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Serial changes in the paroxysmal discharges in rolandic epilepsy may predict seizure recurrence: A retrospective 3-year follow-up study

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ABSTRACT

Objective: The aim of this study was to assess the electrographic criteria related to seizure recurrence and determine age-related seizure recurrence in children with rolandic epilepsy under long-term follow-up. *Methods:* We retrospectively analyzed the data belonging to 109 patients with rolandic epilepsy with sufficient information regarding disease course and follow-up duration longer than 3 years. Patients were divided into two categories: Group A (n: 75), comprised of "patients having fewer than four seizures", and Group B (n: 34), the "recurrence group comprised of patients having more than four seizures in the first three months". The number of spikes per minute during both wakefulness and sleep, the localization of spikes other than centrotemporal region, and the duration of spike-wave activity were evaluated longitudinally, with repeated electroencephalogram (EEG) recordings every 6 months.

Results: The appearance of rolandic spikes in awake EEGs tended to be more prevalent in Group B than Group A. In Group B, spike rates significantly increased in the 12 and 18 months after onset whereas spike rates increased significantly only 6 months after onset in Group A. Seizure recurrence is mostly seen at 6–8 years, and improvement becomes evident by age 12. The mean number of paroxysmal rolandic discharges during sleep was significantly higher in the younger age groups (3–5, 6–8), and the mean number of spikes per minute significantly decreased at ages 9–11 and over 12.

Conclusion: Our study demonstrates that extended periods of high frequency of paroxysmal discharges, initial frontal EEG focus, and persistence of awake interictal abnormalities are highly effective in predicting seizure recurrence in patients with rolandic epilepsy (RE).

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1. Introduction

Rolandic epilepsy (RE) is the most frequent epilepsy syndrome in school-aged children, accounting for 20–25% of all childhood epilepsies [1,2]. Low seizure frequency with infrequent nocturnal seizures and good seizure control is the characteristic finding that has led to the no-menclature of "benign" rolandic epilepsy. About 10% of the cases have only one isolated seizure with an onset just before or after the child starts school [2]. Decision on starting continuous treatment with antiepileptic drugs (AEDs) is often difficult since AEDs have worrisome side effects on cognition and unclear factors about seizure recurrence in these children.

Although the name "benign rolandic epilepsy" and its early descriptions suggested a benign course, there is now substantial evidence for neuropsychological impairment and cognitive and academic problems in affected children. Numerous literature data have shown language defects, impaired reading performance and auditory discrimination, and memory impairment in rolandic epilepsy [3–11]. Several factors could

* Corresponding author. *E-mail address*: zeynep1220@yahoo.com (Z. Ozturk). account for the atypical evolution in these children. Literature studies on neuropsychological impairments in atypical rolandic epilepsy have shown that interictal epileptiform discharges on electroencephalogram (EEG) may be responsible for disrupting brain function and leading to atypical evolutions [9,12–15]. Most children have only rare seizures and, when treated, their sei-

Most children have only rare seizures and, when treated, their seizures respond well to AEDs. However, in a poorly identified subset of children with rolandic epilepsy, more than one AED is required for effective control of recurrent seizures without any atypical evolution. Extensive information on EEG criteria for seizure recurrence in these patients is still lacking, and there is still a need for clinical and EEG markers that predict seizure recurrence in rolandic epilepsy. Thus, there is a continuing debate about the effect of EEG spike–wave activity in children with seizure recurrence without any atypical evolution. There is only one recent study regarding the frequency of paroxysmal EEG discharges and its correlation with seizure recurrence in rolandic epilepsy. Kanemura et al. showed a significant correlation between seizure recurrence and extended periods of paroxysmal EEG abnormalities in their study [16].

This is the first study to assess the EEG criteria related to seizure recurrence in a large group of children with rolandic epilepsy without atypical evolution under long-term follow-up. This study also





represents the first attempt to account for the impact of age on seizure recurrence and their significance in relation to paroxysmal discharges.

2. Patient selection and protocol design

The hospital medical records were searched for all children who were diagnosed with rolandic epilepsy. Data belonging to the patients with rolandic epilepsy with sufficient information regarding disease course and follow-up duration longer than 3 years at Gazi University Faculty of Medicine Pediatric Neurology Department outpatient clinic recruited from March 15, 2006 to December 31, 2013 were included in the study. All patients had their first seizure between March 2006 and December 2013. Patients who had their seizure onset ranging from 3 to 14 years of age with normal neurological examination and magnetic resonance imaging were included in the study. Patients who were not regularly followed, who had a concomitant neurological and psychiatric disorder, and who had received a neurological drug other than an AED were not included in the study. The diagnosis was made on characteristic focal clonic seizure manifestation but may be secondarily generalized and a typical EEG with spikes and sharp waves in either of the centrotemporal region.

