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Source Connectivity Analysis from MEG and its Application to Epilepsy Source Localization

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Abstract

We report an approach to perform source connectivity analysis from MEG, and initially evaluate this approach to interictal MEG to localize epileptogenic foci and analyze interictal discharge propagations in patients with medically intractable epilepsy. Cortical activities were reconstructed from MEG using individual realistic geometry boundary element method head models. Directional connectivity among cortical regions of interest was then estimated using directed transfer function. The MEG source connectivity analysis method was implemented in the eConnectome software, which is open-source and freely available at <http://econnectome.umn.edu>. As an initial evaluation, the method was applied to study MEG interictal spikes from five epilepsy patients. Estimated primary epileptiform sources were consistent with surgically resected regions, suggesting the feasibility of using cortical source connectivity analysis from interictal MEG for potential localization of epileptiform activities.

Keywords

Keywords Epilepsy; MEG; Source imaging; Functional connectivity; Directed transfer function; eConnectome

Introduction

Electrophysiological source imaging of brain activity and connectivity is of importance for neuroscience research and clinical management of neurological and mental disorders (He et al. 2011a, b). Identification of epileptogenic brain regions is of clinical value in the surgical therapy of patients with intractable epilepsy. Electroencephalography (EEG),

magnetoencephalography (MEG), and intracranial EEG have been widely used for localization of epileptiform discharges due to their excellent temporal resolution on the order of milliseconds (He et al. 1987; Ebersole 1991; Shiraishi et al. 2001; Tang et al. 2003; Ding et al. 2007; Zhang et al. 2008; Bai et al. 2010; Ahlfors et al. 2010; Wilke et al. 2010a, b; Cho et al. 2011). Recent studies suggested that the addition of MEG to the clinical evaluation of medically refractory epilepsy patients can improve the postsurgical outcomes of the patients (Stufflebeam et al. 2009; Knowlton 2008), where interictal MEG was used to estimate epileptogenic zones. Different than EEG where ictal EEG source imaging has been shown to provide a means of localizing and imaging seizure sources (Yang et al. 2011), ictal activity is difficult to obtain with MEG, while interictal epileptiform activity is usually observed. Several studies evaluated the consistency of interictal and ictal source localizations by using MEG and indicated that the interictal MEG is a useful tool to predict epileptogenic foci in epilepsy patients (Shiraishi et al. 2001; Tang et al. 2003).

Beyond waveform inspection and field mapping in the sensor space, localization of epileptiform activity with interictal MEG has been advanced by source localization and imaging techniques in the source space. Such inverse techniques are able to identify epileptic sources in the brain more accurately. Common source models for interictal discharges include equivalent current dipoles (ECDs) (He et al. 1987; Ebersole 1991) and distributed current dipoles (Shiraishi et al. 2005). The distributed source model can be used to identify multiple epileptic sources without a priori specification of the number of sources and reveal interictal discharge propagation that is important for understanding the pathophysiology of epilepsy (Lai et al. 2007; Tanaka et al. 2010).

It is challenging to distinguish, from noninvasive electromagnetic signals, primary sources, that initiate the epileptiform activity, from secondary sources, that are generated by the propagation of pathological activity (Ding et al. 2007). Such propagation can be rapid in time and distant from the primary focus (Lai et al. 2007), which can complicate the epileptiform activity and lead to false localization. Efforts have been made to investigate the detection of the primary source of epileptiform activity and the analysis of epileptic propagation from interictal MEG. Ossadtchi et al. used hidden Markov models to infer propagation patterns between several potential epileptogenic regions identified by automatic methods (Ossadtchi et al. 2004) and determined the most likely primary epileptogenic source. Tanaka et al. (2010) extracted waveforms from the source distribution of interictal spikes at the sites corresponding to the locations of frequently spiking intracranial electrodes and used the time differences between the peaks to represent the propagation. Lin et al. (2009) applied bivariate dynamic Granger causality modeling to study the propagation of epileptic interictal spikes.

The directed transfer function (DTF) (Kamiński and Blinowska 1991) is closely related to the Granger causality (Granger 1969). While the Granger causality can only infer directional influence between two time series, the DTF technique can estimate the directional causal interaction for an arbitrary number of signals. The DTF technique has been successfully applied to estimating cortical connectivity from scalp EEG (Babiloni et al. 2005; Astolfi et al. 2007), and to determining the primary epileptogenic sources from secondary sources using ictal EEG (Ding et al. 2007) and ictal and interictal ECoG (Wilke et al. 2010a, b).

