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Significance of interictal occipital epileptiform discharges in children

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ABSTRACT – *Objective*. Interictal occipital epileptiform abnormalities have not been well characterized. The objective of this pilot study was to assess their significance in children. *Methods*. A search was performed on the EEG database for the keywords "occipital", "spike", "sharp wave" and "epileptiform". Patients were divided into two groups based on the absence of all (group 1) or presence of any (group 2) of the following criteria: mental retardation, cerebral palsy, neurological deficits, abnormal MRI and/or intractable epilepsy. Special attention was given to the spike/sharp wave amplitude/duration and background slowing. *Results*. A total of 44 children (eight months to 15 years) were studied. Groups 1 and 2 were each composed of 22 children. Background slowing was more frequent in group 2 (10/22, 45%) compared to group 1 (1/22, 4.5%; p = 0.002). In group 2, 8/22 (36%) had spikes or sharp waves with amplitudes below 50 μV or above 150 μV with a positive predictive value of 89%, and a negative predictive value of 39%. Only 1/22 (4.5%) in group 1 had epileptiform activity outside of the 50-150 μV range. *Conclusions*. The presence of very high or low-amplitude occipital epileptiform abnormalities or background slowing may be indicative of encephalopathy.

Key words: occipital spikes, sharp waves, children, interictal, epileptic encephalopathy, focal idiopathic epilepsy

Occipital spikes can be seen in a variety of entities, including benign childhood epilepsy with occipital paroxysms (CEOP), Angelman's syndrome, mitochondrial diseases, Wolf-Hirschhorn's syndrome, Sturge-Weber syndrome, epilepsy with bilateral occipital calcification, neuronal ceroid lipofuscinosis and others (Westmoreland, 1998). Occipital epileptiform activity can also occur in children with other non-epileptic neurological problems (De Romanis *et al.*, 1988; Silvestri *et al.*, 2007).

Occipital spikes and sharp waves may be dissimilar to epileptiform activity in other locations. Frontal focal spikes have been found to correlate with mostly structural lesions (Van Ness, 1993; Williamson *et al.*, 1985), temporal spikes with complex partial seizures, and centro-temporal spikes

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with benign rolandic epilepsy (Beaumanoir *et al.*, 1974; Lerman, 1992). However, the significance of occipital spikes is less well defined.

Childhood epilepsy with occipital paroxysms (CEOP) is characterized by an EEG pattern of occipital spike and wave complexes that repeats rhythmically at 2-3 Hz per second and occurs with eye closure or intermittent photic stimulation (Gastaut, 1982). Although some investigators have studied ictal occipital lobe EEG discharges (Ludwig and Marsan, 1975), there is a lack of data regarding the significance of interictal morphology of occipital epileptiform discharges and associated outcomes.

The purpose of this pilot study was to assess the significance and clinical correlation of non-ictal EEG in children with occipital epileptiform discharges.

Methods

This study was approved by the institutional review board (IRB) of Drexel University College of Medicine. A search was performed on our Neurophysiology Laboratory EEG database from 2001-2006 for the keywords "occipital", "spike", "sharp wave" and "epileptiform". Epileptiform was defined as a sharply contoured activity lasting less than 200 msec with surface-negative polarity. Patients were selected on the basis of unequivocal evidence of epileptiform activity involving primarily the occipital regions. All cases with unilateral or bilateral epileptiform discharges with occipital maximal amplitude, with or without spread of paroxysmal activity to adjacent areas, were included. Cases with multifocal spikes, evidence of additional minor independent epileptiform foci over more anterior regions, secondary involvement of occipital areas or lack of clinical information were excluded. Forty-four cases fulfilling these criteria were included in the study.

Clinical features

All the clinical data including information on age of onset of symptoms, antiepileptic drugs (AEDs) if any, family history, perinatal history, physical examination, neurological and radiological information were gathered from each patient's medical record. Careful attention was given to the description of symptoms or seizures if present.

