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Transitory Effect of Spike and Spike-and-Wave Discharges on EEG Power in Children

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Abstract

Background—Spikes and spike-and-wave discharges on the EEG of children are a strong biomarker of epilepsy. There is increasing evidence that these EEG abnormalities also impair brain function and result in transitory cognitive impairment. Studies in animal models have shown that EEG spikes alters single cell firing and that such impairment in firing may extend beyond the duration of the spike-and-wave discharge. Whether interictal epileptiform discharges have lasting effects on EEG activity in humans is not known.

Methods and Results—The EEGs of 60 consecutive children with focal or interictal spike-and-wave discharges were evaluated using power spectral analysis to determine if there were any changes in power spectra from before to after the interictal abnormalities. Neither focal spike-and-wave nor generalized spike-and-wave discharges had any effect on the EEG frequency or spectral power following the discharge.

Conclusion—While interictal EEG discharges temporarily alter neural activity during the duration of the spike-and-wave discharge, there is no evidence that alterations of spectral power continue beyond the duration of the interictal discharge. The effects of interictal activity on EEG rhythms therefore appear to be quite transient and confined to the duration of the interictal discharge.

Keywords

spectral analysis; interictal spikes; spike-and-wave; oscillations; EEG

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Introduction

Shortly after the discovery of the EEG by Hans Burger [1,2], interictal spikes (IS) were identified as a marker of epileptic tissue [3]. IS are morphologically defined, episodic, transient EEG discharges that occur as a result of synchronous, paroxysmal depolarization of neurons resulting in a series of action potentials (APs) [4–7]. The localization of focal IS correspond closely to the site of the seizures focus [8,9] and IS remain one of the most important diagnostic features on the EEG [10].

In addition to being a biological marker for epilepsy, there is evidence that IS may have other effects, including causing transitory cognitive impairment (reviewed in [11,12]), endocrine dysfunction [13,14], suppression of seizures [7,15–18] and participation in epileptogenesis [19].

Recent work in rodents has shown that hippocampal spikes that occurred during memory retrieval strongly impaired performance [20]. The effect of IS in animals has been shown to exceed the duration of the actual spike-and-wave. Lebovitz [21], using a penicillin-induced epileptogenic foci in the cat hippocampus demonstrated a suppression of hippocampal single units in the vicinity of the focus for periods up to 10 seconds, far longer than the duration of the IS. Zhou and colleagues [22] showed that in rodents IS were associated with significant decreases in hippocampal action potentials for periods up to two seconds following the IS; when occurring in flurries, IS were associated with an even longer periods of decreased firing. These findings raise the question of IS in humans have a transitory effect confined to the duration of the spike-and-wave or have more sustained periods of disruption.

We undertook this study to determine if focal IS or generalized spike-wave activity has any effect on brain oscillation following the interictal discharge. Here we report that neither focal IS nor generalized spike-and-wave discharges had any discernible effect on EEG rhythms following the end of the discharge.

Methods

The study population consisted of 60 consecutive children (2–18 years of age) referred to the outpatient Clinical Neurophysiology Laboratory at Dartmouth-Hitchcock Medical Center for known epilepsy or suspected seizures with either focal spikes ($n = 30$; mean age 9.5 ± 0.26 years, 18 boys; 12 girls) or generalized spike-and-wave discharges ($n = 30$; mean age 9.7 ± 0.62 years; 15 boys, 15 girls). EEGs were recorded during the fully awake, drowsy and sleep states using the 10–20 System of Electrode placement. A focal spike was defined as a transient, clearly distinguishable from background activity, with a pointed peak and a duration of 20 to <70 ms that had a localized field. Spike-and-wave discharges consisted of generalized bursts of spike-and-wave or polyspike-and-waves occurring in complexes of two or more waveforms.

Two 5 second epochs of waking artifact-free EEG both immediately before and after a focal or generalized spike-and-wave discharge were evaluated (Fig. 1). Attempts were made to assess focal or generalized spike-and-wave discharges when the child was awake, alert and calm and with the eyes closed although in some children may have been drowsy. However,

drowsiness was not considered an issue since EEG was compared immediately before and after the interictal epileptiform discharge, making it unlikely that state change occurred during the period of time when the EEG was analyzed. Records were not used in cases where focal spikes or generalized spike-wave discharges were so frequent that we could not find periods of 5 seconds before and after the discharge. In addition, for each recording we arbitrarily inserted “pseudospikes” or “pseudo-spike-and-wave discharges” into the recording and measured power spectrum for 5 seconds before and after the pseudodischarges. The pseudodischarges were randomly inserted into EEG epochs temporally close to the interictal focal spike or generalized spike-and-wave and during times when the child was alert, the eyes closed and the record free of artifact.