The use of DTF for the estimation of the primary epileptogenic source and epileptic propagation from interictal MEG has not been reported. In the present study, source connectivity analysis with the DTF technique from interictal MEG was investigated in patients with medically intractable epilepsy. Directional connectivity among cortical regions of interest (candidate epileptogenic zones) identified by source imaging was analyzed with the DTF and visualized over the cortical surface using the *eConnectome* software package

(He et al. 2011a; Dai and He 2011) to estimate the primary sources of the epileptiform activities. The estimated primary sources were compared with the surgically resected regions and the surgical outcomes. The interictal discharge propagations in the epilepsy patients were also investigated.

Methods

MEG Connectivity Analysis Functionality in eConnectome

eConnectome is a free and open-source MATLAB software with graphical user interfaces for the mapping and imaging of brain functional connectivity from EEG, ECoG (He et al. 2011a) and MEG signals (Dai and He 2011). MEG data can be preprocessed (e.g. artifact rejection, baseline correction, filtering, time–frequency representation) before further analysis. Connectivity analysis of the preprocessed MEG data can be performed at the sensor level. To reduce connectivity complications that may be caused by head volume conduction, cortical sources can be reconstructed from MEG data and connectivity analysis can then be performed at the source level. Connectivity patterns among MEG sensors and cortical regions of interest (ROIs) can be visualized over the MEG sensor surface and realistic cortical surface respectively. The MEG source connectivity analysis was used to analyze interictal MEG spikes.

Protocol of Source Connectivity Analysis

A diagram outlining the protocol of source connectivity analysis from an interictal MEG spike is shown in Fig. 1. Significant time points around the peak of the interictal spike were selected by visual inspection of the waveform and global field power (see Fig. 1a). Cortical source imaging with an individual realistic three-layer boundary element model across a selected segment (encompassing the selected time points) of the interictal spike was then performed. Cortical regions with significant activity at the selected time points were considered as ROIs and the average waveform (at each time point, the value is the average of estimated cortical currents in the ROI) of each cortical ROI was computed as the representative ROI waveform (see Fig. 1b). Directional connectivity among the cortical ROIs was then estimated from the ROI waveforms using the DTF method, and the connectivity patterns including the information flow and total outflow (see Sect. 2.6) were visualized over the cortical surface (see Fig. 1c). The ROI with the largest total outflow was considered as the most likely primary epileptogenic source for the spike, and the information flows indicated the propagation of the epileptiform activity.

Cortical Source Imaging

The distributed source model (Dale and Sereno 1993) was used to solve the inverse problem from the MEG to cortical current distribution using the minimum norm estimate (MNE) with the aid of the boundary element method (BEM) (He et al. 1987; Hämäläinen and Sarvas 1989). For each patient, the realistic cortical surface and three layers (inner skull, outer skull and skin) (see Fig. 1b) were reconstructed from the anatomical MRI images using the CURRY6 software (Compumedics, Charlotte, NC). The patient-specific BEM model was then constructed with the reconstructed surfaces. Such realistic head models have been suggested to provide improved accuracy in source analysis. The conductivities of the different tissues were assumed to be 0.33 S/m for the skin, 0.0165 S/m for the skull, and 0.33 S/m for the brain (Lai et al. 2005; Zhang et al. 2006). The co-registration of MEG and MRI images was achieved by matching the recorded positions of three fiducial points (nasion, left and right preauricular points) with the locations of these points from the MRI images.

In the forward problem (Mosher et al. 1999), the distributed dipoles were constrained on the cortical surface with their orientations perpendicular to the local surface. The lead field matrix relating MEG sensors to the cortical distributed dipoles was computed with the BEM model using the CURRY6. The cortical surface and lead field matrix were then used in the *eConnectome* software (He et al. 2011a; Dai and He 2011) for the inverse problem and connectivity analysis.

In the inverse problem, the solution of MNE was derived using Tikhonov regularization in the regularization toolbox (Hansen 2007). The inverse solution yielded estimates of continuous time courses of cortical currents. ROI time courses were then computed by averaging estimated cortical currents in the ROI. With the ROI time courses, cortical ROI connectivity was estimated using the DTF method in selected frequency components (Babiloni et al. 2005; Astolfi et al. 2007).

