Pat 1–1–Pat 7; the propagation patterns of MNE and ECoG in Table 2 and Fig. 3. +; resection of initial portion, −; not resected of initial portion, Outc.; outcome based on Engel's classification (Ia–IIIa).

estimated using a noise-normalized linear estimation approach (dynamic statistical parametric maps, dSPM). After recordings, we first estimated the degree of accuracy of MNE source localization using a somatotopic approach. Some factors such as the artifacts, environmental noises, and co-registration always affect the accuracy of MEG source localization, and these factors change day by day. We first estimated the accuracy using SEF, and a pre-trigger period from −200 ms to 0 ms was used for the calculation of the base covariance matrix. After confirmation of the accuracy of source localization, we used the same covariance matrix for the estimation of epileptic charges. The activation patterns derived from the analysis are mapped onto the cortical surface images of each patient.

2.5. ECoG recordings and analysis

All patients underwent ECoG recording via grids and strips covering the convexity of the cerebral cortex, based on the results of presurgical evaluation. ECoGs were recorded using a digital EEG system (EEG1000, Nihon, Kohden, Tokyo, Japan). The sampling rate was 1000 Hz, and the data were low-pass filtered at 120 Hz and high pass filtered at 0.5 Hz for offline analysis.

2.6. Comparisons among ECD, MNE and ECoG

We examined RMS waveforms constructed from recordings of manually selected sensors around spikes. We made comparisons between RMS waveforms and the recordings from some MEG sensors, and finally selected one MEG sensor as a "distinct sensor", being closest to the RMS waveforms. Thereafter, we set three time points (onset, middle and peak) for the selective analysis: the onset time was defined as when the selected spike began, the peak time was when the selected spike achieved its peak, and the middle time was arbitrarily defined as the middle point between the onset and the peak time. For MNE, we defined the initial portion as the area where the epileptic activity began at the time of onset of discharges, and defined the propagated portions as the area where epileptic activity was observed at the middle and peak times in MNE. For ECD, each epileptic discharge was analyzed similarly at the onset, middle, and the peak time. For each analysis, we assessed whether the location of ECD was estimated in the cerebrum and was present in the area where the epileptic discharge was distributed in MNE (Fig. 1). We measured the GOF of the dipoles at each time point and calculated the mean and standard deviation of the GOF for each propagation pattern (Table 2). Although dipoles are usually accepted in our institution when the GOF is above 85%, we decided to accept all

