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Clinical relevance of source location in frontal lobe epilepsy and prediction of postoperative long-term outcome

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ABSTRACT

Purpose: To evaluate the value of magnetoencephalography (MEG) source localization in localization of epileptic activities and predicting surgical outcome in frontal lobe epilepsies (FLE).
Methods: Forty-six patients with presurgical MEG evaluation and intractable FLE surgery (28 male patients) were analyzed retrospectively with a mean follow-up of 5 years. Dipole analysis was performed for MEG source imaging (MSI). The localization of dipole clusters in relation to the dominant hemisphere, lesions, resection cavity and functional cortex were analyzed. The predictive value of MSI in respect to clinical outcome with long-term postoperative follow up was evaluated.
Results: Interictal focal epileptic activities were found in 82.6% (38/46) patients with monofocal activity 81.6% (31/38) and multifocal activities 18.4% (7/38). Seizure free rate was 47.9% at the mean follow-up of 5.0 ± 4.0 years (median 11.5, range 2–57). Seizure recurrence mainly occurred in the first 1 year after surgery. In the monofocal epileptic activity group, 58.1% (18/31) of the patients were seizure free, predicitng postoperative seizure freedom better than multifocal localization 0% (0/7) ($p = 0.028$). Dipole clusters were completely resected in 70.9% of monofocal activity patients, which had higher seizure free rates compared to partial resection ($p = 0.002$). In patients with surgery in the dominant hemisphere, seizure control was less likely ($p = 0.006$).
Conclusion: MSI contributes to the clinical prediction of postoperative outcome in FLE patients. MSI may non-invasively disclose early epileptogenic lesions, pointing to a resectable lesion, and it then facilitates shortcut route of presurgical evaluation.

1. Introduction

Frontal lobe epilepsy (FLE) is the second most likely medically intractable focal epilepsy benefitting from surgical treatment secondary to temporal lobe epilepsy (TLE). Long-term postoperative seizure free rate is 13–47%.[1–4] One reason for less favorable postoperative outcome in FLE is epileptic activity propagates rapidly and localizing the epileptic network in the frontal lobe is difficult even with invasive electroencephalography monitoring (IEEG).[5] Another reason is that important functional cortex is localized in the frontal lobe, for example the motor and eloquent cortex, therefore may lead to incomplete disintegration of the epileptic network.[3]

Despite the continuous improvement of non-invasive diagnostic methods like electroencephalography (EEG), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and

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Table 1
Characteristics of all 46 FLE cases.

	Number of patients	% of total
Characteristic		
Gender		
Female	18	39.1
Male	28	60.9
Onset age (year)	13.9 ± 11.5 (median age 11.5, range 2–57)	
Age at surgery (year)	30.4 ± 11.2 (28.5, 10–58)	
Presurgical evaluation		
MRI		
Lesional	42	91.3
Non-lesional	4	8.7
MEG		
Monofocal activity	31	67.4
Multifocal activity	7	15.2
No activity findings	8	17.4
Ictal-VEEG		
Localized	19	41.3
Non-localized	27	58.7
Interictal-VEEG		
Lateralized	28	60.9
Nonlateralized	18	39.1
Intracranial EEG		
Performed	28	60.9
Not performed	13	28.2
ECoG	5	10.9
Surgical details		
Type of surgery		
Lesionectomy	19	41.3
Lobectomy	14	30.4
Tailored cortical resection	13	28.3
Side of surgery		
Dominant	25	54.3
Non-dominant	21	45.7
Pathology		
Focal cortical dysplasia	8	17.4
Vascular malformation	6	13
Tumor	12	26.1
Tissue defect[a]	15	32.6
Unspecific gliosis	5	10.9
Follow-up years	5.0 ± 4.0 years (5, 0.5–17)	

[a] Tissue defect means postoperative or posttraumatic scars and/or gliosis.

