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Spatial relationship between fast and slow components of ictal activities and interictal epileptiform discharges in epileptic spasms

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HIGHLIGHTS

- The spatial concordance between the fast and slow EEG components differs between ictal activities during epileptic spasms and interictal epileptiform discharges.
- The slow EEG components of ictal activities of epileptic spasms are discordant with the areas of the fast components.
- Generators of the slow EEG components of interictal epileptiform discharges overlap with the areas of the preceding fast EEG components.

ABSTRACT

Objective: We analyzed the spatial distribution and concordance of fast (>10 Hz) and slow (<5 Hz) electroencephalogram (EEG) components of ictal activities and interictal epileptiform discharges (IIED) recorded by intracranial video EEG (IVEEG) in children with epileptic spasms (ES).
Methods: We studied eight children with ES, who underwent IVEEG before resective surgery for epilepsy. We quantified the root-mean-square (RMS) amplitude of the fast and slow components of ictal activities during ES and IIED. We compared the concordance between the spatial distributions of the fast and slow components of ES and IIED.
Results: There was a larger concordance between the spatial distributions of the fast and slow components in IIED than in ES ($p = 0.0206$ and 0.0401).
Conclusions: The spatial concordance between the fast and slow EEG components was significantly different between ES and IIED.
Significance: The mechanisms underlying the generation of slow EEG components may differ between ES and IIED. The slow EEG components of ES might indicate an extensive epileptic network involving remote symptomatic zones for ES in either the cortical or subcortical areas. The high spatial concordance between the fast and slow components of IIED suggests the involvement of a local inhibitory process within the epileptic cortex.

1. Introduction

Epileptic spasms (ES) are commonly seen in generalized epilepsies, such as West syndrome, Ohtahara syndrome, and Lennox–Gastaut syndrome; however, ES have also been reported in focal epilepsies (Gobbi et al., 1987; Ohtsuka et al., 2001). It is common

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for ES to occur in clusters. Until the International League Against Epilepsy categorized ES under "unknown whether generalized or focal" (Berg et al., 2010) ES had been diagnosed and treated as generalized seizures. Nevertheless, a subset of pediatric patients with ES underwent resective epilepsy surgery after identification of the seizure onset zone of ES (Akiyama et al., 2005; Asano et al., 2005; RamachandranNair et al., 2008). Although the mechanism of ES generation is unknown, abnormal interactions between the epileptogenic cortex and the brainstem have been speculated on and are gaining consensus in patients with ES (Chugani et al., 1992; Vigevano et al., 2001).

The distribution of ictal fast waves, especially gamma and high-frequency oscillations (80–200 Hz), in the intracranial video electroencephalogram (IVEEG) is correlated with the localization of the seizure onset zone (Allen et al., 1992; Fisher et al., 1992; Alarcon et al., 1995; Worrell et al., 2004; Ochi et al., 2007; Modur et al., 2011) and the epileptogenic zone (Fujiwara et al., 2012; Park et al., 2012) in adult and pediatric patients with focal epilepsies. Ictal fast waves in ES, including gamma and high-frequency oscillations, have been reported on IVEEG (Akiyama et al., 2005; Asano et al., 2005; RamachandranNair et al., 2008; Nariai et al., 2011a,b) and scalp EEG (Kobayashi et al., 2004, 2007).

Fusco and Vigevano reported ictal EEG patterns of ES consisting of high-amplitude slow waves associated with low-amplitude fast activity and subsequent voltage attenuation (Fusco and Vigevano, 1993). The high-amplitude slow waves were the prominent markers on scalp EEG that were associated with clinical manifestation of ES and rhomboid-shaped discharges on the electromyogram (EMG). They suggested that slow waves in ES probably indicated a far-field potential. Kobayashi et al. reported that ictal slow waves in ES on scalp EEG showed negative potential distributions over the posterior head region or abnormal brain lesions (Kobayashi et al., 2005). Nariai et al. analyzed phase coupling between fast and slow waves on IVEEG in ES and demonstrated that slow waves were near-field synchronized potentials generated by the neocortex (Nariai et al., 2011a).

Interictal epileptiform discharges (IIED) consist of a spike followed by slow waves. The spike corresponds at the cellular level to a paroxysmal depolarization shift (PDS), and the slow wave following the spike is known to be caused by a prolonged hyperpolarization of the cortical neurons (Lothman, 1993). The slow waves of IIED probably reflect local inhibition after excitation within the cortex.