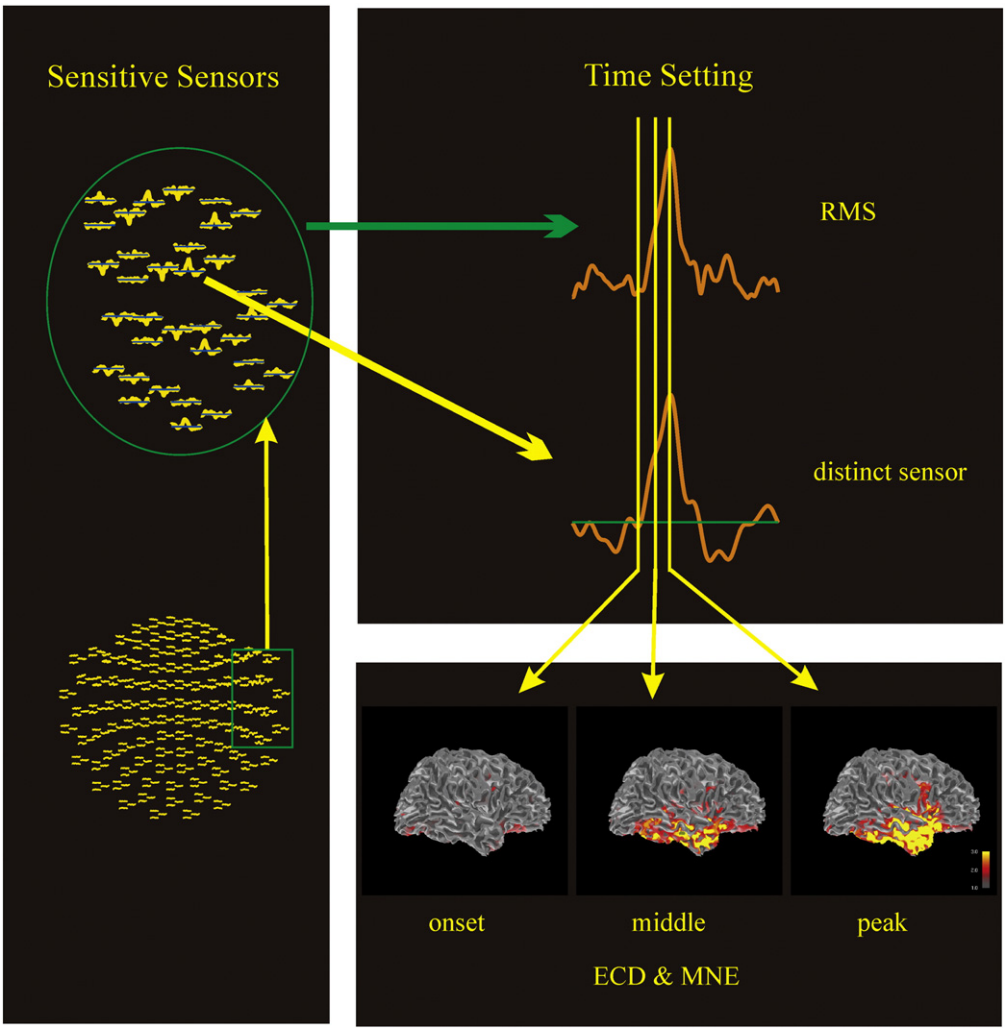

Fig. 1. Procedures for MEG analysis. Four steps were adopted: i) examined RMS waveforms constructed from recordings of manually selected sensors around spikes; ii) selected one MEG sensor as a "distinct sensor" being closest to the RMS waveforms; iii) time setting at onset, middle and peak times of epileptic activity on distinct sensor; and iv) analysis of MEG spikes with the ECD method and MNE. The distributions of current sources are shown on the cortical surfaces in a red/yellow color. The dipole estimated by the ECD method is overlaid on the cortical surfaces as green filled circles.

Table 2
Accuracy of estimation of ECD and location at initial, middle and peak time in each propagating pattern.

Pattern	Number	GoF (%)			Location of dipoles		
		Onset	Middle	Peak	Onset	Middle	Peak
Pat 1–1	25	80.7 ± 2.6	84.4 ± 2.5	87.8 ± 1.9	aT	aT	aT
Pat 1–2	18	54.3 ± 4.1	90.4 ± 3.1	92.4 ± 2.2	–	pT → aT	aT
Pat 1–3	13	86.2 ± 1.9	88.1 ± 2.2	90.1 ± 1.6	iT	iT	iT
Pat 2	31	70.5 ± 2.6	83.9 ± 2.1	87.6 ± 2.1	aT	aT	aT
Pat 3	38	67.1 ± 3.3	88.6 ± 1.8	89.2 ± 1.4	pT	pT → aT	aT
Pat 4	186	87.5 ± 1.7	91.1 ± 1.5	92.1 ± 1.2	P	P	P
Pat 5	13	62.9 ± 4.1	65.2 ± 3.9	80.4 ± 2.2	–	–	iF
Pat 6	40	80.8 ± 2.2	89.1 ± 2.9	92.2 ± 1.3	–	P	P
Pat 7	211	63.1 ± 3.3	96.0 ± 2.5	95.9 ± 1.8	Op	Op	Op

GoF; goodness of fit, aT; anterior temporal, iT; inferior temporal, pT; posterior temporal, P; parietal, iF; inferior frontal, Op; pars opercularis. Propagation pattern (Pat 1–1–7) are shown in Fig. 3.

dipoles irrespective of the GOF to evaluate the relationship between the value of GOF and the three time points. For ECoG, we equally divided the period from the first peak to the last peak of a discharge into three time points (onset, middle, and peak) as with MNE. An initial portion of epileptic activity on ECoG was defined as the area of intracranial electrodes where the spike was observed at the time of onset. Accordingly, the propagated portions of epileptic activity were defined as the areas of intracranial electrodes where the spike was observed at the middle and peak time (Fig. 2). We characterized the propagation patterns of epileptic activities in MNE and ECoG according to the initial portion and the propagated portions, and then two investigators (Y.K. and H.S.) visually judged whether the propagation patterns observed in MNE were identified by ECoG. We also counted how many discharges were involved for each pattern in MNE.

