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Original Article

Magnetoencephalographic Characteristics of Cortical Dysplasia in Children

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ABSTRACT

BACKGROUND AND RATIONALE: Magnetoencephalography has emerged as a tool for preoperative evaluation in children. We aimed to study magnetoencephalography characteristics in subtypes of focal cortical dysplasia and correlate with postoperative seizure outcome. **METHODS:** Inclusion criteria were children ≤18 years who had magnetoencephalography during preoperative workup followed by epilepsy surgery and a histopathologic diagnosis of focal cortical dysplasia between February 2008 and February 2013. Patient demographics, MRI, video electroencephalography, and magnetoencephalography data were reviewed. Postoperative seizure outcome data were categorized per International League against Epilepsy definitions. **RESULTS:** Of 178 magnetoencephalography performed in children during the study period, 33 patients met inclusion criteria. Focal cortical dysplasia type I, II, and III were found on histopathology in 52%, 39%, and 9% of patients, respectively. Thirty patients had positive magnetoencephalography dipoles, including all patients with focal cortical dysplasia type II and III and 82% of patients with focal cortical dysplasia type I. Three patients had magnetoencephalography unique spikes. Brain MRI lesions were noted preoperatively in 21 patients (64%). Twenty-three patients (77%) had surgical resection of magnetoencephalography dipoles and 11 (48%) of them achieved favorable outcome. **CONCLUSIONS:** Magnetoencephalography supplemented scalp electroencephalography data in spike source localization and showed unique spikes in 10% of the focal cortical dysplasia patients. Magnetoencephalography spikes and tight magnetoencephalography clusters were found more frequently in patients with focal cortical dysplasia type II and III as compared with focal cortical dysplasia type I. Presence of an MRI lesion and complete versus incomplete resection of magnetoencephalography cluster did not result in significant difference in postoperative seizure outcome, likely reflecting selection bias of doing magnetoencephalography in only difficult-to-localize epilepsies.

Keywords: magnetoencephalography, focal cortical dysplasia, epilepsy, seizures

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Introduction

Focal cortical dysplasias (FCDs) are malformations of cortical development caused by abnormal neuronal and glial proliferation and migration during early development.[1] The hallmark of FCDs is an abnormal cortical microarchitecture, with loss of the laminar neuronal distribution.[2] They are known to be intrinsically epileptogenic[3,4] and are one of the most common causes of intractable epilepsy in childhood,[5] with up to 76% of patients becoming refractory to

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antiepileptic medications over time.[6] FCDs are also the most common single pathology found in patients undergoing extratemporal epilepsy surgery,[7,8] with incomplete resection of FCD known to be the main predictor of poor postoperative outcome.[9,10]

Various tests used in the preoperative evaluation of children with refractory epilepsy include video electroencephalography (VEEG), magnetic resonance imaging (MRI), and positron emission tomography (PET) scan. Magnetoencephalography (MEG) is another tool and is used to record the extracranial magnetic field generated by the electrical activity of the brain. MEG has excellent temporal and spatial resolution. It has an advantage over electroencephalography (EEG) as the magnetic fields are not distorted or attenuated[11] by the scalp and dura, and accurate localization of the epileptic spike source is possible. Dipole sources in sulci or fissures generating tangential currents are the likely major contributors to the activity recorded by MEG, resulting in several favorable brain areas for MEG source localization.[2]

MEG is used in the evaluation of both lesional and nonlesional epilepsies in children,[12,13] with successful outcomes. It is considered second only to ictal intracranial VEEG in predicting good surgical outcome,[14] and concordance has been shown between interictal spikes localization of MEG sources and the ictal onset zone recorded by intracranial VEEG recordings.[4,15-17] Even when it picks up no new areas of epileptic activity, MEG provides more precise localization than scalp EEG.[18]

There is scarcity of reports in the literature about magnetoencephalographic characteristics of cortical dysplasia. In this study, we aimed to identify MEG characteristics of various subtypes of cortical dysplasias, which may help in their identification preoperatively. We analyzed MEG characteristics according to the subtype of FCD, and correlated MEG with 2 key tools for preoperative evaluation, VEEG, and brain MRI.

