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ORIGINAL ARTICLE

Analysis of serial electroencephalographic predictors of seizure recurrence in Rolandic epilepsy

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Abstract

Purpose We aimed to assess the relationship between electroencephalography (EEG) markers and seizure recurrence in cases with benign epilepsy with centrotemporal spikes (BECT) in a long-term follow-up study.

Methods We analyzed the data of 52 children with BECT who were divided into 2 groups: the isolated group and recurrence group. The clinical profiles and initial/serial visual EEG recordings of both groups were evaluated. The entire follow-up period ranged from 12 to 65 months.

Results None of the clinical characteristics differed between the 2 groups. Serial EEGs showed that the appearance of Rolandic spikes in the frontal region was more prevalent in the recurrence group. Moreover, a significant correlation was found between bilateral asynchronous discharges and seizure recurrence. However, on initial EEG of these patients, neither of the EEG features exhibited statistical significance.

Conclusion The presence of frontal focus and bilateral asynchrony appeared to be hallmarks of BECT patients with higher risk for seizure recurrence.

Keywords BECT · Rolandic epilepsy · EEG · Seizure

Abbreviations

EEG	electroencephalography
BECT	Benign epilepsy with centrotemporal spikes
MRI	Magnetic resonance imaging
AEDs	Antiepileptic drugs
LEV	Levetiracetam
OXC	Oxcarbazepine
VPA	Valproate
CZP	Clonazepam
OR	Odds ratio
CI	Confidence interval
NS	Not significant

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Introduction

Benign childhood epilepsy with centrotemporal spikes, also known as benign Rolandic epilepsy, accounts for approximately 13–25% of cases of epilepsy in school-aged children, and is one of the most common epileptic syndromes in childhood [20]. As the nomenclature indicates, this type of syndrome has good long-term prognosis not only in terms of epileptic seizures, but also with regard to neuropsychological development [2]. The frequency of epileptic seizure is usually low in such cases, with only 1 seizure (isolated seizure) noted in approximately 15% of cases and < 5 seizures noted in two-thirds of cases [2, 11]. However, an increasing amount of evidence has shown that some children with BECT have poor prognosis, intractable seizures, developmental and linguistic regression, and new forms of episodes (atypical absence), which might represent atypical BECT [5, 7, 14, 17]. Several studies have found a relationship between interictal EEG abnormalities and clinical manifestations such as epilepsy recurrence, behavioral disorders, and atypical BECT [1, 8, 9, 12]. In the present study, we aimed to verify the predictive value of EEG in the occurrence of seizures.

Methods

Participants

The data of 52 newly diagnosed children with BECT, from 2013 to 2017, were retrospectively reviewed. The study was conducted at the clinic of Wuxi Children's Hospital. The patients experienced their first seizures between the age of 3–10 years. None of the patients had a history of obstetric injury or asphyxia at birth. Their physical and mental development were normal. Neurological examination and brain magnetic resonance imaging (MRI) revealed no abnormalities. The entire follow-up period ranged from 12 to 65 months. During this period, some patients experienced different clinical courses from others. Thus, patients were divided into 2 groups according to seizure frequency. The recurrence group consisted of 40 children (who had epileptic seizures more than once) ranging in age from 3 to 10 years. All patients exhibited typical EEG abnormalities without atypical forms of seizure and cognitive decline. The isolated group (single seizure episode only) consisted of 12 children ranging in age from 4 to 10 years without seizure recurrence, who were followed for at least 21 months. This study was approved by the medical ethical boards of Wuxi Children's Hospital. All parents or guardians provided informed consent.

EEG assessment

Interictal EEG was performed in all children within 1 month of their first clinical seizures. Repeated EEG was performed at 6- or 12-month intervals. In all cases, EEG was recorded using a digital system with 19 electrodes in both the awake and sleep states without sedation for 2–3 h according to the international 10–20 system. The EEG analysis included background activity, the localization of spikes (unilateral or bilateral hemispheres), the localization of spikes other than the centrotemporal region, the migration of the epileptiform discharge (mainly from one hemisphere to the other), the presence of spikes in the awake state, and synchronicity of discharges in both hemispheres.

Statistical analysis

Statistical analysis was performed using SPSS 22 statistical software. Continuous variables are expressed as means ± standard deviation, whereas categorical variables are presented as frequencies and percentages. Chi-square test, Fisher's test, or Student's t test was used to compare the differences in variables among the 2 groups, as needed. In all analyses, $p < 0.05$ was considered to indicate statistical significance.