Patients were divided into two groups based on the absence of all *(group 1)* or presence of any *(group 2)* of the following criteria: mental retardation, cerebral palsy, neurological deficits, abnormal brain MRI and/or intractable epilepsy. Intractable epilepsy was defined as the persistence of more than one epileptic seizure per month following two different ineffective antiepileptic treatments with appropriate dosing and compliance. This division aimed to separate patients with benign conditions *(group 1)* from patients with encephalopathy and other neurological disorders with worse outcome *(group 2)*.

EEG evaluation

EEGs were digitally recorded with routine (20-30 minutes), ambulatory (24-72 hours, with Digitrace equipment), or inpatient video EEG monitoring. Twenty-one electrodes were placed in accordance with the international 10-20 system of electrode placement. Recording was performed under varying conditions, including wakefulness, drowsiness, sleep, hyperventilation, photic stimulation and eyes open or closed.

The EEG parameters were evaluated independently by three epileptologists who were unaware of the clinical information. The parameters included spike/sharp wave amplitude, duration, frequency of spikes/sharp waves, activation (by photic stimulation, hyperventilation, sleep or eye closure/opening), spread to other regions, unilateral or bilateral location, background activity and presence of background slowing. Each parameter was defined according to Ebersole and Pedley (2003). All the amplitudes were measured using an average referential montage. Special attention was given to the amplitude and duration of the epileptiform discharges and the presence of background slowing.

Statistics

The Chi square testing was used to evaluate the difference in frequency distribution of the different parameters between the two groups. A two-tailed independent sample t-test was used to compare the amplitude and duration means between the groups. The groups were then divided between those whose spike/sharp wave amplitudes fell within the mean ± standard deviation (100 ± 50 μV) of both groups or outside of this range (< 50 and > 100 μV). A value of $p < 0.05$ was considered significant. Odds ratio (OR) and confidence intervals (CI) were given where appropriate. Reliability between scorers was evaluated using the Cronbach alpha reliability score. Reliability between scorers was 0.71 for duration and 0.9 for amplitude of spikes/sharp waves (Cronbach alpha). The average of the three measures was used. All analyses were performed using SPSS statistical software.

Results

A total of 44 children, aged 8 months to 15 years, were included in the study. Each group consisted of 22 children; *group 1* (6.9 ± 4.4 years old) and *group 2* (6 ± 4 years old) *(table 1)*. The male to female ratio in *group 1* and *2* was 12:10 and 11:11, respectively.

Table 1. Patient's characteristics.

Variable	Group 1		Group 2	
Number	22		22	
Female/Male	10:12		11:11	
Age (years ± SD)	6.9 ± 4.4		6 ± 4	
Onset (years)				
< 1	4		7	
1-4	9		9	
5-10	6		4	
≥ 11	3		2	
Positive family history	4		3	
Negative family history	18		19	
Etiology	Gastaut type	6	Hydrocephalus	3
	PS	10	HSV encephalitis	2
	ADHD	2	CVA	1
	Migraine	2	Encephalopathy of unknown etiology	6
	Non-epileptic events	2	Mitochondrial disease	1
			Sturge-Weber syndrome	1
			Angelman's syndrome	2
			TBI	1
			Doose S.	1
			Wolf-Hirschhorn syndrome	1
			Retinoblastoma	1
			Medulloblastoma	1
			Greig's cephalopolysyndactyly syndrome	1
MRI				
Normal	14			4
Abnormal	0			10
N/A	8			8
DD/MR	0			13
Cerebral palsy	0			8
Neurological Exam				
Normal	22			1
Abnormal	0			21

N/A: not performed; PS: Panayiotopoulos syndrome; ADHD: attention deficit and hyperactive disorder; HSV: Herpes simplex virus; CVA: cerebro-vascular accident; TBI: traumatic brain injury; DD: developmental delay; MR: mental retardation, S: syndrome.

Demographics

Family history, physical examination and neurological findings are listed in *table 1*. One patient in *group 2* had developmental regression since the age of nine years. Onset of symptoms was between two to ten years for the majority of children in both groups *(table 1)*.

In *group 1*, ten patients had Panayiotopoulos Syndrome (PS), six Gastaut-type childhood occipital epilepsy (GT), two ADHD and two had migraines. The other two patients in *group 1* had head rocking and staring spells with normal EEG during the clinical events.

