

# World Journal of *Clinical Cases*

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**ABOUT COVER**

Editorial Board Member of *World Journal of Clinical Cases*, Jian-Wu Zhao, PhD, Chief Physician, Professor, Department of Orthopedics, Jilin University Second Hospital, Changchun 130000, Jilin Province, China. [jianwu@jlu.edu.cn](mailto:jianwu@jlu.edu.cn)

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**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Ji-Hong Lin*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lai Wang*.

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Thrice Monthly

**EDITORS-IN-CHIEF**

Bao-Gan Peng, Sandro Vento, Dennis A Bloomfield

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**PUBLICATION DATE**

November 26, 2021

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<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Retrospective Study

# Clinical and electroencephalogram characteristics and treatment outcomes in children with benign epilepsy and centrotemporal spikes

Rui-Hua Chen, Bing-Fei Li, Jian-Hua Wen, Chun-Lan Zhong, Ming-Ming Ji

**ORCID number:** Rui-Hua Chen 0000-0003-1750-7513; Bing-Fei Li 0000-0003-3247-8183; Jian-Hua Wen 0000-0002-4615-6647; Chun-Lan Zhong 0000-0001-6623-7762; Ming-Ming Ji 0000-0001-8021-8496.

**Author contributions:** Chen RH and Li BF designed this retrospective study; Chen RH wrote the paper; Chen RH, Li BF, Wen JH, Zhong CL, and Ji MM were responsible for sorting the data.

**Institutional review board statement:** This study was approved by the Ganzhou Maternal and Child Health Hospital Medical Ethics Committee.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** This is no conflict of interest to disclose.

**Data sharing statement:** No additional data are available.

**Country/Territory of origin:** China

**Specialty type:** Clinical neurology

**Rui-Hua Chen**, Department of Children's Neurology, Ganzhou Maternal and Child Health Hospital, Ganzhou 341000, Jiangxi Province, China

**Bing-Fei Li, Chun-Lan Zhong, Ming-Ming Ji**, Department of Pediatrics, Ganzhou Maternal and Child Health Hospital, Ganzhou 341000, Jiangxi Province, China

**Jian-Hua Wen**, Department of Pediatrics, Ningdu County People's Hospital, Ganzhou 341000, Jiangxi Province, China

**Corresponding author:** Bing-Fei Li, BMed, Chief Physician, Department of Pediatrics, Ganzhou Maternal and Child Health Hospital, No. 106 Dagong Road, Zhanggong District, Ganzhou 341000, Jiangxi Province, China. [jxgzlbf2021@126.com](mailto:jxgzlbf2021@126.com)

## Abstract

### BACKGROUND

Epilepsy is a syndrome characterized by transient, rigid, paroxysmal, and repetitive central nervous system dysfunction. Prevention, control, and improvement of cognitive and behavioral dysfunction are of great significance for improving the patients' intellectual development and quality of life. Electroencephalograms (EEG) can predict an accelerated decline in cognitive function.

### AIM

To determine the clinical and EEG characteristics and treatment results of benign epilepsy in spiking children.

### METHODS

A total of 106 cases of benign epilepsy in children with myocardial spines treated at our hospital from January 2017 to January 2020 were selected. Differences in clinical data and EEG characteristics between treatment-effective/-ineffective patients were analyzed, and children's intellectual development before and after treatment evaluated using the Gesell Development Diagnostic Scale.

### RESULTS

EEG showed that the discharge proportion in the awake and sleep periods was 66.04%, and the peak/peak discharge was mainly single-sided, accounting for 81.13%, while the discharge generalization accounted for 31.13%. There was no

