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Sequential EEG characteristics may predict seizure recurrence in rolandic epilepsy

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ABSTRACT

Purpose: The prognosis of rolandic epilepsy (RE) is considered favorable. Since a moderate proportion of cases presents with isolated seizures, continuous treatment should be considered only for frequent seizures. Clinical and electroencephalogram (EEG) markers to predict seizure recurrence need to be identified. The purpose of this study was to identify EEG criteria related to seizure recurrence in RE.
Methods: There were 10 children (aged 3–10 years; 6 males, 4 females) in the recurrence group and 12 (aged 4–7 years; 6 males, 6 females) in the isolated group. Occurrences of the number of spikes were scored, and the presence of rolandic discharges (RD) in the awake record was evaluated. All patients were evaluated longitudinally, clinically and by EEG, with repeated EEG recordings every 3 months. Clinical and EEG follow-up was performed for ≥4 years.
Results: Seizure recurrence and extended periods of high-frequency paroxysmal EEG abnormalities (>6 months after onset) were significantly correlated ($p < 0.001$). Moreover, the appearance of RD in awake recordings tended to be more prevalent in the recurrence group than in the isolated group (odds ratio 4.714).
Conclusion: In addition to RD in the awake record, a combination of spike rate and extended periods of high-frequency paroxysmal EEG abnormalities may predict seizure recurrence in RE.

1. Introduction

Rolandic epilepsy (RE) is the most common idiopathic, age-specific, epilepsy syndrome of childhood, with an estimated prevalence of 20–25% in school children with epilepsy.[1,2] RE is a sleep-related disorder, and attacks occur predominantly during sleep. Seizures during waking hours are more likely to occur shortly after awakening.[3] In general, RE is associated with a favorable prognosis. Seizure frequency is usually low, and around 10% of cases has only one seizure (isolated seizure).[2] Accordingly, continuous treatment should be considered only in patients with frequent seizures and when the ictal events are disruptive to the patient or family. However, prognostic factors for seizure recurrence remain unclear.[4]

Interictal epileptiform discharges on electroencephalogram (EEG) are regarded as correlated with persistent pathological neuronal discharges.[5] Early descriptions suggested that children with rolandic spikes might be at risk for minor behavioral disturbances or learning difficulties.[6] Atypical cases sometimes occur as a particular syndrome that shares features with other recognized entities or has an unexpected evolution. However, with regard to the frequency of paroxysmal EEG abnormalities and the correlation with cognitive deficits, the association of more frequent discharges or multifocal paroxysms with complicated evolution in RE is a debated subject.[1,7,8] In contrast, in our preliminary study, significant correlations were found between atypical clinical features and extended periods of high-frequency paroxysmal EEG abnormalities in these atypical cases.[9] In another study by Bakke et al., interictal EEG abnormalities were associated with behavioral problems.[10] Moreover, our recent research showed a significant correlation between spike frequency in the frontal region and behavioral problems.[11] Thus, there is continued debate about the importance of paroxysmal EEG abnormalities and their relationships with clinical manifestations such as seizure recurrence and behavioral problems.

Clinical and EEG markers to predict seizure recurrence need to be identified. The purpose of the present study was to determine the EEG criteria related to seizure recurrence in children with RE.

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2. Method

2.1. Participants

A total of 22 patients with normal neurological examinations and brain magnetic resonance imaging (MRI) was followed-up. All children had experienced their index seizure between April 1, 2001 and March 31, 2006. Patients were referred to us from the pediatric departments of University of Yamanashi Hospital and its satellite hospitals. All children were suspected as having RE at the first evaluation. However, the clinical course for some patients diverged from those of others. Some patients demonstrated no seizure recurrence during the follow-up period. Therefore, patients were divided into two groups according to their clinical presentation (Table 1). The recurrence group consisted of children who suffered from typical RE, and the isolated group consisted of children without seizure recurrence. All children in this study were enrolled within 1 week after the appearance of their first seizure. To be included in this study, children (onset of seizures ranging from 3 to 14 years of age) had to have normal neurologic and neuroradiologic examinations. The exclusion criteria were as follows: concomitant neurologic or psychiatric disorders, neurosurgical operation, neurologic medication other than anti-epileptic drugs (AEDs), combination therapy (two or more AEDs), and/or an IQ less than or equal to 70. Patients with Fragile X syndrome were also excluded.

