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Original article

Asymmetrical generalized paroxysmal fast activities in children with intractable localization-related epilepsy

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Abstract

Background: Generalized paroxysmal fast activity (GPFA) consists of burst of generalized rhythmic discharges; 100–200 μV; 1–9 s; 8–26 Hz; with frontal predominance; appearing during NREM sleep. GPFA was originally described as an electrographic feature of Lennox–Gastaut Syndrome (LGS). We analyzed GPFA on scalp video EEG (VEEG) in children to evaluate that GPFA presents in patients with intractable localization-related epilepsy.

Methods: We collected cases with GPFA with intractable localization-related epilepsy who underwent scalp VEEG, MRI, and magnetoencephalography (MEG) prior to intracranial video EEG (IVEEG) and surgical resection. We collected 50 epochs of GPFA per patient during the first night during scalp VEEG. We analyzed amplitude, duration and frequency of GPFA over the bilateral frontal region between surgical resection side with grid placement and non-resection side.

Results: We identified 14 (14%) patients with GPFA on scalp VEEG. The mean amplitude ranged from 145 to 589 μV (mean 293 μV). The mean duration ranged from 1.18 to 2.31 s (mean 1.6 s). The mean frequencies ranged from 9.3 to 14.7 Hz (mean 11.1 Hz). The amplitude (307 ± 156 μV) and duration (1.62 ± 0.8 s) of GPFAs in all the patients over the resection side were significantly higher than those (279 ± 141 μV, 1.58 ± 0.8 s) of the non-resection side ($p < 0.001$). All nine patients who showed significant duration differences between two hemispheres ($p < 0.05$) had longer duration of GPFA over the resection side. Eight of 12 patients who showed significant amplitude differences between two hemispheres ($p < 0.05$) had higher amplitude of GPFA over the resection side. Four of six patients who showed significant frequency differences between two hemispheres ($p < 0.05$) had higher frequency of GPFA over the resection side. Nine (64%) patients became seizure free after surgical resection including multilobar resections in eight patients.

Conclusions: GPFA can exist in localization-related epilepsy with secondary bilateral synchrony. Although EEG shows GPFA on scalp VEEG, the precise localization of the epileptogenic zone using IVEEG could achieve the successful surgical resection.

Keywords: Generalized paroxysmal fast activity (GPFA); Localization-related epilepsy; Intracranial video EEG; Children; Cortico-thalamic epileptic network; Asymmetry; Amplitude; Duration; Epilepsy surgery; Epileptogenic hemisphere

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1. Introduction

Generalized paroxysmal fast activity (GPFA) is a pattern of; (1), 100–200 μV; (2), 1–9 s; (3), 8–26 Hz; (4), bursts of generalized rhythmic discharges with frontal predominance; (5), appearing most frequently during NREM sleep [1]. Jasper and Kershman, first recognized these runs of rapid spikes in sleep as "paroxysmal fast rhythm" [2]. Gastaut detected paroxysmal fast rhythm with tonic seizures in patients with Lennox–Gastaut syndrome (LGS) [3]. Brenner and Atkinson described EEG findings in patients with multiple type of seizures and mental retardation as "generalized paroxysmal fast activity" [4]. Other terms such as grand mal discharges, fast paroxysmal rhythms, rhythmic spikes, and runs of rapid spikes were also used to describe GPFA [1]. Since GPFA was associated with tonic seizures, clonic movements, and subtle jerks in LGS, it has been one of the criteria used in diagnosing LGS [5] as well as a late variant of LGS [6]. GPFA, however, also can be seen in patients with frontal and temporal lobe epilepsy [1]. The paroxysmal fast activities (PFA) of LGS are widespread in distribution and bilaterally synchronous over both hemispheres, with highest amplitude over the frontal and central head regions. Shifting asymmetries of PFA are common, but rarely the pattern may show persistent amplitude asymmetry, unilateral or even focal [7]. EEG and clinical differentiation between LGS and focal epilepsy with secondary bilateral synchrony (SBS) may be difficult or even impossible [8].