**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): 0  
Grade C (Good): C  
Grade D (Fair): 0  
Grade E (Poor): 0

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**Received:** July 6, 2021

**Peer-review started:** July 6, 2021

**First decision:** July 26, 2021

**Revised:** August 8, 2021

**Accepted:** August 27, 2021

**Article in press:** August 27, 2021

**Published online:** November 26, 2021

**P-Reviewer:** Kuczynska J

**S-Editor:** Wang JL

**L-Editor:** Wang TQ

**P-Editor:** Wang LYT



significant difference in any of these variables between sexes and ages ( $P > 0.05$ ). The proportion of patients with early onset ( $< 5$  years old) and seizure frequency  $> 3$  times/half a year was 40.00% and 60.00%, respectively; the incidence rate and seizure frequency in the younger age group ( $< 5$  years old) were significantly higher than those in the treatment-effective group ( $P < 0.05$ ), while the discharge index was significantly lower than that in the treatment-effective group ( $P < 0.05$ ). The discharge index was negatively correlated with fine motor skill and language development ( $r = -0.274$  and  $-0.247$ , respectively;  $P < 0.05$ ), but not with the rest ( $P > 0.05$ ). Logistic regression analysis showed that low age onset ( $< 5$  years old) and seizure frequency were the factors affecting ineffective-treatment of benign epilepsy in children (odds ratio = 11.304 and 5.784, respectively;  $P < 0.05$ ). The discharge index of the responsive group after treatment was significantly lower than that of the unresponsive group ( $P < 0.05$ ). However, there was no significant difference between groups after treatment in gross and fine motor skills, adaptability, language, and personal social development ( $P > 0.05$ ).

**CONCLUSION**

The EEG of children with benign epilepsy due to spinal wave in central time zone has characteristic changes, and the therapeutic effect is influenced by age of onset and attack frequency.

**Key Words:** Centrottemporal spikes; Benign epilepsy; Children; Electroencephalogram; Therapeutic effect

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**Core Tip:** The electroencephalogram of children with benign epilepsy with centrottemporal spikes has characteristic changes, and the therapeutic effect is affected by the age and attack frequency of the children at the time of onset.

**Citation:** Chen RH, Li BF, Wen JH, Zhong CL, Ji MM. Clinical and electroencephalogram characteristics and treatment outcomes in children with benign epilepsy and centrottemporal spikes. *World J Clin Cases* 2021; 9(33): 10116-10125

**URL:** <https://www.wjgnet.com/2307-8960/full/v9/i33/10116.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v9.i33.10116>

**INTRODUCTION**

Epilepsy is a syndrome characterized by transient, rigid, paroxysmal, and repetitive central nervous system dysfunction, generally caused by excessive neuron synchronization in the brain and self-limited abnormal discharge caused by various etiological factors. As a common disease among children, the incidence rate of epilepsy has shown an increasing trend in recent years. Benign epilepsy in children with centrottemporal spike waves is an age-dependent epileptic syndrome, which generally peaks between 6–8 years old, with normal mental and motor development[1,2]. At present, the primary goal of antiepileptic treatments is to completely control epileptic seizures, while simultaneously considering prevention, control, and improvement of cognitive and behavioral dysfunction is of great significance for improving the patients' intellectual development and quality of life. Electroencephalogram (EEG) is an important external validator of normal brain structure and function and useful to detect some brain alterations. Cognitive function, an important aspect of brain function, is also based on brain morphology and/or function. Studies have shown that abnormal EEG can predict an accelerated decline in cognitive function[3,4]. In this study, the clinical and EEG characteristics of children with benign epilepsy and centrottemporal spikes were analyzed, and the children's treatment and outcomes also discussed.

## MATERIALS AND METHODS

### Patients

A total of 106 cases of benign epilepsy, including 66 males and 40 females, in children with spinous waves in the central temporal region were treated at our hospital from January 2017 to January 2020. Their ages ranged from 3 to 12 years old, and their average age was  $7.15 \pm 1.82$  years old. The inclusion criteria were: (1) The diagnosis met the criteria for the epilepsy diagnosis and treatment guidelines of the International League Against Epilepsy; (2) First-time treatment; (3) Aged 3–12 years old; (4) Complete clinical, EEG, and follow-up data; (5) Had intelligence tests; and (6) Informed consent from the child's guardian. The exclusion criteria were: (1) A history of encephalitis, meningitis, brain developmental malformation, and other brain diseases; (2) Other diseases such as connective tissue disease, nephrotic syndrome, and immunodeficiency; and (3) Patients with a history of glucocorticoid and other treatments within 6 mo before treatment in our hospital.

### Treatment and follow-up

The children were treated with levetiracetam and lamotrigine. The levetiracetam dose was 10 mg/kg/d, and the final therapeutic dose was 10–30 mg/kg/d. Lamotrigine was administered at doses from 0.3–0.6 mg/kg/d, gradually increasing to 3–6 mg/kg/d. Each child was followed for 1 year after treatment, and the treatment was considered ineffective if there were clinical epileptic seizures during the follow-up period, and effective if there were no clinical epileptic seizures.