Directed Transfer Function

The Directed Transfer Function (DTF) is a frequency-domain estimator of causal interaction based on the multivariate autoregressive (MVAR) modeling (Kamiński and Blinowska 1991). To calculate the DTF measures, N ROI time courses $Y(t)$ were firstly modeled as the following MVAR process:

$$\sum_{k=0}^p \Lambda(k)Y(t-k) = E(t), \text{ with } \Lambda(0) = I \quad (1)$$

where $E(t)$ was a vector of a multivariate zero-mean uncorrelated white noise process, $\Lambda(1)$, $\Lambda(2)$, ... and $\Lambda(p)$ were the $N \times N$ matrices of model coefficients and the model order p was determined using the Final Prediction Error (FPE) criterion (Akaike 1971) and Schwarz Bayesian Criterion (SBC) (Schwarz 1978). In order to investigate the spectral properties of the examined process, Eq. (1) was transformed to the frequency domain:

$$\Lambda(f)Y(f) = E(f), \text{ where } \Lambda(f) = \sum_{k=0}^p \Lambda_k e^{-j2\pi f \Delta t k} \quad (2)$$

This equation was then rewritten as:

$$Y(f) = \Lambda^{-1}(f)E(f) = H(f)E(f) \quad (3)$$

where $H(f)$ was the inverse of the frequency-transformed coefficient matrix, $\Lambda(f)$, and was defined as the transfer matrix of the system. From the transfer matrix, the DTF measure, $\gamma_{ij}^2(f)$, which described the directional connectivity from ROI j to ROI i , was defined by the elements of the transfer matrix in the spectrum domain (Kamiński and Blinowska 1991; Babiloni et al. 2005):

$$\gamma_{ij}^2(f) = \frac{|H_{ij}(f)|^2}{\sum_{m=1}^N |H_{im}(f)|^2} \quad (4)$$

Statistic Assessment of Connectivity

Since the DTF measures have a highly nonlinear relation to the time series from which they are derived, it is difficult to apply traditional parametric statistical methods. Instead, a

nonparametric method based on surrogate data was used to assess the significance of the estimated connectivity measures (Theiler et al. 1992; Palus and Hoyer 1998; Ding et al. 2007). The original ROI time courses were transformed to the Fourier space, in which the phases were randomly shuffled without changing the magnitude. The surrogate data in the Fourier space were then transformed back to the time domain. The phase shuffling process destroyed the causal connections between ROIs while preserved the spectral structure of the time courses, which is critical since the DTF is measure of frequency-specific causal interactions. After shuffling, the connectivity estimation was applied to the surrogate data. The shuffling and connectivity estimation procedures were repeated 1,000 times, yielding a distribution of the DTF values under the null hypothesis that no connectivity existed. Based on this empirical distribution, the critical value of significance was set at the level $P < 0.05$ (Ding et al. 2007).

Visualization of Connectivity Patterns

Two connectivity patterns (the information flow and total outflow, see Fig. 1c) from the significant DTF measures were visualized over the cortical surface (Babiloni et al. 2005). The information flow pattern was represented by arrows pointing from source ROIs toward target ROIs. The arrow's color and size coded the strength of the estimated significant connectivity (significant $\gamma_{ij}^2(f)$, see Eq. (4) and Sect. 2.5) from the source to the target. The total outflow pattern was represented by spheres on the ROIs, where the color and size of the sphere were linearly related to the total outflow from the ROI. The total outflow of the ROI was defined as the sum of the significant connectivity (significant $\gamma_{ij}^2(f)$, see Eq. (4) and Sect. 2.5) over the frequency bands of interest from the ROI toward the other ROIs. The frequency bands of interest were selected according to the average time–frequency representation of the ROI time courses. The time–frequency was calculated using the Complex Morlet's wavelet (Qin et al. 2004; Qin and He 2005).

Patients and Data Acquisition

Five patients with medically intractable epilepsy (two with single epileptogenic focus and three with multiple epileptogenic foci) were studied using a protocol approved by the Institutional Review Boards of the University of Minnesota and Allina Hospitals and Clinics. The patients were randomly selected according to the following criteria: (1) anatomical MRIs and interictal MEGs were recorded pre-operatively; (2) the patients underwent resection of epileptogenic zones identified clinically; (3) the patients had at least 1 year follow-up after the surgical resection. The epileptogenic foci in the patients were identified by experienced epileptologists according to ictal onset zones localized using intracranial EEGs. In all the patients, intracranial EEG electrodes were placed under the guidance of routine clinical MEG performed at MSI center of Minnesota Epilepsy Group and United Hospital. The patients were seizure free or had significant seizure reduction with AEDs (anti-epileptic drugs) after surgical resection.

