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Original article

Magnetoencephalography localizing spike sources of atypical benign partial epilepsy

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Abstract

Rationale: Atypical benign partial epilepsy (ABPE) is characterized by centro-temporal electroencephalography (EEG) spikes, continuous spike and waves during sleep (CSWS), and multiple seizure types including epileptic negative myoclonus (ENM), but not tonic seizures. This study evaluated the localization of magnetoencephalography (MEG) spike sources (MEGSSs) to investigate the clinical features and mechanism underlying ABPE. *Methods:* We retrospectively analyzed seizure profiles, scalp video EEG (VEEG) and MEG in ABPE patients. *Results:* Eighteen ABPE patients were identified (nine girls and nine boys). Seizure onset ranged from 1.3 to 8.8 years (median, 2.9 years). Initial seizures consisted of focal motor seizures (15 patients) and absences/atypical absences (3). Seventeen patients had multiple seizure types including drop attacks (16), focal motor seizures (16), ENM (14), absences/atypical absences (11) and focal myoclonic seizures (10). VEEG showed centro-temporal spikes and CSWS in all patients. Magnetic resonance imaging (MRI) was reported as normal in all patients. MEGSSs were localized over the following regions: both Rolandic and sylvian (8), peri-sylvian (5), peri-Rolandic (4), parieto-occipital (1), bilateral (10) and unilateral (8). All patients were on more than two antiepileptic medications. ENM and absences/atypical absences were controlled in 14 patients treated with adjunctive ethosuximide. *Conclusion:* MEG localized the source of centro-temporal spikes and CSWS in the Rolandic-sylvian regions. Centro-temporal spikes, Rolandic-sylvian spike sources and focal motor seizures are evidence that ABPE presents with Rolandic-sylvian onset seizures. ABPE is therefore a unique, age-related and localization-related epilepsy with a Rolandic-sylvian epileptic focus plus possible thalamo-cortical epileptic networks in the developing brain of children.

Keywords: Epileptic negative myoclonus; Focal seizure; Atypical absence; Centro-temporal spike; Continuous spike and waves during sleep; Secondary bilateral synchrony

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1. Introduction

Atypical benign partial epilepsy in childhood (ABPE) initially presents with the following signs and symptoms: (i) onset age of 2.5–6 years; (ii) multiple seizure types including focal motor, atypical absences and myoclonic-atonic seizures; (iii) electroencephalography (EEG) showing central and mid-temporal spikes and diffuse slow spike-wave activities during drowsiness or sleep; and (iv) normal development or mild mental retardation [1]. Despite multiple seizure types and slow spike and waves on EEG, ABPE is distinguished from Lennox–Gastaut syndrome by its characteristic spontaneous remission, lack of tonic seizures or developmental delay, and normal awake EEG background activity. Since hemi-convulsive seizures during sleep and contralateral/bilateral centro-temporal epileptiform discharges are present at the beginning, the electro-clinical findings of ABPE are indistinguishable from those of benign epilepsy with centro-temporal spikes (BECTS) [2–5]. BECTS is the most well-recognized, age-related idiopathic focal epilepsy with occasional epileptic seizures despite frequent centro-temporal spikes on EEG. In contrast, ABPE patients tend to develop atypical absences or myoclonic-atonic seizures during the course of their condition. Tovia et al. [6] showed that 0.5% of patients with BECTS were categorized as atypical variants, while Doose et al. [7] found that 29% of the relatives of ABPE patients had some abnormal activities on EEG. Finally, Gobbi et al. [8] reviewed several subtypes of idiopathic focal epilepsies to categorize ABPE as a "Rolandic epilepsy-related disorder"; these age-related epilepsies including ABPE and BECTS were attributed to a maturational continuum with different manifestations.

Epileptic negative myoclonus (ENM) is one of the characteristic seizure patterns in ABPE. Oguni et al. [6] analyzed the ictal EEG findings of ENM and demonstrated generalized, bilateral synchronous discharges, while ictal magnetoencephalography (MEG) of an ABPE patient showed that the spike sources of ENM were localized at the peri-sylvian region [7].

MEG is a relatively new clinical technique that uses superconducting quantum interference devices (SQUIDs) to measure and localize sources of extracranial magnetic fields generated by intraneuronal electric currents. Current MEG machines have a whole-head array of more than 100 sensors contained within a helmet-shaped Dewar, which effectively covers most of the brain surface. MEG has been increasingly used for localization of the epileptic zone and functional mapping in epilepsy patients. MEG in BECTS patients showed spike sources with an anterior–posterior oriented perpendicular to the Rolandic fissure [8,9]. No case series of ABPE have thus far used MEG to localize epileptic spike sources.

We conducted a multi-center study to collect clinical, EEG and MEG findings in ABPE patients, with MEG used to characterize the spike sources (MEGSSs) in ABPE. We hypothesize that the epileptic network in ABPE is localized in both the Rolandic-sylvian cortex and thalamo-cortical networks, based on their unique clinical and electrophysiological features.

2. Patients and methods

We collaborated with four institutions on this study: the Department of Pediatrics, Hokkaido University School of Medicine (HU); Department of Pediatrics, Tohoku University School of Medicine (TU); Department of Pediatrics, National Center of Neurology and Psychiatry (NCNP), Japan; and the Division of Neurology, The Hospital for Sick Children (HSC), Toronto, Ontario, Canada.

2.1. Patients

We studied 18 patients with ABPE (nine females and nine males). We diagnosed ABPE according to the triad of diagnostic criteria as follows: (1) focal motor seizures, absences/atypical absences, atonic seizures including ENM, myoclonic seizures and drop attacks described by parents; (2) EEG findings of central and middle temporal spikes and generalized slow spike-wave activity during drowsiness or sleep similar to continuous spike and slow waves during sleep (CSWS); (3) normal development or mild mental retardation during the clinical course.

2.2. EEG

Scalp video EEGs were recorded using the international 10-20 electrode placement system and electromyography (EMG) electrodes for bilateral deltoid muscles to capture ENM. Awake and sleep EEGs were recorded in all patients.

2.3. MEG and magnetic resonance imaging

Initial MEG studies were conducted at the onset of ENM. Seven patients had multiple MEG studies up to six times. Parents or guardians of all patients provided written informed consent for the MEG studies. MEG and EEG were done in a magnetically shielded room. MEG was recorded using a system with 306 SQUIDs (Vectorview; Elekta-Neuromag Ltd., Helsinki, Finland) at HU, NCNP and TU, and with an Omega system (151 channels, VSM MedTech Ltd., Port Coquitlam, BC, Canada) at HSC. MEG data were recorded with a band pass filter of 0.03–133 Hz at HU, NCNP and TU, and of 1–208 Hz at HSC. Sampling frequency was 400 Hz at HU, 600 Hz at NCNP and TU, and 625 Hz at HSC. EEGs were recorded using the international 10-20 system, with additional electrocardiogram (ECG)