ELSEVIER

Brain & Development 35 (2013) 762–770

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Cortical contribution to scalp EEG gamma rhythms associated with epileptic spasms ☆

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Received 27 April 2012; received in revised form 16 December 2012; accepted 29 December 2012

Abstract

The cortical contribution for the generation of gamma rhythms detected from scalp ictal EEG was studied in unique cases of epileptic spasms and a review of the related literature was conducted. Ictal scalp gamma rhythms were investigated through time–frequency analysis in two cases with a combination of focal seizures and spasms and another case with spasms associated with cortical dysplasia. In the two patients with combined seizures, the scalp distribution of ictal gamma rhythms was related to that of focal seizure activity. In the third patient, an asymmetric distribution of the ictal scalp gamma rhythms was transiently revealed in correspondence to the dysplasic cortex during hormonal treatment. Therefore, the dominant region of scalp gamma rhythms may correspond to the epileptogenic cortical area. The current findings have reinforced the possibility of the cortical generation of ictal scalp gamma rhythms associated with spasms. The detection of high frequencies through scalp EEG is a technical challenge, however, and the clinical significance of scalp gamma rhythms may not be the same as that of invasively recorded high frequencies. Further studies on the pathophysiological mechanisms related to the generation of spasms involving high frequencies are necessary in the future, and the development of animal models of spasms will play an important role in this regard.

Keywords: Epileptic spasms; Gamma rhythms; High frequency oscillations; Ictal scalp EEG; Combined seizure; Cortex

1. Introduction

Epileptic spasms, or infantile spasms, are a cardinal seizure type in age-dependent epileptic encephalopathy (ADEE), including West syndrome (WS), Ohtahara syndrome, and early myoclonic encephalopathy (EME) [1,2]. Seizures that are reminiscent of epileptic spasms are also observed in Lennox–Gastaut syndrome (LGS) [3]. The generation of epileptic spasms is traditionally considered to involve the brain subcortical structures, especially the brainstem, as well as pathological interaction with the cortex [4]. However, some evidence indicates cortical contribution to the generation of epileptic spasms. For example, some patients with epileptic spasms have been cured by cortical resection [5,6].

The detection of cortical high-frequency oscillations (HFOs) associated with epileptic spasms also supports the hypothesis of the contribution of the cortex to the generation of spasms. It has been suggested that high frequencies are related to epileptogenicity and ictogenicity; it is of note that the resection of cortical lesions that gen-

☆ Part of this work has been presented at the International Symposium on Surgery for Catastrophic Epilepsy in Infants (ISCE), the Fourteenth Annual Meeting of ISS, Tokyo, February 18–19, 2012.

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http://dx.doi.org/10.1016/j.braindev.2012.12.012

erate HFOs resulted in the suppression of epileptic spasms [7–9]. HFOs include ripple (80–200 Hz) and fast ripple (250–500 Hz) oscillations, and they have a closer relation to epileptogenicity than gamma oscillations (<100 Hz).

Spasm-associated gamma rhythms in the EEGs recorded through the scalp may reflect a slower part of the ictal cortical high frequencies because a faster part of cortical high frequencies tends to be filtered out by the skull and scalp [10,11]. Herein, we report on three unique cases of epileptic spasms that exhibited ictal scalp gamma rhythms with an asymmetric distribution. These cases reinforce the possibility of cortical contribution to the generation of spasms. Two of these cases were spasms combined with focal seizures, a rare phenomenon that provides a cue regarding the relation between spasms and cortical abnormalities [12–14]. The third case of spasms was associated with cortical malformation; ictal gamma rhythms were exhibited with a transient asymmetric distribution during hormonal treatment. In addition, the literature related to scalp gamma and cortical HFOs associated with epileptic spasms is reviewed so as to understand their clinical meaning.

2. Patients and methods

2.1. Patient 1

This patient is a boy with no abnormal family history who was born normally after an uneventful pregnancy. Spasms in clusters appeared at about 2 months of age. One month later, brief partial seizures with right-side-dominant tonic posturing began to occur immediately preceding a series of spasms, and he was admitted to Okayama University Hospital.

The patient was developmentally retarded and had no head control or visual following. His tendon reflexes were bilaterally hyperactive, and right hemiparesis was noted. Myoclonus was not observed. His cranial MRI revealed atrophy of the left temporal lobe (Supplementary Fig. 1). Both waking and sleeping interictal EEGs revealed a left-hemisphere-dominant suppression-burst pattern, and we therefore diagnosed him with Ohtahara syndrome.

We performed synthetic ACTH-Z (tetracosactide Zn) treatment. At his follow-up visit at 7 years, 7 months of age, the patient had no unambiguous seizures. His development was slow; he had no spoken language and he needed assistance to stand. EEG revealed multifocal spike-waves over the left hemisphere in particular.

2.2. Patient 2

This patient is a boy who was born normally after an uneventful pregnancy. His brother had febrile seizures, but the family history was otherwise unremarkable. He began to suffer from spasms in series at 4 months of age, which resulted in his admission to Okayama University Hospital. At that time, he exhibited no signs of developmental retardation or neurological abnormality. MRI detected no organic brain lesion. Hypsarrhythmia was observed in interictal EEG, and he was diagnosed with WS.

At one point, the patient had a status of spasms in clusters mixed with frequent motion-arrest seizures with tonic posturing. This status persisted for approximately 30 min and was suppressed by an intravenous injection of secobarbital. These motion-arrest seizures did not recur thereafter. We performed ACTH-Z treatment, and at his follow-up visit at 7 years, 9 months of age, he was free from seizures. Although he had no spoken language, he could walk without assistance. Multifocal spike-waves remained in EEG.

2.3. Patient 3

This patient is a boy who was born without asphyxia. He began to smile and achieved head control at 3 months of age. The patient started to have a few clonic seizures per day that involved the extremities and had left-side dominance at 3 months of age. EEG revealed focal spikes over the right centrotemporal region. One month later, epileptic spasms commenced and his EEG abnormalities gradually evolved into hypsarrhythmia. When he was admitted to Okayama University Hospital, he had lost the ability to smile and his head control; paresis of the left upper extremity was also observed. MRI revealed widespread dysplasic lesions involving the right hemisphere, particularly in the frontal and parietal lobes (Supplementary Fig. 2).

ACTH-Z treatment was only transiently effective at suppressing seizures. After two months, they reappeared and a ketogenic diet was ineffective. A functional right hemispherectomy was performed at 12 months of age, and the patient became free from seizures and there was a dramatic improvement in EEG. His spasms recurred at 4 years of age. His development was slow; he had no spoken language and he required assistance to walk at the follow-up visit at 4 years, 6 months of age.

2.4. Ictal EEG and frequency analysis

The ictal EEG was recorded with a digital sampling frequency at 500 Hz with Nihon-Kohden Neurofax, which used a low-cut filter at 0.016 Hz before digital sampling. The international 10–20 electrode system was used, and video was simultaneously recorded.

The conventional traces of EEG were initially reviewed to identify the ictal events using a time constant of 0.1 s. The traces of ictal EEG were then temporally expanded with a time constant of 0.03 s (corresponding to a high-pass filter of 5.3 Hz) to study the gamma activity details.