2.7. Statistics

The difference of GOF at each analysis time was analyzed by one-way repeated-measures ANOVA with Tukey–Kramer's test using JMP 8.0. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Clinical profiles of our cases

Table 1 provides an overview of the case profiles. The epileptic foci detected by EEG existed in the temporal region in six patients and in the frontal region in one patient. MRI revealed that three patients had no lesion, three patients had focal cortical dysplasia (FCD) and one patient had a dysembryoplastic neuroepithelial tumor (DNT). Of note, one patient (case 2) had three lesions: FCD, cavernous angioma (CA) and hippocampal sclerosis (HS). According to the results of the presurgical evaluation, including ECoG, the epileptogenic zone was assumed to exist in the lateral temporal lobe in four patients, in the mesial temporal lobe in two patients, in the parietal lobe in one patient and in the frontal lobe in two patients.

3.2. Comparison of the findings between MNE and ECD methods

The locations of dipoles are also depicted in Fig. 3, and Table 2 summarizes the results obtained with the ECD method. The ECD method failed to estimate the current source in the cerebrum in three patterns (Pat 1–2 [case 1], Pat 5 [case 5] and Pat 6 [case 6]) at the onset time and also failed to estimate the source in one pattern (Pat 5 [case 5]) at the middle point. However, ECDs were successfully estimated in the cerebrum in all cases at the peak time and they were located in the propagated portion that was estimated by MNE (Table 2 and Fig. 3).

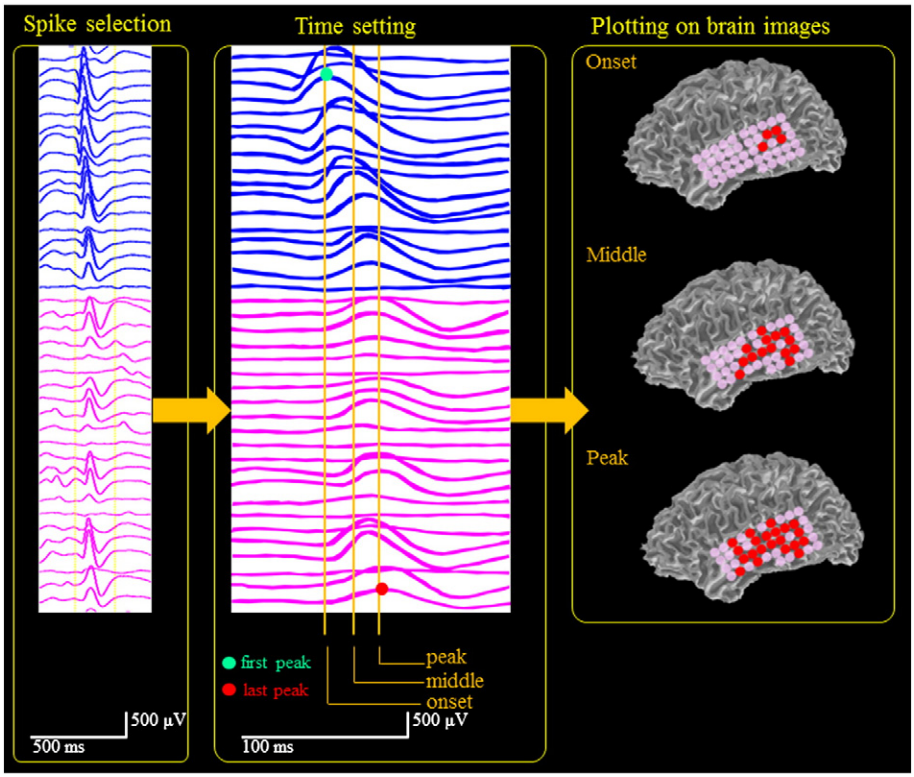

Fig. 2. Three-step procedure for ECoG analysis. Three steps were adopted: i) picking up the interictal spikes from ECoG recorded in each case; ii) time setting of onset, middle and peak times for epileptic activity; and iii) displaying the activated electrodes at each time. The pink dots represent the subdural grid electrodes and red dots indicate the distribution of spikes.

