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Original article

Scalp-recorded high-frequency oscillations in childhood epileptic encephalopathy with continuous spike-and-wave during sleep with different etiologies

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Abstract

Objective: To investigate high-frequency oscillations (HFOs) in epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS) with different etiologies.

Methods: Twenty-one CSWS patients treated with methylprednisolone were divided into structural group and genetic/unknown group. Comparisons were made between the two etiological groups: selected clinical variables including gender, age parameters, seizure frequencies and antiepileptic drugs; distribution of HFOs in pre-methylprednisolone electroencephalography (EEG) and percentage changes of HFOs and spikes after methylprednisolone treatment.

Results: There were 7 patients (33%) in structural group and 14 patients (68%) in genetic/unknown group. No significant difference was found between the two groups regarding selected clinical variables. HFOs were found in 12 patients in pre-methylprednisolone EEG. The distribution of HFOs was focal and accordant with lesions in 5 of structural group, and it was also focal but in different brain regions in 7 of genetic/unknown group. The percentage reduction of total HFOs and spikes was 81% (158/195) and 19% (1956/10,037) in structural group, while 98% (315/323) and 55% (6658/12,258) in genetic/unknown group after methylprednisolone treatment.

Conclusion: The etiologies had no distinct correlation with some clinical characteristics in CSWS. HFOs recorded on scalp EEG might not only be used as makers of seizure-onset zone (SOZ), but also have association with functional disruption of brain networks. Both HFOs and spikes reduced more in genetic/unknown patients than that in structural patients after methylprednisolone treatment and HFOs were more sensitive to treatment than spikes.

Keywords: High-frequency oscillations; Epileptic encephalopathy with continuous spike-and-wave during sleep; Scalp electroencephalography; Time-frequency analysis

1. Introduction

Electrical status epilepticus in sleep (ESES) can be present in various evolutionary stages of a spectrum of disease. Atypical benign partial epilepsy (ABPE) may be considered milder manifestations of the

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electroclinical continuum in which epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS) represents the more severe end [1–4]. CSWS is heterogeneous with various etiologies, and structural lesions such as developmental lesions have been identified as one important etiology of CSWS [5–9]. For CSWS management, standard antiepileptic drugs are most commonly used and corticosteroids were generally regarded effective to improve or even resolve ESES [7,10–12]. Because the seizures and ESES of CSWS usually remit before adolescence, surgical treatment is restricted to highly selected cases, even for patients with definitely unilateral structural lesions [8,13–16].

High-frequency oscillations (HFOs) play a crucial role in both physiological and pathological brain functions [17]. It has been established that both ictal and interictal HFOs recorded in intracranial electroencephalography (EEG) identified the seizure-onset zone (SOZ) better than traditional spikes [18–20] and the resection of the brain regions containing HFOs correlates with good post-surgical seizure outcome [18,20–23]. Great strides have been made in detecting ictal and interictal HFOs on scalp EEG and HFOs recorded on scalp EEG could also be used to identify SOZ [24–27]. Recently, it was suggested that the applications of HFOs in scalp EEG could not only be used to localize SOZ assisting with epileptic surgery, but also be applied to assess disease activity and treatment response [28].

As our previous study found that HFOs could reflect the severity of epilepsy and were more sensitive to methylprednisolone treatment than spikes in ABPE [29]. Different from ABPE in which structural brain abnormalities were very infrequent, it was reported that 33–50% of CSWS patients were due to structural lesions [7,30]. The present study aimed to retrospectively investigate the characteristic of interictal HFOs occurring on scalp EEGs in CSWS patients with structural etiology and genetic/unknown etiology.

2. Material and methods

2.1. Patients

A total of 67 patients were diagnosed with CSWS in the Pediatric Department of Peking University First Hospital from January 2006 to December 2016. Twenty-one consecutive patients were included in the study. The inclusion criteria were as follows: (1) Diagnosis of CSWS: a. an age-related seizure disorder, b. neuropsychological regression in at least two dominants of development, and c. an age-related ESES pattern on EEG. (2) Three courses of methylprednisolone treatment: each course included methylprednisolone intravenous infusion at a dose of 15–20 mg/kg/d for 3 days, followed by oral administration at a dose of 1–2 mg/kg/d for 4 days. After three courses, prednisolone (1–2 mg/kg/d) was tapered off in 6 months. (3) at least 1 brain magnetic resonance imaging (MRI) study results available for review. (4) with at least 1 EEG recording in 6 months before and after methylprednisolone treatment, respectively. In our study, the ESES pattern was defined as a peculiar EEG pattern with continuous epileptic activity at 2–3 Hz occupying ≥85% of non-rapid eye movement (NREM) sleep. The predominant discharges might distribute in the anterior, posterior or rolandic regions [31].

This study was approved by the Ethical Committee of Peking University First Hospital, and written informed consents were obtained from the legal guardians (parents) of the subjects.

2.2. Classification of etiology

All patients had at least one brain MRI and a pediatric neuroradiologist (S.P.P) blinded to clinical diagnosis reviewed all MRI scans. For the purpose of this study, we separated all patients into structural group and genetic/unknown group according to MRI findings and history of pregnancy and delivery. The patients who had early developmental lesions on MRI with or without history of perinatal brain injury were assigned to structural group and those that had normal MRI findings and no history of abnormalities in pregnancy and delivery were included in genetic/unknown group. We considered any specific brain structural lesion, either malformative or destructive, that occurred prenatally or during the first 2 years of life as early developmental lesions.

2.3. EEG recording and event identification

EEG was recorded using the standard international 10–20 system, with a sampling frequency of 500 Hz (Neurofax; Nihon-Kohden, Tokyo, Japan). A low-cut filter at 0.016 Hz was used before digital sampling. A 4-h video-EEG monitoring was performed. All children were tested with intermittent photic stimulation, hyperventilation, and polyelectromyography (PEMG) recording the activity from deltoid and quadriceps femoris. The sleep status for 30–60 minutes was recorded in all subjects and all recordings in this study.

In each EEG record, continuous EEG segments with spindle waves and low electromyogram (EMG) power of above 5 minutes were visually reviewed in a referential montage and selected as stage Ⅱ NREM sleep data. As suggested by Kobayashi et al. [32], a brain-mapping expert initially reviewed sleep EEG using a bipolar montage including the derivations of Fp1-F7, Fp2-F8, F3-C3, F4-C4, T3-T5, T4-T6, P3-O1, and P4-O2 to determine clean data without apparent artifacts nor muscle activity, and then selected NREM sleep data with duration of 60 s including minimum artifacts in our study.

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