In *group 2*, clinical entities included hydrocephalus, Greig's cephalopolysyndactyly syndrome, post-herpes simplex (HSV) encephalitis, stroke, chronic static encephalopathy, mitochondrial disease, Sturge-Weber Syndrome, Angelman's syndrome, traumatic brain injury, Doose's Syndrome, Wolf-Hirschhorn syndrome, retinoblastoma and medulloblastoma *(table 1)*.

Seizure remission, greater than one year in patients with epilepsy, was found in four patients in *group 1* and three patients in *group 2* (one patient had Sturge-Weber syndrome, one patient encephalopathy and the other patient medulloblastoma status post-ventriculoperitoneal shunt). The presence of seizures within the last year in some patients of *group 1* was not indicative of a bad outcome or poor seizure control since many of them had been diagnosed for less than a year. Current antiepileptic medications are shown in *table 2*.

Table 2. Antiepileptic drugs.

	Group 1	Group 2
Carbamazepine	6	5
Phenobarbital	0	4
Lamotrigine	0	4
Valproic acid	2	2
Topiramate	2	3
Levetiracetam	1	1
Zonisamide	0	3
Oxcarbazepine	0	3

EEG Pattern

EEG data are presented in *table 3*. The mean amplitude of spikes/sharp waves in *group 1* was 96 ± 35 μV compared to 101.8 ± 74 μV in *group 2* (p = 0.6, t-test). However, in *group 2*, 8/22 (36%) had spikes or sharp waves with amplitudes below 50 μV or above 150 μV, with an OR of 2.1, CI: 1.1-3.7, a positive predictive value of 89%, and a negative predictive value of 39% (p = 0.037, Chi Square). Only 1/22 (4.5%) in *group 1* had spikes/sharp waves outside of the 50-150 μV range. When broken down by age groups (six months to three years, three to eight years and older than eight years) only the middle group showed statistical significance (p = 0.047). There was not enough data to reach significance for the other two age groups. Not surprisingly, significant background slowing was found in *group 2* (10/22, 45%) compared to *group 1* (1/22, 4.5%), p = 0.004. There were no significant differences regarding the localisation of discharges, or in response to eyes opening or closing, between the groups. Spread of discharge mainly involved the rolandic, mid-temporal, or centro-temporal areas. There was no correlation between the presence of spread of discharge and clinical manifestation. The morphology of occipital epileptiform discharges were spikes, sharp waves or polyspikes. In *group 1*, 5/22 patients had polyspikes in comparison to 3/22 patients in *group 2*, which was not statistically significant (p = 0.6, chi square). The mean duration of spikes/sharp waves was similar in both groups (77.4 ± 22 msec in *group 1*, 76 ± 30 msec in *group 2*, p = 0.88, t-test). The majority of patients in both groups had spike/sharp wave duration between 70-100 ms (sharp waves). Multiple EEGs were obtained in 18/44 (41%) of our patients. Evolution pattern in patients with multiple EEGs is noted in *table 3*.

Table 3. EEG Data.

		Group 1 (n = 22)	Group 2 (n = 22)
Side	U/L	10	11
	B/L independent	6	6
	B/L synchronous	6	5
Morphology	Spike	16	14
	sharp waves	13	14
	Polyspikes	5	3
Duration	< 70 ms	8	7
	70-100 ms	13	13
	> 100 ms	1	2
Amplitude	Mean ± SDEV (μV)	96 ± 35	101.8 ± 74
	< 50 uV	0	4
	50-150 uV	21	14
	> 150 uV	1	4
Spread		17	17
Activation	Photoparoxysmal	2	1
	Hyperventilation	1	1
	Sleep	4	7
	Attenuation to eye opening	2	1
Background slowing		1	10
Spike frequency	Frequent > 10/ record and in trains (> 3/3 sec)	16	19
	< 10/record and not in trains	7	3
Ictal recording		2	2
Evolution pattern	MF → O	2	4
in patients with	Normal → O	2	1
multiple EEGs	O → C or T	2	0
	O → nl	3	0
	O → MF	0	1
	O / → hyps/LGS	0	1

U/L: unilateral; B/L: bilateral; MF: multifocal; O: occipital; C: central; T: temporal; hyps: hypsarrhythmia; LGS: Lennox-Gastaut syndrome, nl: normal; SDEV: standard deviation.