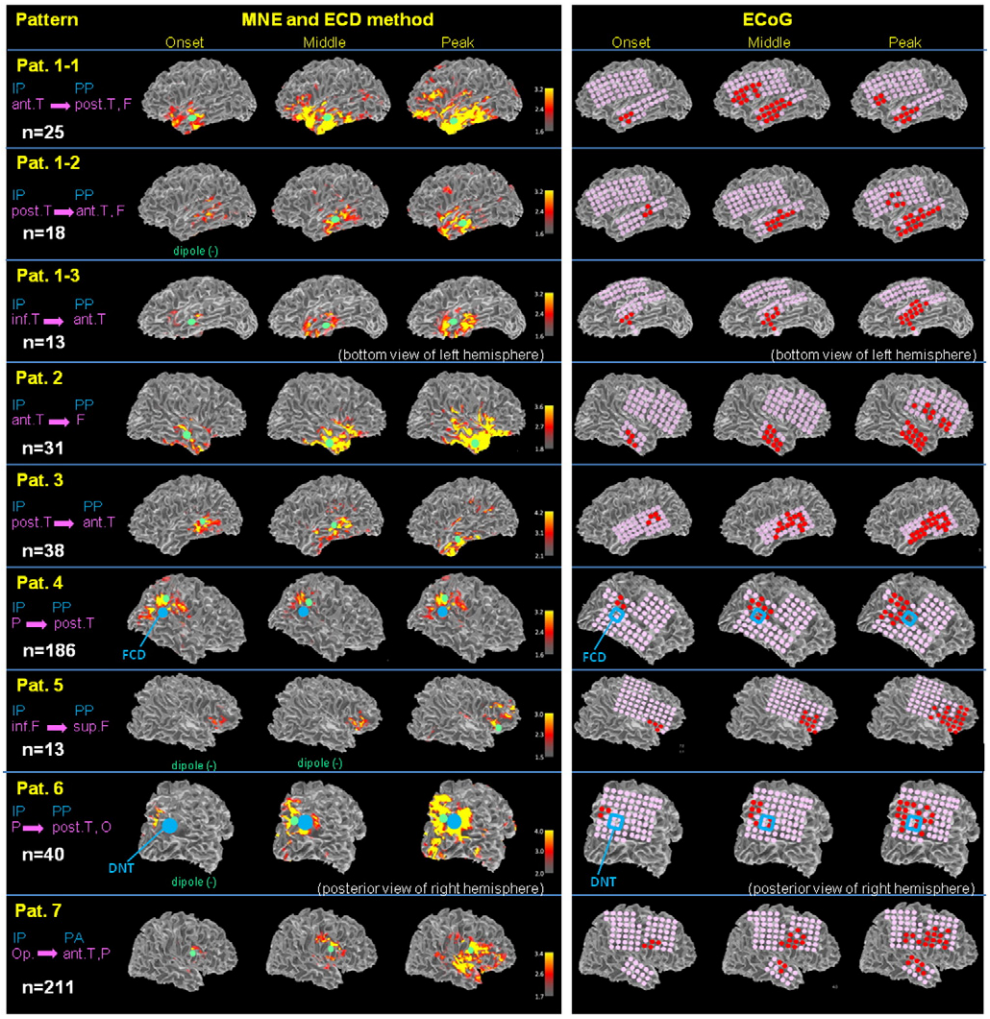

Fig. 3. Propagation patterns of MNE and ECoG. Pat 1–3 and Pat 6 are shown in bottom and posterior views, respectively. In Pat 4 and Pat 6, the location of FCD and DNT detected by MRI are overlaid on the cortical surface as blue areas. Pat 1–1–Pat 7 correspond to cases 1–7 in Table 1 and Pat 1–1–Pat 7 in Table 2. IP; initial portion, PP; propagated portions, ant; anterior, post; posterior, inf; inferior, sup; superior, F; frontal lobe, T; temporal lobe, P; parietal lobe, O; occipital lobe, Op; pars opercularis, "dipole (−)" means that the dipole is not estimated in the cerebrum at that time.

Among the six patterns in which dipoles were estimated in the cerebrum at the time of onset, only one pattern (Pat 3 [case 3]) showed a different location of dipoles between the onset time and the peak time. Table 2 also shows the GOF of the dipole for each pattern. GOF was the highest at the peak time and was higher at the middle time than at the onset time ($F [2, 575] = 1005.724$; $p < 0.0001$: ANOVA, Fig. 4).

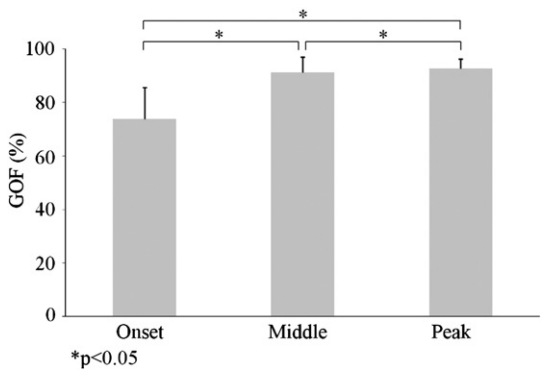

Fig. 4. Differences in goodness of fit (GOF) among the three time settings. Note that GOF is the highest at the peak time.