Materials and Methods

Study design

We retrospectively studied all pediatric patients (≤18 years) who had MEG study performed at the Cleveland Clinic between February 2008 and February 2013 as part of their preoperative workup. Patients who underwent surgical resection, had a histopathology confirmed FCD, and had at least 6 months' follow-up after surgery were then identified and included. Charts were reviewed for the following information: demographics including age and gender, epilepsy risk factors, number of antiepileptic drugs, seizure types and frequency, MEG results including location of abnormalities and presence of MEG clusters or scatters, VEEG abnormalities, preoperative MRI for identification of epileptogenic lesion, postoperative MRI to assess resection of MEG spikes, type and location of surgery, FCD subtype, and seizure outcome as reported by caregivers at least 6 months after surgery.

MEG data acquisition and co-registration

MEG with a whole head system of 204 gradiometers and 102 magnetometers was performed with simultaneously recorded 10/20 scalp EEG for 60-minute periods during awake and sleep conditions. Acquisition parameters included 1000 Hz sampling rate and 0 to 300 Hz recording bandpass, followed by post-processing with the temporally extended signal space separation method (VectorView, Neuromag, Helsinki, Finland). At review time, the MEG and EEG data were subsequently bandpass-filtered to 0.5 to 50 Hz. All of the recorded MEG and EEG channels were visually reviewed, and spikes were manually identified from either MEG or EEG. Epochs (usually 0.5 to 1 second) containing epileptic spikes were further filtered to 5 to 50 Hz (to emphasize the spikes over the slower background), and the MEG spikes were subjected to single equivalent current dipole modeling localization applied within a spherical head model using the source modeling software supplied by the vendor (Xfit, Neuromag, Helsinki, Finland). A single dipole location was obtained for each spike, at or slightly before the peak, with dipole fits accepted if they fulfilled all of the following criteria: dipolar pattern on the magnetic field topographic display, reduced chi-square less than 2, confidence volume less than 1500 mm^3, goodness of fit greater than 85%, amplitude between 150 and 500 nA-m.[19]

MEG spikes were classified as tight clusters if ≥5 dipoles were identified across two gyri and one sulci; loose clusters if ≥5 dipoles were identified in a sub-lobar region; and the rest as scatters (less than five dipoles or greater than five dipoles in a wide distribution). Prolonged VEEG (electroencephalography) monitoring was performed using scalp electrodes placed according to the International 10-20 system, and information from the most recent evaluation before surgery was collected. High-resolution MRI was performed on all patients using Siemens 1.5 or 3 Tesla SP system (Siemens, Erlangen, Germany) using a standardized epilepsy protocol that included high-resolution T1-weighted volume acquisition, T2-weighted, and fluid-attenuated inversion recovery sequences. Most of the patients also had a fluorodeoxyglucose-positron emission tomography or FDG-PET scan.

Results of the noninvasive evaluation were discussed in a multidisciplinary patient management conference where the decision was made to either proceed with a resection or to perform an invasive evaluation for further investigation. All patients in this study eventually had surgical resection of identified epileptogenic region. Post-resection tissue sections were evaluated for the presence of FCD by the neuropathologist (RP) and classified per International League against Epilepsy (ILAE)[20] classification into different FCD subtypes. MRI scans were obtained after surgery and evaluated by 2 authors (NA and RCB) to ascertain whether complete, partial, or no resection of MEG dipole sources was achieved. Clinical outcome was determined at the last clinical follow-up available (at least >6 months after surgery) and classified as per ILAE classification.[21] Favorable outcome was defined as ILAE class I + II and unfavorable outcome as class III + IV +V. The study was approved by Cleveland Clinic Institutional Review Board (IRB).

Statistical analysis

Statistical analysis was performed using chi-square test (χ^2). *P* values <0.05 were considered significant.

Results

A total of 178 MEG studies were performed on children aged 18 years or less during the study period. Of these, 54 patients underwent surgical treatment, and cortical dysplasia was identified in 33 patients on postoperative pathology analysis. All patients had at least 6 months' clinical follow-up after surgery (range six months to 39 months). Mean age at seizure onset was 3.9 years (range zero days to 12 years). Mean number of antiepileptic drugs used before surgery was 2.39 (range one to four) with a male-to-female ratio of 2.3. Histopathology confirmed FCD type I was found in 17 (52%) patients, FCD type II in 13 (39%), and FCD type III in 3 patients (9%).

FCD subtypes and MEG

Thirty patients (91%) were found to have positive MEG studies, and 3 patients (9%) had normal studies. Twenty-