Power spectral analysis (PSA) was conducted using Twin® EEG software (Grass Telefactor) using an average reference montage. Frequencies from 0–25 Hz were analyzed using a Fast Fourier Transform (FTT) with Hamming windowing, a sampling rate of 200 Hz, and epoch size of 256 Hz with a frequency resolution 0.781 Hz. For focal IS the channel with maximum amplitude on a reference montage was analyzed. For spike-and-wave discharges all channels (referred to as the total PSA) were obtained. Mean, median, edge and peak frequency, percentage of total power in the delta (0–4 Hz), theta (4–7 Hz), alpha (8–12) and beta (13–25) bandwidths and total, delta, theta, alpha and beta power were calculated.

Statistical analysis

All data was assessed to determine if the data came from a Gaussian distribution using the D’Agostino and Pearson omnibus normality test. Mean, peak and median frequencies, relative percentage of power accounted for by delta, theta, alpha and beta frequencies and total power were compared before and after the focal IS or generalized spike-and-wave discharge. Correlations coefficients using the Pearson *r* were performed between generalized spike-and-wave discharge duration and spectral measures before and after the spike-and-wave discharge. Data is presented in means $\pm$ SE and a *p* value of <0.05 was considered statistically significant.

Results

There were no differences between i) edge, mean, median and peak frequency; ii) percentage of total power in the delta (0–4 Hz), theta (4–7 Hz), alpha (8–12) and beta (13–25) bandwidths; and iii) total, delta, theta, alpha and beta power before and after the focal spikes or generalized spike-and-wave discharge (Figs. 1 and 2). Likewise no differences in any of the measures were seen from before and after the pseudospikes and pseudo-spike-and-wave discharge. There was no correlation between length of the spike-and-wave discharge (mean = 1.55 ± 0.12 sec, range 1–3 sec) and any of the spectral measures before and after the generalized spike-and-wave discharge (Pearson *r* : edge = -0.06115 ; mean = -0.1186 ; peak = 0.2121 ; median = 0.1877 , in delta = 0.08224 ; in theta = -0.2306 ; in alpha = -0.1511 ; in beta = 0.2133 , $p > 0.05$ in all). Likewise, there was no relationship between age of patient and EEG changes after the spike-and-wave discharge (Pearson *r* : edge = -0.07844 ; mean = 0.1329 ; peak = 0.1131 ; median = 0.01168 , in delta = 0.1618 ;

in theta = -0.09572 ; in alpha = -0.0434 ; in beta = 0.2453 , $p > 0.05$ in all). There was no relationship between location of focal spikes and any of the EEG measures (data not shown).

In a post-hoc analysis we examined changes in frequency and spectral power for 1 second epochs before and after focal spikes and generalized spike-and-wave and pseudospikes and pseudo-spike-and-wave discharges. No differences were seen (data not shown). We also attempted to find records where there were flurries of spikes with adequate EEG 5 seconds before and after the flurry of spikes (arbitrarily defined as 3 or more spikes in 5 or fewer seconds). Most records did not have adequate artifact and interictal spike-free periods that permitted such an analysis and we feel our sample size was not adequate to make any definitive conclusions.

Discussion

In addition to seizures, there is increasing evidence that IS can result in cognitive impairment. Several clinical studies have demonstrated that IS can result in transitory cognitive impairment [23–29]. Patients with temporal lobe epilepsy and IS have also been shown to have declines in working memory during periods of IS [30,31]. Generalized spike-and-wave discharges also are known to alter function during the discharge, particularly those lasting longer than 3 secs [32,33].

In lieu of animal data showing that interictal discharges had effects on neural firing that persisted beyond the duration of the IS, we asked the simple question of whether focal spikes and generalized spike-and-wave discharges had effects on the EEG that occurred beyond the end of the discharge. We found no evidence that IS altered frequency or power of EEG following the end of the discharge. The effects of interictal discharges therefore appear to be transient and limited to the duration of the IS or generalized spike-and-wave discharge.

While we found no long-lasting effects of focal spikes and generalized spike-and-wave discharges on EEG oscillatory activity, our findings should be interpreted cautiously. We assessed changes in far-field potentials using surface EEG electrodes. Spectral power of the EEG measures voltage fluctuations resulting from ionic current flows within neurons over time separated into frequencies and measured as power (energy) per hertz. Animal data demonstrates that focal interictal spikes alter single cell firing (action potentials), which cannot be measured using surface EEG recordings. Studies using intracranial electrodes with both macro- and microelectrodes will be needed to address this question fully.

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Fig. 1.

Example of focal interictal spike-and-wave and generalized spike-and-wave discharge. Spectral analysis was performed for 5 sec before and after the epileptiform discharges. The vertical black lines show the beginning and end of the discharge.

Fig. 2.

Comparison of spectral analysis before and after focal spikes. A. Mean edge, peak, mean and median frequencies; B. Percentage of total power in the delta, theta, alpha and beta bandwidths; C. Total power and power in the delta, theta, alpha and beta bandwidths. No significant differences were noted before and after the focal spikes.

Fig. 3. Comparison of spectral analysis before and after generalized spike-and-wave discharge. A. Mean edge, peak, mean and median frequencies; B. Percentage of total power in the delta, theta, alpha and beta bandwidths; C. Total power and power in the delta, theta, alpha and beta bandwidths. No significant differences were noted before and after the spike-and-wave discharge.