The interictal MEG data were recorded by Magnes 2500 WH (148 MEG channels, 4D Neuroimaging). The patients lay in a magnetically shielded room without motion during MEG recording. Two patients were recorded under sedation with intravenous propofol. They were allowed to go to sleep and the lights were turned down or off. The interictal MEG data were sampled at 508.63 Hz and continuously acquired with an online 1 Hz high-pass filter. The anatomical MRIs for source imaging include a three dimensional T1 weighted sequence, acquired on a 1.5T or 3T GE scanner. The interictal MEG data were filtered with a 30 Hz low-pass filter (zero-phase filtering) to remove high frequency artifacts but preserve frequency components up to beta band. Corrupted channels were rejected by visual inspection. For each patient, significant interictal spikes were selected by experienced

epileptologists. In this pilot study, only four out of all the selected spikes were analyzed for each patient to initially evaluate the proposed source connectivity analysis method. The four spikes for each patient were selected manually and randomly without any a priori information. Each spike is a segment of 2 s encompassing the spike peak. The source connectivity analysis was applied to each spike to estimate the primary epileptogenic source and epileptic propagation.

Results

The clinical information of the five patients with medically intractable epilepsy is summarized in Table 1. There were three females and two males, with ages from 3 to 32. The patients had cortical tubers, gliosis or astrogliosis (see Table 1 for details). After surgical resection of the clinically identified epileptogenic zones, three patients were seizure free and the other two patients had significant seizure reduction. The patients were followed up for 3–6 years. All patients remained on antiepileptic medications before and after resection.

For each interictal spike, the time points that represented significant activities (such as early, main and late activities) (Merlet and Gotman 1999) around the peak were selected by visual inspection of the waveform and global field power (Michel and He 2011) for the determination of regions of interest. The most likely primary epileptiform source (the ROI with the largest total outflow, see Sect. 2.6) for the interictal spike was compared with the surgically resected regions visually. The interictal spikes are illustrated as compared in Table 2, which shows that the estimated primary sources for each patient were within or overlapping with the surgically resected regions.

Figure 1 shows representative source connectivity analysis results of an interictal spike from patient 1 who had cortical tubers and gliosis in the right frontal and temporal lobes. Epileptogenic tubers were clinically identified in the right temporoparietal lobes. Four cortical ROIs were selected for connectivity analysis and the primary source identified by the source connectivity analysis method (see Fig. 1c) agreed with the temporoparietal tubers. The information flow pattern suggested the propagation of the epileptiform activity initiated from the right temporoparietal, temporal and frontal lobes to the region around the right inferior frontal lobe.

Patient 2 was a 3-year-old female with right frontal and parietal cortical tubers and subcortical gliosis. A spike from the patient is shown in Fig. 2a. Cortical current distributions were calculated for the spike. The sensor-space field maps and source images at two time points around the peak of the spike are shown in Fig. 2b, c respectively, which indicated right frontal activation. Three related ROIs were selected and the directional connectivity among the ROIs was estimated from the ROI time courses. The connectivity patterns of information flow and total outflow are displayed in Fig. 2d, e respectively. The estimated primary source of the interictal spike in the right frontal cortex agreed with the right frontal resection (by comparing the primary source with the clinically resected zone visually, see Fig. 2e, f. The information flow pattern (see Fig. 2d) illustrated the propagation of the epileptiform activity from the right frontal cortex to the right posterior and inferior frontal cortices. The patient has remained seizure free with anti-epileptic drugs (AEDs) after right frontal and parietal topectomy.

There was astrogliosis pathologically in the right temporal lobe of the 13-year-old patient 3. The source connectivity analysis results of a spike from the patient were shown in Fig. 3. Two time points at the peak were selected (see Fig. 3a), and three ROIs were determined according to the field maps and source images (see Fig. 3b, c) at the time points. The

information flows among the ROIs (see Fig. 3d) and total outflows of the ROIs (see Fig. 3e) indicated the primary source was in the right temporal lobe, and the propagation of the epileptiform activity was from the right temporal lobe to the right anterior and posterior frontal lobes. The identified primary source was overlapping with the clinically resected zone (see Fig. 3f) and the propagation possibly suggested an epileptic brain network from the epileptogenic area to the right anterior and posterior frontal lobes. The patient has reported a single simple partial seizure while remaining on AEDs after performance of a right temporal lobectomy including mesial structure.