2.1.1. The recurrence group

This group consisted of 10 children ranging in age from 3 to 10 years (mean age, 5.5 years; 6 males, 4 females). All patients demonstrated the typical EEG abnormalities of this condition with normal neurological examinations, and they fulfilled the following criteria of typical RE[2]: (1) nocturnal partial seizures associated with centrotemporal spikes on EEG; (2) onset of seizures ranging from 3 to 14 years of age; (3) normal routine laboratory examination and normal results on screening for metabolic diseases (blood gas, lactate, pyruvate, and amino acid analyses); (4) normal brain MRI; and (5) absence of other types of unprovoked seizures. All patients were treated with antiepileptic drugs such as carbamazepine (CBZ) after their third seizures (2–6 months after seizure onset). All participants began therapy with CBZ, and one participant was switched to sodium valproate (VPA) because of a CBZ-related skin rash. Accordingly, nine children were treated by CBZ (mean dose, 6.3 mg/kg/day; mean trough concentration, 4.2 μg/mL) and one was treated by VPA (dose, 11.4 mg/kg/day; trough concentration, 48.8 μg/mL). The start of therapy was not related to deterioration in the EEG.

Table 1
Clinical profiles of the isolated and RE groups.

	Recurrence group (n = 10)	Isolated group (n = 12)
Sex	M:F = 6:4	M:F = 6:6
Age at seizure onset	5 y 0 mo	4 y 10 mo
Family history of febrile seizure	3/10 (30%)	2/12 (16.7%)
Family history of epilepsy	2/10 (20%)	3/12 (25%)
Previous history of febrile seizure	0	0
Seizure type	PS:SG = 8:2	PS:SG = 10:2
Seizure lateralization	Rt:Lt:Bil = 4:4:2	Rt:Lt:Bil = 4:6:2
Seizure duration (>5 min)	0	0
Laterality of spike foci	Rt:Lt:Bil = 3:4:3	Rt:Lt:Bil = 4:5:3
Comorbidities	0	0

M, male; F, female; PS, partial sensorimotor; SG, secondary generalization; Rt, right; Lt, left; Bil, bilateral.

2.1.2. The isolated group

This group consisted of 12 children ranging in age from 4 to 7 years (mean age, 5.3 years; 6 males, 6 females). All patients fulfilled the above-mentioned criteria for RE. Accordingly, it was initially impossible to differentiate these patients from those in the recurrence group. None were given any treatment such as AEDs. All patients had no seizure recurrence.

2.2. Assessment of interictal EEG abnormalities

Assessment of interictal EEG abnormalities has been described in our previous report.[9] A brief outline of the assessment is provided. The EEGs were recorded without sedation for 20–40 min using a digital system with the international 10–20 array of electrode placement. All EEGs in this study were recorded during both awake and sleep states. Three minutes of hyperventilation and intermittent photic stimulation in wakefulness were performed during each EEG recording session in all patients. The EEG readers were blinded to the clinical details and groupings. Two child neurologists analyzed EEG recordings with the words "rolandic," "central," "centrotemporal," or "centro-temporal." The EEG reports chosen for analysis were solely those for which two child neurologists agreed that the EEG findings showed RE. In addition, the dominant region was defined by the localization of spikes in cases where spikes were more frequent and higher in amplitude. The occurrence of spikes in both the awake and sleep states was scored as follows: (1) the number of spikes with bipolar montage; (2) the localization of spikes, especially the term for frontal EEG focus; and (3) the duration of spike activity. The highest number of spikes from each state was used. The number of spikes was greater in sleep stages 1 and 2 than in the awake state. Accordingly, the rates of discharges were computed in sleep stages 1 and 2 and expressed as the number of discharges per minute. In addition, the presence of spikes in the awake state was also evaluated. These evaluations were made by visual inspection. The spikes were quantified by the same EEG readers. Moreover, EEG readers quantified the spikes in the same EEG recording at least twice, and confirmed the data as intra-rater and inter-rater reliabilities.

EEG recordings were started within 8–14 days after the patients' first seizures in all patients. Accordingly, EEG recordings were obtained in the recurrence group before CBZ treatment. All patients were evaluated longitudinally, clinically and by EEG. Repeated EEG recordings were obtained for all patients every 3 months. EEG follow-up was performed for at least 4 years for all patients, and all patients were re-evaluated at the end of follow-up. All EEG recordings from all patients in both groups were analyzed.

2.3. Seizure frequency and type

Clinical profiles such as seizure frequency and type were evaluated. All patients were reviewed, and the results were unanimously agreed by all authors. Clinical follow-up for at least 4 years was performed for all patients, and all patients were re-evaluated at the end of follow-up.

2.4. The neuropsychological evaluations

The Wechsler Intelligence Scale for Children version III (WISC-III) or the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) was evaluated by age in all patients at the onset of seizures and every year.

2.5. Statistical methods

Statistical analysis was done using SPSS, version 19 (IBM, New York, NY, USA). All data are presented as means of each measure.