Results

A total of 52 patients with BECT were included in this study. None of the patients had atypical seizures, oromotor deficits, or obvious cognitive impairment. Among these patients, 12 (23.1%) experienced only 1 seizure, 25 (48.1%) experienced 2–5 seizures, and 15 (28.8%) experienced > 5 seizures. The study population consisted of 28 males and 24 females, with a male to female ratio of 1.17:1. The mean follow-up duration was 37.7 ± 14.0 months. There were no significant differences in age at onset, gender, diurnal episodes, mean follow-up duration, previous febrile seizure, and family history of epilepsy between the isolated and recurrence groups (Table 1). Antiepileptic drugs (AEDs) were administered to patients with ≥ 2 episodes. Eighteen patients were initially treated with levetiracetam (LEV), 16 with oxcarbazepine (OXC), and 3 with valproate (VPA). In 1 child, VPA was initiated due to OXC failure, and in 2 other children, clonazepam (CZP) was administered in addition to OXC. Seizures were found to be well controlled at the final follow-up in all cases.

The background activities were normal in all cases. Tables 2 and 3 separately list the initial and serial EEG characteristics of the 2 groups. The serial EEGs showed that Rolandic spikes were present in 39 cases (75%) during the awake state; during the initial EEG examination, this value

Table 1 Clinical profiles of the isolated and recurrence groups

	Isolated group	Recurrence group	p value
Male	6 (50%)	22 (55%)	NS
Age at onset (years)	6.9 ± 1.9	6.8 ± 2.0	NS
Diurnal episode	0 (0%)	7 (17.5%)	NS
Family history of epilepsy	0 (0%)	2 (5%)	NS
Previous febrile seizure	1 (8.3%)	4 (10%)	NS
Follow-up duration (months)	38.5 ± 15.5	37.4 ± 13.7	NS
Comorbidities	0 (0%)	0 (0%)	NS

NS not significant

Table 2 Initial EEG characteristics of the 2 groups

	Isolated group	Recurrence group	*P* value	Total
Spikes in the frontal region (initial EEG) (%)	2 (16.7%)	14 (33.3%)	NS	16 (30.1%)
Bilateral asynchronous discharges (initial EEG) (%)	3/7 (42.9%)	9/12 (75%)	NS	12/19 (63.2%)
Spikes in the awake recordings (initial EEG) (%)	6 (50%)	18 (45%)	NS	24 (46.2%)

was 24 (46.2%). There was no significant difference in the appearance of Rolandic spikes between the 2 groups during the awake state.

On serial examination, 15 children had right-sided, 10 children had left-sided, and 27 children had bilateral interictal Rolandic discharges. Discharge migration from one side to the other was noted in 13 (25%) children.

However, among the 27 cases with bilateral discharges, asynchrony was detected in 95% (19/20) of the cases in the recurrence group and 42.9% (3/7) of cases in the isolated group. Asynchronous bilateral Rolandic spikes (seen in Fig. 1) tended to be more prevalent in the recurrence group than in the isolated group ($p = 0.009$, odds ratio [OR]: 25.3, confidence interval [CI]: 2.065–310.757; Tables 3 and 4).

In addition, frontal discharge was noted in 24 (60%) cases and 2 (16.7%) case in the recurrence and isolated groups, respectively (Table 3). Although the difference in these values was significant ($p = 0.008$, OR: 7.5, CI: 1.448–38.846) (Table 4), no such difference was noted on initial EEG (Table 2).

An abnormal discharge was also noted in the frontal region that temporarily disappeared. In 4 patients, the frontal discharge disappeared after 1 year of treatment and reappeared in the next year of follow-up. During the follow-up, we observed that the EEGs of 7 children returned to the normal baseline condition. The recovery time of EEGs was 5 months and 25 months in 2 patients with an isolated episode. The other 5 cases had < 5 seizures, and the recovery time of EEGs after drug treatment ranged from 11 to 30 months (average, 17 months).

Discussion

Patients with BECT exhibit characteristic EEG changes, including a normal background with centrotemporal stereotyped spikes or sharp waves followed by slow waves, unilaterally or bilaterally, which can be synchronized or asynchronized on both sides. The epileptiform activities can migrate from side to side, and even extend to adjacent brain regions such as the frontal or occipital areas [3]. Sleep can activate many epileptiform activities, and hence, the onset of BECT is closely related to sleep. In the present study, only 7 of 52 (13.4%) children had diurnal episodes when they were conscious, and they all belonged to the recurrence group. However, initial and serial EEGs did not reveal any significant differences in the appearance of Rolandic spikes recorded during the awake state.