Patient 4 was an adult female who had moderate to marked astrogliosis in left temporal and frontal lobes. Seizure onset was at the age of 10. Initial resection at that time revealed a dermoid cyst of left temporal lobe. The patient continued to have complex partial seizures following this original resection. She had epilepsy surgery consisting of left temporal lobectomy and frontal topectomy in 11/2005. She has remained on AEDs and had two simple partial seizures after the resective surgery. The interictal MEG recorded prior to her second resective surgery was analyzed in this study. The information flow patterns from two interictal spikes are illustrated in Fig. 4. The information flows suggested the epileptic propagations of the spikes and the primary sources agreed with the clinically resected zones (see Fig. 4c).

Patient 5 was an adult with mild astrogliosis in the left temporal lobe. Fig. 5 shows the information flow patterns from two interictal MEG spikes from the patient. The information flow patterns suggested the propagations of the epileptiform activity initiated from the left temporal lobe to the anterior and posterior of the frontal lobe, which suggested the epileptic propagations of the spikes and the primary source were in agreement with the temporal lesion. The patient underwent left temporal lobectomy including mesial structure and has remained seizure free with AEDs.

Discussion

In this study, we examined source connectivity analysis of interictal MEG for estimating the most likely primary epileptiform sources and the propagations of the epileptiform activities in randomly selected medically intractable epilepsy patients. The proposed MEG source connectivity analysis method mainly included two steps: cortical source imaging from MEG and cortical ROI connectivity analysis. The distributed source model with the three-layer BEM and MNE was used for cortical source imaging, and the DTF was employed for the calculation of directional connectivity among multiple cortical ROIs. The source connectivity analysis was applied to study five patients who underwent surgical evaluation for the treatment of medically intractable epilepsy. The present pilot data (see Table 2) suggest that the primary sources estimated from the interictal spikes in each patient partially agreed with the epileptogenic zones identified clinically. The estimated propagations of the epileptiform activities, which were related to the outcome of epilepsy surgery, might represent epileptic networks.

A number of methods can be used to estimate the directional connectivity from multiple time courses. The widely used DTF has shown to reliably recover the connectivity patterns under a wide range of signal-to-noise ratios and recording lengths (Astolfi et al. 2005; Ding et al. 2007). One of the shortcomings of the DTF method is the potential inclusion of the indirect pathways. With partial directed coherence (PDC) (Baccala and Sameshima 2001), the potential limitation is presumably reduced by the exclusion of indirect pathway information in the connectivity calculation. Another estimation method, direct DTF (dDTF) (Korzeniewska et al. 2003), has also been proposed to accommodate for the indirect pathway by combining the DTF with PDC. However, a recent study (Astolfi et al. 2007)

found in simulation data that the DTF had the lowest error variance in the calculation of the direct pathways compared to the PDC and dDTF. Furthermore, there was no significant difference in the estimation of the causality drivers and sinks of the cortical sources using the three methods on experimental data of the Stroop protocol.

While the source connectivity analysis with the DTF technique can be used to infer causal interactions among a selection of cortical ROIs, it remains challenging to estimate all separate primary sources with this method alone. In the present study, we considered the ROI with the largest total outflow as the most likely primary source for epileptogenesis, which was based on the hypothesis that there was only a single primary source for a spike. Consequently, the ROIs with smaller total outflows may be overlooked with this method of analysis. As in patient 1 (see Sect. 3.1 and Fig. 1), three brain regions were surgically resected (right temporal, parietal and frontal topectomy), but only the most significant primary source corresponding to the tubers was identified without a priori information on the number of separate primary sources. In addition to analyzing all spikes to localize every possible primary source, another potential solution for more accurate localization may be to take the total outflow as a probability of primary source and determine separate primary sources with assistance of evidences from other modalities (e.g. intracranial ictal EEG or ictal EEG imaging (Yang et al. 2011)).

The epileptic propagation estimated from each spike was from the identified primary source to irritated brain regions, which suggested a possible epileptic brain network. For each patient, the propagation pattern might vary from spike to spike. The spikes might initiate at the same epileptogenic foci but propagated to different connected brain regions. The variance of the propagation might be due to different signal-to-noise ratios of the spikes. The underlying actual epileptic brain network might respond to a spike with a particular distinguishable signal-to-noise ratio, which led to a particular propagation pattern. The average spike or statistical analysis of the propagation patterns may be used to estimate the actual epileptic network, which should be addressed in future investigations.