### EEG examination

We employed an EEG-1200C manufactured by Japan Optoelectronics Co., Ltd with the following parameters: Gain, 50  $\mu$ V; high-pass filtering conducted at 45 Hz; time constant, 0.3 s; accuracy, 16 bit; frequency, 200 Hz; and scalp resistance,  $\leq 5000$  M $\Omega$ . Reference electrodes were placed on the bilateral earlobes and we used 16 recording electrodes in total. EEG signals were recorded in a quiet and eye-closed state for 5 min, and the complexity was calculated. The human electroencephalogram frequency was (0.5–30) Hz, including  $\beta$  (13.5–30.0) Hz,  $\alpha$  (8.0–13.0) Hz,  $\theta$  (4.0–7.5) Hz, and  $\delta$  (1.0–3.5) Hz.

### Intelligence development test

The development of children's intelligence was assessed using the Gesell Development Diagnostic Scale, which included five domains, namely, gross motor, fine motor, adaptability, language, and personal-social ability. The test result of each domain is expressed as development quotient (DQ), and a DQ > 85 was considered normal.

### Statistical analysis

SPSS22.0 software was used for data analyses. Measurement data with a normal distribution are expressed as the mean  $\pm$  SD, and *t* test was used for comparison between groups. Count data are expressed as *n* (%), and inter-group comparisons were performed by the chi-square test. Pearson correlation analysis for correlation, and logistic regression analysis for multivariate analysis were also performed. *P* values < 0.05 were considered statistically significant.

## RESULTS

### Children's EEG characteristics

Among the 106 children, the EEG showed a discharge proportion in the awake and sleep periods of 66.04%, a spike/sharp wave discharge rate of 81.13% (mainly unilateral discharge), and a discharge generalization rate of 31.13%, as shown in [Table 1](#).

### Comparison of children's EEG characteristics with respect to sex and age

There was no significant difference in the proportion of discharge, spike/sharp wave unilateral discharge, and discharge generalization between the sexes and among all age groups either during the awake or asleep period (*P* > 0.05), as shown in [Table 2](#).

**Table 1** Electroencephalogram characteristics of children

Electroencephalogram characteristic	Number of cases	Proportion (%)
Discharge period		
Awake and sleep periods	70	66.04
Sleep period	36	33.96
Spine/spike discharge		
Unilateral	86	81.13
Bilateral	20	18.87
Discharge generalization	33	31.13

**Table 2** Comparison of electroencephalogram characteristics of children of different sexes and ages

Group	Number of cases	Awake and sleep discharge (%)	Spike/sharp wave unilateral discharge (%)	Discharge generalization (%)
Gender				
Man	66	42 (63.64)	55 (83.33)	19 (28.79)
Woman	40	28 (70.00)	31 (77.50)	14 (35.00)
$\chi^2$		0.450	0.554	0.448
<i>P</i> value		0.502	0.457	0.503
Age				
≤ 7 yr	34	25 (73.53)	26 (76.47)	11 (32.35)
> 7 yr	72	45 (62.50)	60 (83.33)	22 (30.56)
$\chi^2$		1.253	0.711	0.035
<i>P</i> value		0.263	0.399	0.852

### Comparison of clinical data of treatment responsive/unresponsive children

The proportion of children with young-age onset (< 5 years old) and attack frequency > 3 times/half a year in the treatment unresponsive group was significantly higher than that in the treatment responsive group ( $P < 0.05$ ), and the discharge index significantly lower ( $P < 0.05$ ). There was no significant difference in sex, age, or discharge period between the treatment responsive/unresponsive groups ( $P > 0.05$ , Table 3).

### Correlation between discharge index and Gesell scale

Pearson correlation analysis showed a negative correlation between the discharge index and fine motor skills and the language development quotient ( $r = -0.274$  and  $-0.247$ , respectively;  $P < 0.05$ ), but no significant correlation was observed in any other parameters ( $P > 0.05$ ), as shown in Table 4 and Figure 1.

### Results of multivariate analysis

Logistic regression analysis was performed using the above statistically significant indicators as independent variables and treatment effectiveness as the dependent variable. The results showed that low age (< 5 years old) and seizure frequency were the factors affecting the lack of treatment response in children with benign epilepsy and centrotemporal spike wave (Odds ratio = 11.304 and 5.784, respectively;  $P < 0.05$ ), as shown in Table 5.