3.3. Comparison of the findings between MNE and ECoG

Among seven patients, nine common propagation patterns were observed using MNE methods. Fig. 3 shows representative results of analysis for each pattern. These distributions coincide with those obtained by ECoG recordings. In both MNE and ECoG, epileptic activity seemed to be generated within a limited area at the time of onset, and then propagate to other areas at the middle and peak times. In our cases, the initial portion was located in the anterior temporal lobe in two patterns (Pat 1–1 [case 1], Pat 2 [case 2]), in the posterior temporal lobe in two patterns (Pat 1–2 [case 1], Pat 3 [case 3]), in the inferior temporal lobe in one pattern (Pat 1–3 [case 1]), in the parietal lobe in two patterns (Pat 4 [case 4], Pat 6 [case 6]), in the inferior frontal lobe in one pattern (Pat 5 [case 5]) and in the opercular part of the frontal lobe in one pattern (Pat 7 [case 7]). MNE showed two different manifestations of propagation patterns. In seven patterns (Pat 1–1 [case 1], Pat 1–3 [case 1], Pat 2 [case 2], Pat 4 [case 4], Pat 5 [case 5], Pat 6 [case 6] and Pat 7 [case 7]), the epileptic activity propagated around the initial portion, however, in two patterns (Pat 1–2

[case 1] and Pat 3 [case 3]), the center of activity moved according to propagation with maintained activity of the initial portion even at the peak time.

3.4. Operative outcome

Table 1 summarizes the surgical methods and prognosis of the evaluated cases. Cases 1 and 2 whose epileptogenic zones were assumed to be in both the mesial and lateral temporal lobes underwent both hippocampectomy and lateral temporal lobectomy. Case 1 also underwent multiple subpial transection (MST) of the posterior temporal lobe. Case 3 underwent anterior temporal lobectomy and MST of the posterior temporal lobe. Cases 4, 5, 6 and 7 underwent focus resection or tumor resection. As a result, the initial portions estimated by MNE and recorded by ECoG were resected in the cases showing six of nine patterns and MST was carried out in the cases showing two of three patterns for which the initial portions were not resected. After the operations, seizures disappeared or rarely occurred in five of seven patients (Engel's class I or II). The other two patients (Cases 1 and 3) who underwent MST at the posterior temporal lobe, and whose histological abnormalities were not remarkable, achieved partial improvement (Engel's class III).

4. Discussion

MEG analysis with the ECD method is established as a useful tool for the evaluation of epileptic discharges (Knowlton and Shih, 2004). However, there are several methods that can be used to estimate the current source from magnetic fields such as the ECD method, MNE and Beamformer. In the present study, we used MNE analysis of interictal MEG spikes to represent the pattern of propagation of spike activity. We also compared the distribution and propagation patterns between MEG and ECoG. Although the intracranial electrodes were not always located widely, we found that similar distribution and propagation patterns were observed with the two modalities in all cases. More importantly, MNE can depict the initial portion of epileptic activity detected by ECoG. A previous ECoG study showed that removal of the initial portion of epileptic discharge was essential to achieve seizure control (Alarcon et al., 1997). Therefore, MNE may provide an important source of information regarding the area that needs to be treated surgically.

4.1. The advantage of MNE over the ECD method

The application of MNE to the analysis of MEG spikes has been reported previously (Shiraishi et al., 2005; Tanaka et al., 2009). These studies showed that MNE could provide better information on the interictal (Shiraishi et al., 2005) and ictal activity (Tanaka et al., 2009) of patients with epilepsy compared with the conventional means of source analysis such as the ECD method. We employed a sphere model for the ECD while we employed a BEM realistic model for the MNE analysis, because these are most conventional approaches. For verification, we compared the ECD method using both the sphere model and BEM, and the differences were not large. In the present study, we compared the locations of spikes estimated by the ECD method and MNE at the onset, middle and peak times of the epileptic activities. The ECD method estimates the current sources as points while MNE estimates them as areas. At the peak time, the locations of the current sources estimated with ECDs were present in areas estimated by MNE. Meanwhile, the GOF of the dipole at the onset was lower than that at the peak time in all patterns and the ECD method failed to detect the initial portion in three of nine patterns. However, this does not directly indicate that the ECD method is unsuitable for estimating the initial portion. Several studies have revealed that good surgical outcomes are achieved in those patients whose area of MEG spike localizations estimated using ECD method are located within the resected area (Genow et al., 2004; Placantonakis et al., 2010; Ramachandran Nair et al., 2007). As shown in Fig. 3, epileptic activity was generated from the initial portion and propagated to other areas, maintaining the high activity of the initial portion at the peak time in seven of nine patterns. Additionally, when dipoles were estimated on the cerebrum using the ECD method at the onset time, the location of the dipole did not change at the peak time in five of six patterns. These findings suggest that the dipole estimated at the peak time exists at the initial portion of the epileptic discharge in many cases. Therefore, the ECD method is still useful for determining the area that is to be resected. However, our results showed that the initial portions were not detected with the ECD method in three out of nine patterns (Pat 1–2, 5, 6). The locations of the dipole estimated at the peak time did not coincide with the initial portion in one pattern (Pat 3). Even in such cases, MNE could estimate the same initial portion as ECoG. In other words, MNE is superior to the ECD method in that MNE can estimate the onset area of an epileptic discharge despite distinctions of the propagation patterns.

