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Electro- and magneto-encephalographic spike source localization of small focal cortical dysplasia in the dorsal peri-rolandic region

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HIGHLIGHTS

- Six epilepsy patients presented with a single small magnetic resonance (MR) imaging lesion suggesting focal cortical dysplasia (FCD) within a single gyrus.
- All 6 patients had a single small FCD lesion in the dorsal peri-rolandic region on MR imaging, which had been previously overlooked.
- Source localization of EEG and magnetoencephalography spikes confirmed the diagnosis of a single small FCD lesion in the 5 patients with leg sensori-motor seizures.

ABSTRACT

Objective: Small focal cortical dysplasia (FCD) may be ambiguous or overlooked on magnetic resonance (MR) imaging. Source localization of EEG and magnetoencephalography (MEG) spikes was evaluated to confirm the diagnosis of small FCD.
Methods: This study included 6 epilepsy patients with a single small lesion on MR imaging suggesting FCD within a single gyrus among 181 consecutive epilepsy patients admitted to our epilepsy monitoring unit over 27 months. Stereotypical interictal spikes were detected on simultaneous EEG and MEG recordings and the onset-related source of averaged spikes was estimated.
Results: All 6 patients had unique clinical characteristics as follows: leg sensori-motor seizures in 5 patients and eye version in 1 patient; a small MR imaging lesion suggesting FCD in the dorsal peri-rolandic region, which had been overlooked until our evaluation; and both EEG and MEG dipoles were estimated adjacent to the MR imaging lesion.
Conclusions: Source localization of EEG and MEG spikes can confirm the diagnosis of FCD based on a single small MR imaging lesion, which was overlooked by previous examination of MR images.
Significance: Examination of MR images should be based on spike source localization as well as seizure semiology to identify subtle MR imaging abnormalities.

1. Introduction

Focal cortical dysplasia (FCD) is a major cause of pharmacoresistant epilepsy (Widjaja et al., 2008; Lerner et al., 2009; Palmini, 2010). Therefore, identification of FCD lesions by magnetic reso-

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nance (MR) imaging is essential to improve surgical outcome. Surgical resection resulted in seizure-free outcomes in 70% of patients with a focal lesion identified by MR imaging, but in only 41% of patients without such a lesion (Widdess-Walsh et al., 2007). MR imaging may fail to detect FCD lesions such as small dysplasia, although the MR imaging detection rate is generally high (60–90%). Smaller FCD was reported to be located in a deeper region, at the bottom of the sulcus, which is called "bottom of sulcus" dysplasia (Besson et al., 2008; Hofman et al., 2011). However, routine MR imaging overlooked 81% of small FCD lesions at the bottom of the sulcus (Besson et al., 2008).

^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) can reveal focal hypometabolism corresponding to FCD lesions not detectable by MR imaging. However, FDG-PET can only detect an extended functional deficit area. Therefore, a focal small lesion may not be detected by any type of neuroimaging studies including FDG-PET and MR imaging. Electroencephalography (EEG) and magnetoencephalography (MEG) source localization can show a focal irritative zone arising from such a single small lesion rather than those arising from multiple or extended lesions (Ebersole, 2000; Yoshinaga et al., 2002), but no studies have evaluated subtle MR imaging abnormalities in patients with small FCD.

The present study investigated whether source localization of EEG and MEG spikes can confirm the existence of abnormalities associated with single small FCD lesions, which have been overlooked by serial MR imaging.

2. Methods

2.1. Patients

This study included 12 patients with MR imaging findings suggesting FCD among 181 consecutive epilepsy patients admitted to our epilepsy monitoring unit over 27 months. Six of these 12 patients, 2 men and 4 women aged 15–41 years, had a single small lesion within a single gyrus detected by MR imaging. This study was approved by the Ethics Committee of Tohoku University Graduate School of Medicine, and informed consent was obtained from each patient.