Halasz hypothesized that the mechanism of GPFA is the permanent or momentary breakdown of the GABAergic inhibitory process operating during the generation of spike-wave discharge [9]. The usual spike and wave complex is thought to consists of a balance of excitatory (spike components) and inhibitory (slow components) components [10]. Therefore, the lack of slow waves during GPFA suggests an absence of inhibitory processes. As well, Halasz et al., reported GPFA in three patients with non-malignant seizures to prove that GPFA can be a possible electrographic variant in certain generalized epilepsies showing atypical features [11]. These authors concluded that GPFA could be seen in patients with treatable epilepsy with a better seizure outcome than that seen in patients with LGS.

Sueda et al. differentiated the localized origin and propagation of PFA in patients with epileptic spasms, in contrast to bilaterally generated PFA in patients with LGS, using time–frequency analyses of magnetoencephalography (MEG) [12].

To our knowledge, there have been no reports on GPFA in patients undergoing epilepsy surgery, prior to their receiving the surgery. The characteristics of GPFA and its correlation with the epileptogenic zone as defined by intracranial video EEG (IVEEG) and seizure outcome remain unclear. We analyzed GPFA on scalp recordings performed in pediatric patients with intractable localization-related epilepsies, who subsequently underwent IVEEG for epilepsy surgery. We hypothesized that asymmetry of GPFA would be present in patients with intractable localization-related epilepsy secondary to the resectable epileptogenic zone, and further that there are characteristic features of GPFA in the intractable localization-related epilepsy.

2. Patients and methods

We selected patients with GPFA among the patients who underwent intracranial video EEG between 2004 and 2012 at the Hospital for Sick Children. All patients were admitted to the epilepsy monitoring unit (EMU) for scalp video EEG (VEEG) between 1 and 5 days. In addition, MRI, neuropsychological assessment and magnetoencephalography (MEG) were performed. Thereafter, because the data were concordant for localization of an epileptogenic zone, the patients underwent intracranial video EEG (IVEEG) to delineate the epileptogenic zone pursuant to resective surgery. Parents or guardians gave informed consent for all procedures. This study received prior approval from the Research Ethics Board at The Hospital for Sick Children.

We recorded scalp video-EEG (HARMONIE 5.4, Stellate, Montreal, PQ, Canada) using 19 or 25 scalp electrodes placed according to the International 10–20 system (subtemporal electrodes; F9, F10, T9, T10, P9 and P10 or midline electrodes; F1, F2, C1, C2, P1 and P2). A single reference was placed at Oz, Pz' (located 1 cm behind Pz), or FCz, whichever was the most inactive electrode. Sampling rate was 200 or 500 Hz.

We selected the first 50 GPFAs for each patient during NREM sleep, at the first and/or second night of admission. We followed three criteria to select GPFAs (1) amplitude of 100–200 μV; (2) duration of 1–9 s; (3) frequency of 8–26 Hz, for bursts of generalized rhythmic discharges with frontal predominance [1]. We applied a band pass filter of 5–70 Hz without notch filter for the selection and analysis of GPFA. We used a program "Signal statistics" (HARMONIE 5.4, Stellate, Montreal, PQ, Canada) to analyze the amplitude, duration and frequency. We analyzed the amplitude of GPFAs using each of electrodes on referential montage EEG (ex, Fp1-Ref, Fp2-Ref, F3-Ref, F4-Ref). Single Oz electrode was used for the reference. If a patient has the lesions and/or epileptic zone around the occipital lobe, Pz electrode is used for the reference. During the period of GPFA, we measured the amplitude difference between minimum and maximum amplitudes of each GPFA. We compared the amplitude for paired electrodes, Fp1-Ref v.s. Fp2-Ref or F3-Ref v.s. F4-Ref. First, we found the electrode with the maximum amplitude among four electrodes. Second, we compared the paired electrodes, one of which had maximum