Single Photon Emission Computed Tomography (SPECT), a single method alone is only rarely available to provide comprehensive localization information to proceed to surgery. Invasive methods on the other hand may cause unbelievable suffers and sometimes severe complications[6,7] which also have only a limited field of view. MEG and EEG source localization as non-invasive evaluation methods in the presurgical evaluation of patients with epilepsy may additionally contribute to detection and localization of focal epileptic activity and also to the functional mapping of eloquent cortex.[8–13] Only few studies, with a limited number of patients and short follow-up time, focus on clinical relevance of source localization in FLEs.[8–13] Recent studies have shown that MEG is able to guide invasive EEG implantation and resections.[8,14–16] Others show MEG can localize the hypothetical epileptogenic zone and subsequent 'clusterectomy' relates to better outcome.[8,13,17–20] To truly evaluate the value of MEG source localization in the specific population of FLE patients, large study populations are needed, taking into account the location of equivalent current dipole (ECD) clusters in relation to the lesion and resection cavity with a long-term postoperative outcome.

In the present retrospective study, a large number of patients with presumable FLE and a presurgical MEG investigation followed by resective epilepsy surgery and long term follow-up were included. Correlation of outcome over time with MEG localization relative to the lesion, etiology and completeness of resection were investigated. We hypothesized that complete resection of MEG epileptic clusters in FLE may cause at least a considerable improvement or even long term seizure freedom.

2. Materials and methods

2.1. Patients

We reviewed all patients meeting the following inclusion criteria at the Epilepsy Center of the University Erlangen Hospital from 1991 to 2012, and the Reference Center for Refractory Epilepsy of Ghent University Hospital from 2009 to 2012: patients with (1) diagnosis of drug resistant focal FLE; (2) MEG, EEG (scalp-Video EEG or/and IEEG), MRI and neuropsychological evaluation during their presurgical evaluation; (3) resective epilepsy surgery and with a postoperative follow-up of at least 6 months; (4) availability of histopathology. Cortical resection were performed in forty six FLE (28 male). The characteristics of the 46 patients with FLE are listed in Table 1.

2.2. Presurgical evaluation protocol

Before surgery, all patients underwent a spectrum of noninvasive or invasive diagnostic investigations. All patients underwent scalp-video EEG monitoring with 21–27 or 48 EEG electrodes placed using the international 10/20 system (Usingen, Germany). All recruited patients underwent high-resolution and fluid-attenuated inversion recovery (FLAIR) imaging MRI using a 1.5 or 3 T SP system (Siemens, Erlangen, Germany) with a standardized epilepsy protocol. MEG was also performed in all patients (see below). Neuropsychological tests (e.g. Wada test) were performed to confirm the dominant hemisphere. Results of noninvasive evaluation were discussed in a multidisciplinary conference, where the decision was made to proceed to surgery, obtain more noninvasive testing, or perform an invasive evaluation.

2.3. MEG

MEG data at Ghent University Hospital were acquired using the whole head 306 channel Elekta Neuromag system (Vectorview & MaxShield; Elekta Neuromag Oy, Helsinki, Finland) installed at the ULB-Hospital Erasme (Brussels, Belgium), the characteristics of which have been described in former publication.[21,22] MEG data at University Hospital Erlangen were acquired using a 74-channel, two-sensor system (Magnes II; 4-D Neuroimaging, San Diego, CA, USA) in a magnetically shielded room (Vakuumschmelze, Hanau, Germany) from 1995 to 2009. Each MEG sensor consisted of 37 first-order gradiometers with a 5-cm baseline and an average distance between channels of 2.8 cm. In 2010 and 2011, patients were investigated at the Department of Neurology, University Hospital Magdeburg, Germany, using a 148 magnetometer- and a 248-magnetometer whole-head system (WHS2800, WHS3600, 4-D Neuroimaging, San Diego, CA, USA). Starting 2012, patients

Table 2
Relationship among MEG clusters, surgery and Engel classification (patients).

MEG localization	Seizure freedom	Non-seizure freedom							
	IA	IB	IC	ID	IIA	IIB	IIIA	IVA	IVB	Total
Monofocal activity	18	2	2	0	2	2	3	0	2	31
Completely resected	15	2	2	0	1	2	0	0	0	22
Incompletely resected	2	0	0	0	1	0	2	0	1	6
Not resected	1	0	0	0	0	0	1	0	1	3
Multifocal activity	0	0	0	1	0	1	3	2	0	7
No activity found	5	0	1	0	0	1	0	0	1	8
Total	23	1	3	1	2	3	6	2	3	46

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