Discussion

In this pilot study, we present the characteristics of interictal occipital epileptiform discharges in a group of children with and without epilepsy. Occipital spikes and sharp waves can be associated with various clinical entities with a wide spectrum of significance from benign to less benign. EEG in these cases can provide additional information for diagnosis and possible prognosis. Occipital epileptiform activity has mainly been described in idiopathic CEOP (Chahine and Mikati, 2006; Engel, 2001). Two sub-types have been recognized, the early onset with autonomic symptoms and ictal vomiting, Panayiotopoulos syndrome (Koutroumanidis, 2007; Lada *et al.*, 2003; Martinovic, 2001; Parisi *et al.*, 2007; Tedrus and Fonseca, 2006) and the later onset Gastaut type (GT) (Gastaut, 1982; Loiseau, 1993).

Occipital spikes can also be seen in a wide variety of disorders and physiological conditions including ADHD (Hughes *et al.*, 2000), symptomatic occipital lobe epilepsy (Ajmone-Marsan and Ralston, 1957; Blume, 1991),

blindness (Westmoreland, 1998; Kellaway, 1980), Sturge-Weber syndrome (Westmoreland, 1998), Angelman's syndrome (Dan and Boyd, 2003; Laan and Vein, 2005), Wolf-Hirshhorn syndrome (Kacinski *et al.*, 2005; Kagitani-Shimono *et al.*, 2005), migraine (De Romanis *et al.*, 1988), neuronal ceroid lipofuscinosis (Caraballo *et al.*, 2005), and myoclonus epilepsy with ragged red fibres (MERRF) (So *et al.*, 1989).

Seven out of 44 patients in our study did not have epilepsy. We found that the frequency, location and spread of spikes did not determine clinical manifestations, severity or frequency of seizures. In our study, high (> 150 mV) or low (< 50 mV) amplitude epileptiform discharges were observed in 8/22 patients in *group 2* and only 1/22 patients in *group 1*. Very high amplitude epileptiform discharges have been seen in epileptic encephalopathies and symptomatic epilepsies such as infantile spasms (West syndrome) and Angelman's syndrome. A recent study showed that very high or low amplitude spikes occurred during infantile spasms (Curatolo *et al.*, 2001; Vigevano *et al.*, 2001). A study by Watanabe *et al.* (2007) described six patients with localisation related epilepsy who had clusters of epileptic spasms preceded by focal seizures. Their patients had high amplitude occipital spikes during REM sleep, but the amplitude was not reported. The neurophysiological and anatomical basis for high or low amplitude occipital spikes and sharp waves, and the biological relationship with outcome or symptomatic epilepsies remains elusive, but in our experience it may indicate the presence of encephalopathy.

The presence of background slowing is a non-specific finding that in the correct clinical setting may indicate diffuse encephalopathy. Children with benign localisation related epilepsies usually have a normal background (Lerman and Kivity, 1991). This study also emphasizes the importance of carefully analyzing the background activity.

Our study suggests that when occipital spikes are present on the EEG, it is important to evaluate their amplitude. Our findings support the concept that the presence of very high or low-amplitude occipital interictal epileptiform abnormalities or background slowing is indicative of encephalopathy or symptomatic epilepsy. The presence of occipital spikes with amplitudes between 50 and 150 microvolts and absence of background slowing suggest a maturational type of benign epilepsy or the presence of fortuitous spikes in patients with migraine or other non-epileptic conditions. Larger prospective studies classifying patients by age and in more homogeneous groups are needed to confirm these findings and support this clinical significance on a long-term basis. □

Disclosure.

This study was approved by the institutional review board (IRB) of Drexel University College of Medicine. None of the authors has any conflict of interest to disclose.

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