In contrast, Kanemura et al. [9] reported that spikes were more frequent during the awake state in the recurrent seizure group than in the isolated group. The researcher's other study [8] indicated that awake interictal abnormalities showed a trend towards a higher risk of developing atypical BECT. Arhan et al. [1] found that Rolandic spikes in awake EEGs tended to be more prevalent in patients with > 5 episodes than in those with < 5 seizures. The difference in grouping may have contributed to the discrepancy between our results and those of previous studies. We did not include children with atypical seizures, and the severity of the illness in children enrolled in the recurrence group might be inconsistent with previous studies. In contrast, the recording time of EEG differed in various studies. Due to a relatively long recording time (2–3 h in our population), the rate of Rolandic spike detection during the awake state on the initial EEG was 46.2%, although the frequency of spikes was apparently low as compared with that in the sleep state. Some studies [15, 16, 19] have already indicated the relationship between the frequency of spikes during wakefulness with cognitive function, and hence, we believe that the frequency of paroxysmal discharges in the awake state is more suitable for predicting seizure recurrence.

Table 3 Serial EEG characteristics of the 2 groups

	Isolated group	Recurrence group	*P* value	Total
Spikes in the frontal region (%)	2 (16.7%)	24 (60%)	0.008	26 (50%)
Spikes in the awake recordings (%)	9 (75%)	30 (75%)	NS	39 (75%)
Bilateral spike foci (%)	7 (58.3%)	20 (50%)	NS	27 (51.9%)
Laterality of the spike foci (R:L)	3:2	12:8	NS	15:10
Epileptic focus migration	2 (16.7%)	11 (27.5%)	NS	13(25%)
Bilateral asynchronous discharges (%)	3/7 (42.9%)	19/20 (95%)	0.009	22/27 (81.5%)

Epileptic focus migration refers to movement of the discharge from one hemisphere to the other