2.2. Neuroimaging study

All patients underwent 3T MR imaging with either Magnetom Trio (Siemens AG, Erlangen, Germany) or Intera Achieva (Philips Healthcare, Best, The Netherlands). The protocol consisted of axial T1-weighted, T2-weighted, and fluid-attenuated inversion recovery (FLAIR) imaging (slice thickness, 7 mm), and/or coronal FLAIR imaging (slice thickness, 3.8 mm). Axial three-dimensional T1-weighted imaging was also performed (slice thickness, 1 mm). Maximum diameter of the lesion was measured on the axial FLAIR image. Axial raw data were obtained using a PET scanner (Biograph Duo or Biograph 40; Siemens AG) 60 min after intravenous injection of FDG at a mean dose of 0.1 mCi/kg during the interictal period of each patient. FDG-PET and T1-weighted MR images were co-registered to evaluate the anatomical distribution of glucose hypometabolism with image processing software (Amira version 5.4; VSG, Burlington, MA). The MR images were examined by a neuroradiologist and two epileptologists (K.J. and M.I.), whereas the MR images had been reviewed by neuroradiologists with general neurologists or neurosurgeons in previous studies.

2.3. Simultaneous EEG and MEG recording

MEG studies used a 160- or 200-channel axial gradiometer system (MEG vision PQ1160C; Yokogawa Electric, Tokyo, Japan) in a magnetically shielded room. EEG was simultaneously recorded using 42-channel electrodes, with approximately double the density of the standard 10–20 system. EEG and MEG data were acquired with sampling at 1000 Hz and band-pass filtering between 0.16 and 200 Hz. EEG and MEG recordings were performed for 30–60 min periods for each patient during awake, drowsy, and sleep conditions.

2.4. Source analysis of interictal EEG and MEG spikes

Typical EEG and MEG spikes were identified manually and used as templates to search for similar spatiotemporal spike patterns. Using spike detection software (BESA Research 5.3; BESA GmbH, Gräfelfing, Germany), similar spikes were detected, averaged, and high-pass filtered (1.6 Hz) to enhance the spike onset (Bast et al., 2004). Single equivalent current dipole (ECD) models were used to localize the onset-related source. To visualize the EEG and MEG spike sources, the EEG and MEG dipoles were superimposed onto individual MR images. The distance was measured between the center of the MR imaging lesion and the source location of the EEG/MEG spikes. The distance was also measured between the EEG and MEG dipoles. The center of the lesion was identified on axial and/or coronal FLAIR MR images by neuroradiologists.

3. Results

3.1. Electro-clinical and neuroradiological findings

Seizure semiology, EEG findings, and MR images of the 6 patients are summarized in Fig. 1 (Cases 1–6). All 6 patients suffered sensori-motor seizures as the initial symptoms, occurring as leg sensori-motor seizures in 5 patients and eye version in 1. Interictal EEG revealed stereotyped spikes around the vertex region in all patients. MR imaging had been considered to show no abnormalities until our evaluation revealed a single small lesion in the dorsal peri-rolandic region in all patients. The lesions were less than 20 mm in diameter. FDG-PET coregistered with individual MR images showed no focal hypometabolism in any of the patients.

3.2. Source analysis of interictal EEG and MEG spikes

All detected EEG and MEG spikes used for the averaged spikes showed goodness-of-fit >95% and >80%, respectively, in 5 patients (Cases 1–5), whereas no spikes were found by either EEG or MEG in one patient (Case 6). Both EEG and MEG dipoles of the averaged spikes were adjacent to the MR imaging lesion and well correlated with the seizure semiology in these 5 patients (Cases 1–5) (Fig. 2). The distance between the center of the lesion and the EEG/MEG spike source was less than 20 mm in all 5 patients. The distance between the EEG and MEG spike sources was also less than 20 mm in all patients except one, with a distance of 26.4 mm (Table 1).

4. Discussion

Our 6 patients had unique clinical characteristics as follows: (i) semiology, leg sensori-motor seizures in 5 patients and eye version in 1; (ii) neuroimaging, a single small MR imaging lesion suggesting FCD in the dorsal peri-rolandic region, which had been overlooked until our evaluation, and no focal hypometabolism detectable by FDG-PET; and (iii) EEG/MEG, interictal epileptiform discharges around the vertex region detected by scalp EEG and MEG, with ECDs located close to the MR imaging lesion.