The major limitation of the present study is the limited patient population and limited number of interictal spikes analyzed. Due to the challenges in localizing primary epilepsy sources from patients with multiple identified foci, the results reported here do not provide a validation of the MEG source connectivity analysis method in localizing primary epilepsy sources. Rather, it reports the first attempt, to our knowledge, to estimate primary epilepsy sources from the approach we are proposing, by solving MEG inverse source imaging problem and then performing connectivity analysis on the source domain with the DTF technique. Further validation studies should be carried out in a large number of patients before any conclusions can be drawn with regard to the power of such approach to localize primary epilepsy sources.

In summary, the present pilot results suggest the feasibility of using cortical source connectivity analysis from interictal MEG for the localization of primary sources and propagations of epileptiform activities in a small group of patients. The MEG source connectivity analysis may have other applications in localizing and imaging brain activity and connectivity.

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Fig. 1.

Protocol of source connectivity analysis from the interictal MEG spike. The waveform and global field power of the interictal spike were inspected for the selection of significant time points around the peak of the spike (see **a**). Cortical current distributions were reconstructed from the interictal spike with an individual realistic three-layer boundary element model, and cortical regions with significant activity at the selected time points were considered as regions of interest (see **b**). Representative waveforms for the cortical regions of interest were computed. Directional connectivity among the cortical ROIs was estimated from the ROI waveforms using directed transfer function, and visualized over the cortical surface (see **c**). *L* left view, *R* right view

Fig. 2.

Source connectivity analysis from Patient 2. Three cortical ROIs with significant activity at two time points around the peak of an interictal spike were selected (see (a, b, c)). The information flows among the ROIs (see d) and the total outflows of the ROIs (see e) indicated the primary source of the interictal spike in the right frontal lobe. Epileptiform activity propagated from the right frontal lobe to the right posterior and inferior frontal regions. The identified primary source was in the clinically resected zones. *R* right view

Fig. 3.

Source connectivity analysis from Patient 3. Three cortical ROIs with significant activity at two time points around the peak of an interictal spike were selected (see **a**, **b**, **c**). The information flows among the ROIs (see **d**) and the total outflows of the ROIs (see **e**) indicated the primary source in the right temporal lobe. Epileptiform activity propagated from the right temporal lobe to the right anterior and posterior frontal lobes. The identified primary source was overlapping with the clinically resected zone. *R* right view

Fig. 4.

Source connectivity analysis from Patient 4. **a** Two ROIs were determined from spike 1 and the information flow indicated the primary source in the left temporal lobe. **b** Three ROIs were determined from spike 2 and the information flows indicated the primary source in the left frontal lobe. The identified primary sources agreed with the clinically resected zones (see **c**). *L* left view

Fig. 5. Source connectivity analysis from Patient 5. Two ROIs were determined from spike 1 (see **a**) and spike 2 (see **b**). The information flows indicated the primary source in the left temporal lobe. The identified primary source agreed with the clinically resected zone (see **c**). *L* left view

Table 1

Clinical information for the patients

Patient	Gender	Age of onset of seizures	Seizure type and frequency presurgically	Age at surgery	Pathology	Surgery	Surgery date	Outcome	Engel score
1	Female	2 months	Complex partial seizure, daily	11	Cortical tubers and gliosis	Right temporal, parietal and frontal topectomy	5/2005	Seizure free remained with AEDs since surgery	IA
2	Female	19 months	Complex partial seizure, daily	3	Cortical tubers and gliosis	Right frontal and parietal topectomy	2/2008	Seizure free with AEDs since surgery	IA
3	Male	5 years	Complex partial seizure, 8–10/week	13	Astroglia	Right temporal lobectomy including mesial structure	10/2006	Single simple partial seizure remained with AEDs since surgery	IB
4	Female	10 years	Simple and complex partial seizure, monthly	32	Moderate to remarked astroglia	Left temporal lobectomy and frontal topectomy	11/2005	2 simple partial seizures remained with AEDs since surgery	IB
5	Male	27 years	Complex partial seizure	31	Mild astroglia	Left temporal lobectomy including mesial temporal structure	10/2007	Seizure free with AEDs since surgery	IA

Table 2

Source identification results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
+	4	3	4	3	4
-	0	1	0	1	0
Total	4	4	4	4	4

Total: the number of interictal spikes analyzed

+ the estimated primary source is within or overlapping with the clinically resected zones

- the estimated primary source is away from the clinically resected zones