### Comparison of discharge index and Gesell scale between treatment responsive/unresponsive children before and after treatment

The discharge index after treatment in the treatment responsive group was  $34.47 \pm 10.02\%$ , significantly lower than that in the unresponsive group ( $P < 0.05$ ). In the treatment responsive group, fine motor skills, adaptability, and language development quotient improved after treatment ( $P < 0.05$ ). There was no significant difference in gross and fine motor skills, adaptability, language, or personal-social ability

**Table 3 Comparison of clinical data of children with and without effective treatment, *n* (%)**

Clinical data	Treatment ineffective ( <i>n</i> = 20)	Treatment effective ( <i>n</i> = 86)	<i>t/χ<sup>2</sup></i>	<i>P</i> value
Gender			0.554	0.457
Man	11 (55.00)	55 (63.95)		
Woman	9 (45.00)	31 (36.05)		
Age (yr)	7.15 ± 1.98	7.15 ± 1.80	0.000	1.000
Discharge period			0.883	0.347
Awake and sleep periods	15 (75.00)	55 (63.95)		
Sleep period	5 (25.00)	31 (36.05)		
Spike/sharp wave discharge			2.081	0.149
Unilateral	19 (95.00)	67 (77.91)		
Bilateral	1 (5.00)	19 (22.09)		
Discharge generalization	8 (40.00)	25 (29.07)	0.904	0.342
Low age onset (< 5 yr)	8 (40.00)	6 (6.98)	12.690	0.000
Seizure frequency			9.582	0.002
> 3 times/half a year	12 (60.00)	21 (24.42)		
≤ 3 times/half a year	8 (40.00)	65 (75.58)		
Discharge index (%)	65.05 ± 7.74	73.28 ± 9.17	-3.714	0.000
Gesell scale				
Gross motor (points)	85.70 ± 6.62	85.28 ± 7.29	0.236	0.814
Fine motor (points)	88.60 ± 5.99	86.62 ± 8.00	1.040	0.301
Adaptability (points)	87.60 ± 7.02	86.08 ± 7.20	0.854	0.395
Language (points)	88.15 ± 7.13	86.33 ± 7.92	0.942	0.348
Individual-social ability (points)	85.40 ± 8.61	85.99 ± 8.22	-0.287	0.775

**Table 4 Results of correlation analysis**

Gesell scale	Discharge index	
	<i>r</i>	<i>P</i> value
Gross motor	-0.014	0.887
Fine motor	-0.274	0.005
Adaptability	-0.068	0.488
Language	-0.247	0.011
Individual-social ability	0.098	0.316

development quotient between the treatment responsive/unresponsive group after treatment (*P* > 0.05, Table 6).

## DISCUSSION

Epilepsy is a brain disease mainly characterized by transient central nervous system dysfunction caused by abnormal neuron discharge. Repeated epileptic seizures are often accompanied by a variety of neurobiological, cognitive, psychological, and social dysfunctions. Benign epilepsy with spinous waves in the central temporal region is the most common partial epilepsy in childhood, with an onset age between 3-13 years and accounting for 15%-24% of all kinds of epilepsy in children[5]. Several studies have shown that children with epilepsy and centrottemporal spikes have various degrees of

Table 5 Results of multivariate analysis

Index	$\beta$	SE	Wals	P value	OR (95%CI)
Incidence at a young age (< 5 yr)	2.425	0.696	12.131	0.000	11.304 (2.888-44.251)
Attack frequency	1.755	0.593	8.760	0.003	5.784 (1.809-18.490)
Constant term	-2.686	0.480	31.254	0.000	-

OR: Odds ratio.