There are no reports in the literature on the relationship between slow EEG wave components in ictal activities during ES and IIED. We analyzed the spatial distribution and concordance of the slow and fast components of ES and IIED recorded in pediatric patients who underwent IVEEG. We hypothesized that the mechanism of slow-wave generation in ES is distinct from that of slow waves in IIED and that the spatial distributions of the fast and slow components in IIED correlate strongly while those in ES correlate weakly.

2. Methods

2.1. Patients

We retrospectively identified patients with intractable epilepsy with ES occurring in clusters who underwent IVEEG monitoring prior to epilepsy surgery at the Hospital for Sick Children in Toronto, Canada between 2005 and 2011. IVEEG was performed in patients with localized or lateralized IIED on scalp EEG concordant with the dipole localization of IIED in magnetoencephalography (MEG). We reviewed the patients' clinical histories, EEG, MEG, and magnetic resonance imaging (MRI) findings, pathologies, and surgical outcomes. Ethics approval was obtained from The Research Ethics Board at The Hospital for Sick Children.

2.2. Extra-operative intracranial video EEG

The technique of implantation of intracranial electrodes, mapping of the possible epileptogenic zone, and intraoperative and extra-operative functional mapping of the eloquent cortex was done as described previously (Pang et al., 2009; Benifla et al., 2009). Center to center spacing of the contacts was 6.5–10.5 mm in subdural electrodes and 7 mm in depth electrodes (Ad-Tech Medical Instrument, Racine, WI, USA). IVEEGs were recorded using the Stellate Harmonie system (Natus, San Carlos, CA, USA) with two electrodes over the brain regions without active spikes used as linked references. These references could be changed during monitoring depending on the EEG findings. The EEG signals were sampled at 1 kHz after band-pass filtering at 0.016–300 Hz. We recorded the EMGs of bilateral deltoid muscles simultaneously to monitor muscle activities during seizures.

2.3. Resective surgery

The resection margin was determined based on visual analysis of ictal EEG discharges, spectral analysis of EEG at ictal onset and during early spread (Ochi et al., 2007), interictal spikes on IVEEG, the localization of dipole cluster by MEG, and the location of eloquent cortices revealed by functional mapping using direct cortical stimulation and sensory-evoked potentials.

2.4. EEG selection for analysis

All EEG data were reviewed and analyzed by an in-house program written in MATLAB (The MathWorks, Natick, MA, USA). EEG data were remontaged to an average reference to reduce noise and contamination from the recording reference, to eliminate the effect of changes of recording reference during EEG monitoring, and to obtain the reference-free topographic maps described later (Crone et al., 2001). We excluded depth electrodes and contralateral strip electrodes to concentrate on the spatial distributions of the fast and slow components on the brain surface of the presumed epileptogenic hemisphere.

For each patient, we selected 10–20 ictal EEG sections of consecutive ES in a single cluster. ES with a spasm preceding by no more than 2 s or with a subsequent spasm within 3 s were excluded. For each ES we placed a marker at the onset of the fast components in the ictal EEG using a 10 Hz high-pass filter with the MATLAB program. The time point where the marker was placed is referred to as 'time zero' in the following analysis. Five-second sections of unfiltered ictal EEGs starting from 2 s before the marker (i.e., −2 to +3 s) were saved for later analysis. This duration of 5 s was determined so that the selected EEG sections would be long enough to perform the analysis described later.

For IIED, we selected a group of representative spike-waves in each patient. For this purpose, we used Reveal software (Persyst, Prescott, AZ, USA) for automated spike detection with a default setting for a maximum 30 min interictal EEG in each patient. Next, we used Spike Review software (Persyst, Prescott, AZ, USA) with a default setting for automated clustering of spikes based on their topographic distribution and morphology. Spike Review software generates a clustering tree of spikes according to the dissimilarity level (Fig. 1). The lower the dissimilarity level of a cluster (group), the more alike the spikes in the cluster. A spike cluster can be further divided into subclusters (subgroups) with lower dissimilarity levels consisting of more homogeneous spikes. Starting from the stem of the clustering tree, we chose the branch with the lower dissimilarity level when we reached a branching point. When the