The information on each patient included the family history of epilepsy; febrile convulsion history; age at onset; the duration, frequency, and number of seizures; and the seizure semiology. According to the clinical presentation, patients were divided into two categories: Group A, comprised of "patients having fewer than four seizures", and Group B, the "recurrence group comprised of patients having more than four seizures in the first three months". These groups were determined based on the clinical data of the patients.

- Group A This group consisted of 75 patients who had their first seizures at the age of 4 to 8. All patients had the abovementioned criteria of rolandic epilepsy. They had four or fewer seizures at follow-up.
- Group B This group consisted of 34 patients who first had their seizure at the age of 3 to 7. All patients fulfilled the typical electroclinical characteristics of rolandic epilepsy. Because of seizure recurrence, routine laboratory examination and routine metabolic disorder screening were performed on all these patients. None of these patients had a seizure other than a rolandic or a secondarily generalized seizure.

Carbamazepine (CBZ, 15 mg/kg/day) was the first choice, and sodium valproate (VPA, 20 mg/kg/day) was prescribed if CBZ did not control the seizures.

3. Assessment of interictal EEG findings

We evaluated the serial EEGs of the patients from the onset of the seizures. Interictal EEG was recorded using a digital system with 18 electrodes according to the International 10–20 system during both wakefulness and sleep without sedation. Intermittent photic stimulation and hyperventilation were performed routinely in each patient. Two electroencephalographers (EA, AS) who were blinded to the clinical details and the grouping of the patients analyzed the EEG according to the below mentioned analysis. The dominant region was defined as the localization where spikes are most frequent and higher in amplitude. The readers analyzed the following:

- a. the number of spikes per minute
- b. the localization of spikes, unilateral or bilateral centrotemporal
- c. the localization of spikes other than the centrotemporal region
- d. the duration of spike-wave activity

The number of spikes was computed during both wakefulness and NREM sleep stages 1 and 2.

The number of spikes was expressed as the number of discharges per minute. These evaluations were made by visual inspection by each reader separately. Interobserver agreement was high ($\kappa = 0.91$).

Initial EEG recordings were performed within 7–10 days after the initial seizure of all patients. In the recurrence group, EEG obtained just before AED administration was selected as the first EEG for evaluation. Repeated EEG recordings were obtained for all patients every 6 months. Electroencephalogram was made at least 3 years for every patient. All EEG recordings from all patients were analyzed in order.

The patients were evaluated in relation to age at first occurrence for each group. First, age at seizure onset was noted for each group. Second, from this pool, the age at which the most frequent seizure recurrence occurred and the number of spikes per minute during both sleep and wakefulness in Group B was evaluated. These data were evaluated on the basis of 4 stages of development. Those age groups were 3–5, 6–8, 9–11, and over 12 years.

3.1. Cognitive function assessment

At onset, all patients were evaluated using the Wechsler Intelligence Scale for Children version II (WISC-II). However, cognitive functions were not evaluated by neuropsychological assessments but only through parental and teacher reports. Families were contacted by phone and if they agreed to participate in the study, questions were then asked about school performance and behavioral aspects of the patient at that time. Therefore, a longitudinal follow-up for cognitive functions could not be evaluated.

4. Statistical analysis

The following parameters were included in the statistical evaluation: the age at onset, gender, family history of epilepsy, and history of febrile seizure. All data are expressed as means of each measure. Continuous variables are expressed as means \pm SD, and categorical variables are presented as frequencies and percentages. Fisher's test, McNemar's test, repeated analysis of variance (ANOVA), Dunnett's test, and Student's *t*-test were used to compare the differences in categorical variables among the two groups, as appropriate. For statistical analysis, SPSS 20.0 statistical software (SPSS, Chicago, IL, USA) was used. In all analyses, p < 0.05 was taken to indicate statistical significance. This study was approved by the Ethics Committee of Gazi University Medical Faculty, Turkey.

5. Results

A total of 109 patients with rolandic epilepsy were included in this study. The study population consisted of 59 males (54.1%) and 50 females (45.9%) with a mean follow-up duration of 48.7 \pm 18.1 months (3-10 years). The first three-year follow-ups were evaluated, and all assessments were performed during this period. The number of patients as distributed to the groups according to the clinical presentation was as follows: Group A, n = 75 (68.8%), and Group B, n = 34 (31.2%) (Table 1). The clinical profiles of Groups A and B are given in Table 1. Neurologically, they all appeared to have normal development. There were no differences between the two groups in age at seizure onset, history of neonatal seizure, previous febrile seizure, and laterality of spike foci. Family history of epilepsy (p = 0.041) and the number of males were significantly higher in Group B when compared with Group A (Table 1). None of the patients in either of the groups had atypical seizures including atypical absences, negative myoclonus, or oromotor symptoms. There was no difference in seizure semiology between the two groups. Carbamazepine was initiated after two or more seizures. In Group A, the mean seizure frequency was 1.5 seizures, and the mean interval between the first and the second seizure was 1.2 months for patients who had more than one seizure. In Group B, the mean

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