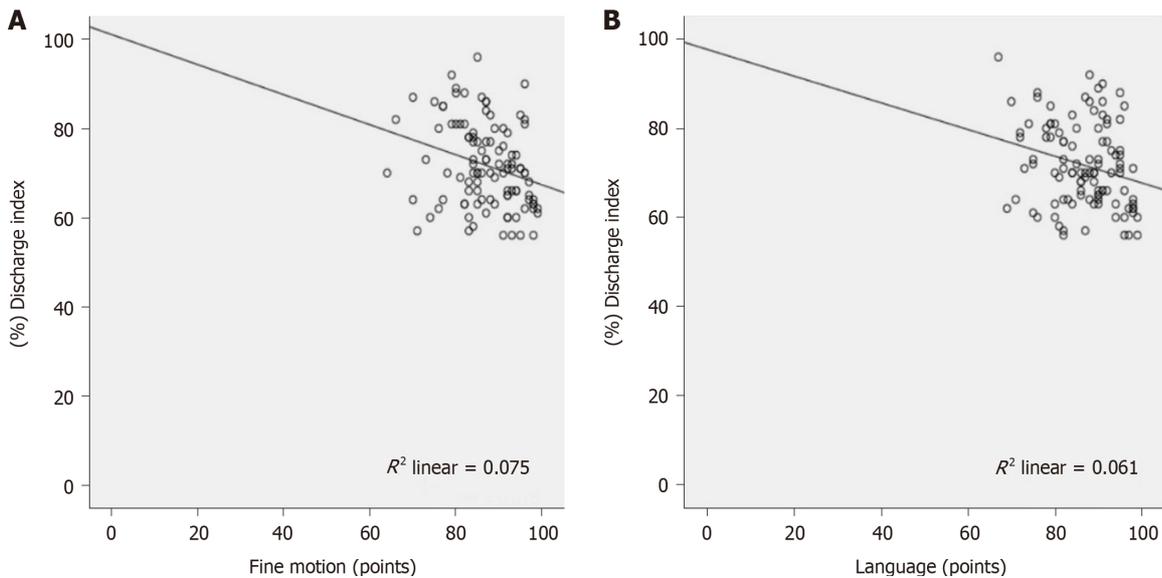
cognitive and behavioral damage[6,7], while other reports have found that the cognitive impairment in these children is not caused by seizures but related to frequent clinical discharge. Neuropsychological and sociological problems exist in half of these children after adulthood[8,9]. Although the primary goal of antiepileptic treatment is to completely control epileptic seizures, prevention, control, and improvement of cognitive and behavioral dysfunction must be simultaneously considered. Therefore, clinicians must achieve a balance between controlling the epileptic seizures as much as possible and preserving cognitive and behavioral functions[10]. Long-term outbreaks of spike-and-slow wave rhythm and bilateral asynchronous spike-and-slow wave distribution cause more severe cognitive impairment than single spike waves[11]. EEG monitoring, a common modern auxiliary examination method for the clinical diagnosis of mild cognitive impairment diseases, induces no physical trauma and has confirmed value in the diagnosis of brain diseases. However, comprehensive analyses, as well as other experimental and auxiliary examinations, need to be conducted based on specific symptoms and signs; therefore, it is of great clinical significance to explore chemical markers of brain damage[12]. EEG represents the waveforms formed by the brain spontaneous potential; these waveforms can be divided into  $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\theta$ , and  $\delta$  waves according to their frequencies, with different waveforms being shown at different ages, in various consciousness states, and at various brain function levels[13,14]. Some studies have shown that abnormal EEGs can predict an accelerated decline in cognitive function. In children with epilepsy, EEGs accompanied by spinous waves in the central temporal region during the attack stage are often characterized by tonic-clonic seizures, where the initial fast wave activity of low amplitude in the central or middle temporal region on one side gradually increases in amplitude and decreases in frequency, gradually evolving into the alternating appearance of spinous and slow waves, which can be generalized to the ipsilateral hemisphere or even spread to the contralateral one[15]. At present, EEGs are considered to be highly related to epilepsy with spinous waves in the central temporal region. And compared with those of healthy peers, an increase in extremely high-amplitude spinous and slow waves in the high Rolandic region can be observed in the awake period, along with a widespread rhythmic outbreak of 2-3 Hz high-amplitude spinous and slow waves in the awake period. However, the discharge is significantly increased in the sleep period, and the spinous and slow wave discharge index is > 50% during the non-rapid-eye-movement sleep period[16]. In epilepsy accompanied by centrotemporal spikes, the presence of a status epilepticus EEG during sleep is known to cause nerve damage and cognitive changes; the higher the abnormal discharge index in the EEG, the more severe the cognitive damage in children. Therefore, we should actively diagnose, treat, and observe the therapeutic effects in children with epilepsy accompanied by centrotemporal spikes[17,18]. In this study, correlation analysis revealed that the discharge index was negatively correlated with fine motor performance and the language development quotient. Logistic regression analysis showed that an early age of onset (< 5 years old) and seizure frequency were influencing factors for the unresponsive treatment of benign epilepsy with centrotemporal spikes in children, indicating that monitoring the EEG discharge index could be used to preliminarily determine the children's fine motor skills and language development quotient. During treatment, great attention should be given to children with early-onset and frequent seizures in whom clinical treatment has a poor effect. Frequent attacks can lead to delayed reaction time or even reaction loss in children, suggesting that abnormal discharges may be accompanied by transient cognitive function changes under clinical conditions, which reminds us that seizure control should not be the target of clinical treatment but the inhibition of clinical discharge and subsequent improvement in patients' cognitive function[19,20]. An early age of onset is an important factor leading to poor treatment effect in children with benign epilepsy and centrotemporal spikes. Given the lack of clear clinical data