4.2. Operative results and necessity of ECoG

The operative outcomes were worse in cases 1 and 3 than in the others. Because the initial portions of Pat 1–2 [case 1] and Pat 3 [case 3] were considered to have verbal functions, MST was selected. Case 4 had a good outcome without removal of the initial portion of the epileptic discharge estimated by MNE. The initial portion of the interictal epileptic discharge was located at the parietal lobe which neighbored the FCD at the posterior temporal lobe; however, the ictal activity on ECoG was recorded from the intracranial electrode just above the lesion. As a result, focus resection limited to FCD was carried out. In this case, the analysis of the interictal of MNE and ECoG provided only a clue as to the portion that should be removed. The analysis of early ictal spikes has been found to be useful for estimating the seizure onset zone (Assaf et al., 2003; Tilz et al., 2002) and it has been reported that MEG could serve this purpose (Tanaka et al., 2004). At present, however, the discharges detected by MEG in epilepsy patients are usually interictal ones because MEG is not suitable for long-duration recording. ECoG is fit to record to detect ictus for a long time and has an important role as a tool for brain mapping. Therefore, the information derived from intracranial electrodes is still necessary for deciding on a surgical plan.

4.3. Usefulness of MNE and its role in presurgical evaluation

Implantation of intracranial electrodes has some risk not only when the operation is performed but also while intracranial EEG is performed (Hamer et al., 2002; Wong et al., 2009). Therefore, intracranial electrodes are usually implanted in the minimum area that is thought to be necessary to detect epileptic discharges as a result of EEG and brain imaging. As mentioned above, MNE provides a clue to the epileptogenic zone, which exists on the convexity of the cerebrum. This characteristic suggests that MNE can be a useful tool with which to decide where intracranial electrodes should be implanted. Necessary and sufficient implantation of electrodes may introduce good operative outcomes.

4.4. Accuracy of MNE and future works

MNE has some parameter settings and these settings affect the resolution and accuracy; therefore, we should discuss this issue. In principle, approximately 340,000 vertices were defined based on the gray-white matter boundaries, and these vertices provide millimeter-level resolution (Fischl et al., 1999). However, to reduce the computational cost, the source space was created by decimating these vertices with a controlled distance of around 4.9 mm (Molins et al., 2008) with the parameter setting "–ico −6". For the spatial smoothing we always use '5', and smooth parameters provide some interpolation for the original vertices automatically. Because of the nature of the nature

of this problem the resolution of the MEG inverse solution is not straightforward. In this study the purpose of performing MNE was to estimate the proper location prior to ECoG recording, and thus, submillimeter-level accuracy is not required. The resolution of ECoG is 5 mm to 1 cm and by making comparisons between MNE and ECoG (Fig. 3), it might be possible to evaluate that we have at least 5 mm to 1 cm accuracy resolution using an MNE approach. This resolution is sufficient for pre-surgery purposes.

Another important factor is the setting of the threshold level for visualization. At the beginning of this study, we focused on this issue and hypothesized that by making comparisons between ECoG and MNE results for the three latencies (onset, middle, and peak) we would be able to find some criteria to evaluate systematically. Some tendencies were observed; however, we cannot yet conclude this issue and will address this in future work.

5. Conclusions

Our study clearly demonstrated that MNE can represent a similar distribution and propagation pattern of epileptic discharges recorded by ECoG. MNE may be superior to the ECD method because MNE can detect the initial portion of epileptic activity, even when the ECD method fails. In this sense, MNE is a useful method of analysis as part of the presurgical evaluation of patients with epilepsy.

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