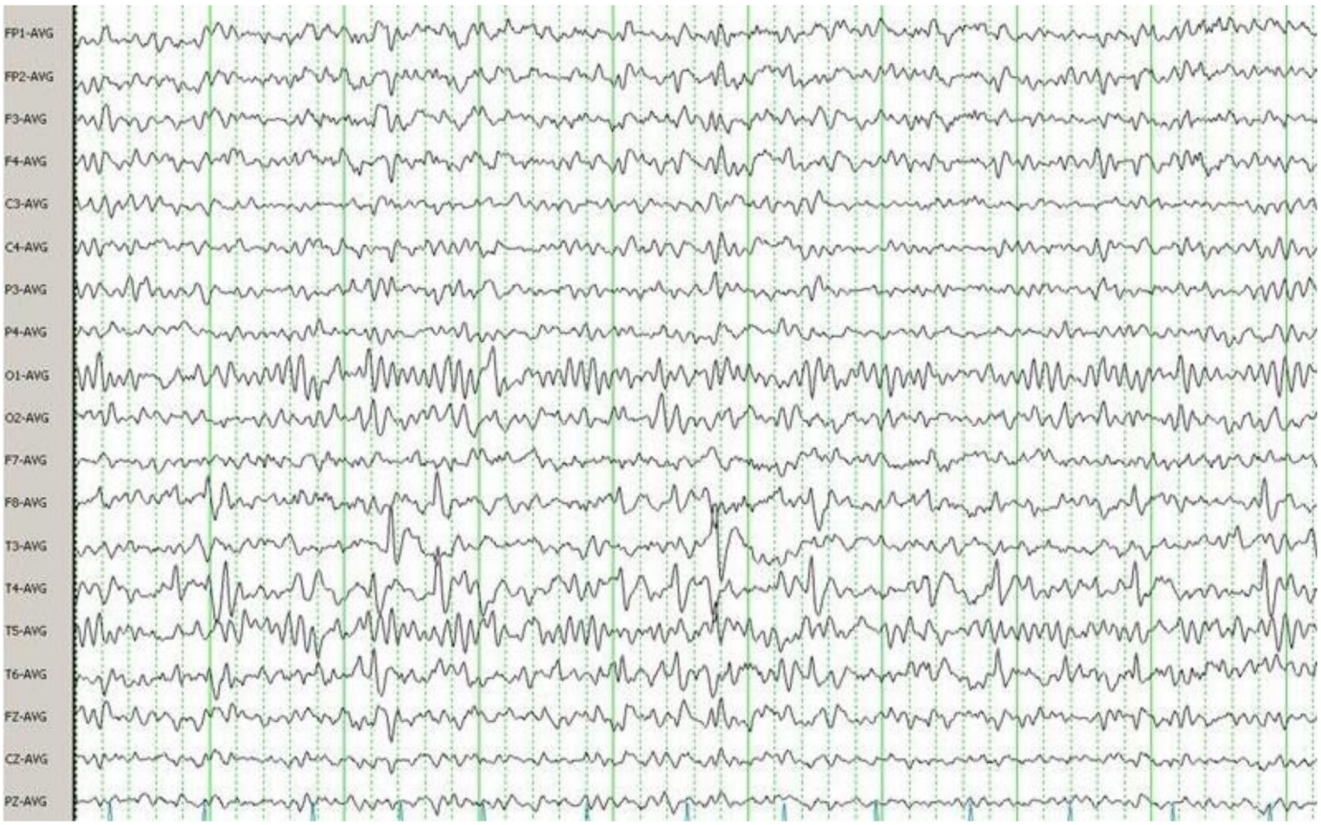

Fig. 1 Bilateral asynchronous Rolandic spikes

The propagation of epileptic activation triggered by an earlier centrotemporal discharge is most often observed in the frontal region [1]. In the present study, serial EEGs showed that the total presence of frontal paroxysmal abnormality (a propagation from a centrotemporal discharge) was 50% (26/52). The occurrence of frontal spikes was significantly higher in the recurrence group than in the isolated group, consistent with previous studies [1, 8, 9]. Moreover, an extended period (> 10 months) of frontal EEG focus was also suggested to indicate a higher risk of developing atypical BECT and cognitive/behavioral impairment [8], whereas the latter has not been verified in other research [1]. In the recurrence group in the present study, 14 children had extended periods of frontal EEG focus, whereas 4 experienced temporal frontal focus disappearance and recurrence after 1 year. None of these children exhibited cognitive and behavioral deficits or fluctuation. Transient cognitive impairment is known to accompany frequent interictal spike discharge [13], and hence, we believe that a high frequency of spikes is vital. Accordingly, an extended period of frontal EEG focus and high spike frequency may be related to poor cognitive function.

The lateralization of the predominant focus was stable in 25 patients. Interictal discharges involving the unilateral hemisphere showed a right prevalence in both groups. This right predominance was consistent with that noted in a previous study [12]. Moreover, lateralization shifted from one hemisphere to the other in 13 patients; this was more commonly noted in the recurrence group, but there was no significant difference between the 2 groups. Bilateral interictal epileptiform discharges were more frequent and were mainly asynchronous in the present study. The serial EEGs indicated that, in children with discharges on both sides, the asynchrony differed between the 2 groups.

Table 4 The appearance of Rolandic spikes in the frontal region and presence of bilateral asynchronous discharges on both sides in serial EEGs

	Spikes in the frontal region		Bilateral asynchronous discharges	
	+	–	+	–
Recurrence group	24	16	19	1
Isolated group	2	10	3	4
Odds ratio	7.5		25.3	
95%CI	1.448–38.846		2.065–310.757	

CI confidence interval

Bilateral asynchronous discharges were more prevalent in the recurrence group than in the isolated group. Previous studies [4, 12, 13] have shown that bilateral synchronous discharges are caused by epileptiform activity through the corpus callosum and do not result in cognitive impairment. However, bilateral asynchronized discharges—generated by an earlier focal epileptic activity or created by multifocal epileptic circuits—may affect cognition [6, 10]. Nevertheless, the asynchronous foci spontaneously regressed over time in our patients and did not cause cognitive dysfunction.

Based on the findings of serial EEGs, we concluded that the presence of frontal focus and bilateral asynchrony may be correlated with the recurrence of BECT. However, neither of these 2 EEG features differed on initial EEG recording between the 2 groups. Thus, we confirm that it is difficult to predict the occurrence of a second seizure on the basis of the initial EEG following the first clinical seizure, as reported in a previous study [18]. Our retrospective study also offers potential clues for identifying patients with a higher risk of recurrent seizures. However, as frontal focus and bilateral asynchrony may appear later or disappear temporally on serial EEGs, we might not be able to recognize the risk of seizure recurrence at an early stage. Therefore, in the future, more sophisticated EEG analyses, such as high-frequency oscillations (ripples), should be used to enable the prompt prediction of seizure recurrence in cases with BECT.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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