**Table 6 Comparison of discharge index and Gesell scale scores between treatment-effective and treatment-ineffective children before and after treatment**

Index	Treatment ineffective (n = 20)	Treatment effective (n = 86)	t	P value
Discharge index (%)				
Before treatment	65.05 ± 7.74	73.28 ± 9.17	-3.714	0.000
After treatment	40.15 ± 5.36	34.47 ± 10.02	2.449	0.016
t	11.828	26.498		
P value	0.000	0.000		
Gross motor (points)				
Before treatment	85.70 ± 6.62	85.28 ± 7.29	0.236	0.814
After treatment	85.90 ± 5.47	86.20 ± 6.47	-0.192	0.848
t	-0.104	-0.875		
P value	0.918	0.383		
Fine motor (points)				
Before treatment	88.60 ± 5.99	86.62 ± 8.00	1.040	0.301
After treatment	91.20 ± 2.69	89.24 ± 5.29	1.605	0.111
t	-1.771	-2.533		
P value	0.085	0.012		
Adaptability (points)				
Before treatment	87.60 ± 7.02	86.08 ± 7.20	0.854	0.395
After treatment	88.50 ± 5.04	88.26 ± 5.38	0.182	0.856
t	-0.466	-2.249		
P value	0.644	0.026		
Language (points)				
Before treatment	88.15 ± 7.13	86.33 ± 7.92	0.942	0.348
After treatment	89.35 ± 6.02	88.55 ± 5.99	0.537	0.592
t	-0.575	-2.073		
P value	0.569	0.040		
Personal-social ability (points)				
Before treatment	85.40 ± 8.61	85.99 ± 8.22	-0.287	0.775
After treatment	86.95 ± 6.78	87.91 ± 6.27	-0.607	0.545
t	-0.633	-1.722		
P value	0.531	0.087		

on the specific scope of early-onset benign epilepsy with centrotemporal spikes, an early age at onset can be used as a relevant factor to predict treatment prognosis in these children. In this study, early age of onset was < 5 years old.

The analysis of the results of this study showed that the two antiepileptic drugs levetiracetam and lamotrigine could effectively control epileptic seizures and inhibit epileptic discharge, thus improving children's cognitive function. However, this study has various limitations. Due to the limited number of enrolled children, there may be some deviation and error in the evaluation of discharge index, which may lead to a lack of generalizability. Therefore, further research expanding the sample size and extending follow-up time is needed.



**Figure 1 Correlation analysis.** A: Fine motion; B: Language.

## CONCLUSION

In summary, the EEG of children with benign epilepsy and centrotemporal spikes has characteristic changes, and therapeutic effects are affected by the age and attack frequency at the time of onset.

## ARTICLE HIGHLIGHTS

### Research background

The primary goal of antiepileptic treatments is to completely control epileptic seizures, while simultaneously considering prevention, control, and improvement of cognitive and behavioral dysfunction is of great significance for improving the patients' intellectual development and quality of life.

### Research motivation

In this study, the clinical and electroencephalograms (EEG) characteristics of children with benign epilepsy and centrotemporal spikes were analyzed, and the children's treatment and outcomes also discussed.

### Research objectives

This study aimed to determine the clinical and EEG characteristics and treatment results of benign epilepsy in spiking children.

### Research methods

A total of 106 benign epilepsy children with myocardial spines were included. Differences in clinical data and EEG characteristics between treatment-effective/-ineffective patients were analyzed, and children's intellectual development before and after treatment evaluated using the Gesell Development Diagnostic Scale.

### Research results

EEG showed that the discharge proportion in the awake and sleep periods was 66.04%, and the peak/peak discharge was mainly single-sided, accounting for 81.13%, while the discharge generalization accounted for 31.13%. The discharge index was negatively correlated with fine motor skill and language development, but not with the rest. The discharge index of the responsive group after treatment was significantly lower than that of the unresponsive group.

### Research conclusions

The EEG of children with benign epilepsy and centrotemporal spikes has charac-

teristic changes, and therapeutic effects are affected by the age and attack frequency at the time of onset.

### Research perspectives

Further research expanding the sample size and extending follow-up time is needed.

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