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Surgical treatment of children with drug-resistant epilepsy involving the Rolandic area

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ABSTRACT

Objective. We retrospectively analysed the clinical features and prognostic factors of surgery in children with drug-resistant epilepsy involving the Rolandic area, and the relationship between the stable compound muscle action potentials (CMAPs) of intraoperative neurophysiological monitoring (IONM) and good motor function outcomes postoperatively.

Methods. A study was conducted on the clinical data of 91 patients with epilepsy who underwent epilepsy surgery involving the Rolandic area and IONM from November 2015 to February 2019.

Results. In total, 91 patients were included in this study. The median age at seizure onset was 1.3 years old. The median age at surgery was 4.4 years old. Twenty-seven patients (29.7%), with age at onset below three years old, had epileptic spasms. The central operculum was the most common surgical region in 52 patients (57.1%). The most common pathology was focal cortical dysplasia (FCD) in 67 patients. At the last follow-up visit, 69 patients (75.8%) were seizure-free. Interictal epileptiform discharges in the Rolandic area were associated with good seizure outcome (p=0.016). Out of 91 patients, successful IONM was performed in 88 patients (96.7%). Stable CMAP was seen in 79 of 88 patients (89.8%), and irreversible disappearance of CMAP was seen in nine patients (10.2%). New permanent motor deficit was observed in 13 of 88 patients (14.8%). There was a significant correlation between stable CMAP and good motor function outcome (p<0.001).

Significance. This is the largest reported cohort of children with drug-resistant epilepsy involving the Rolandic area who received surgery from a single centre. Epileptic spasms were only observed in young children with age at onset below three years old. The major aetiology was FCD. The rate of seizure freedom was 75.8%. Epileptiform discharges in the Rolandic area were the main prognostic factor affecting surgical outcome. Stable CMAP can predict good motor function outcome postoperatively.

Key words: surgery; Rolandic area; compound muscle action potentials; intraoperative neurophysiological monitoring; new permanent motor deficit

For drug-resistant epilepsy, the purpose of radical epilepsy surgery is to remove the epileptogenic cortex, control seizure attacks, and help patients improve their quality of life. However, when the epileptogenic zone (EZ) is adjacent to, or located in eloquent cortical regions, the surgical strategy of how to balance seizure control and functional protection has always been a challenge for epilepsy surgery. When the lesion involves the motor eloquent cortex, improper protection of the primary motor cortex may cause different degrees of new permanent motor deficit (NPMD) after surgery. Therefore, it is necessary to accurately locate the EZ and eloquent cortex to avoid impairing motor function.

There have been few reports about Rolandic epilepsy surgery in children, and some early studies have limitations in methods and techniques. In recent years, location techniques in epilepsy surgery have developed rapidly. However, it is still too difficult to perform non-invasive techniques (e.g., functional magnetic resonance imaging [fMRI] or magnetoencephalography [MEG]) and invasive techniques (e.g., cortical electrical stimulation [CES]) in very young children to precisely locate the eloquent cortex. How to protect motor function effectively while achieving seizure-free status after surgery is a great challenge for paediatric epilepsy surgeons. In our study, we retrospectively analysed the presurgical evaluation and surgical treatment of children with drug-resistant Rolandic epilepsy in our epilepsy centre in recent years. Our aim was to summarize clinical characteristics, intraoperative neurophysiological monitoring (IONM), and seizure and motor function outcomes in order to improve the surgical outcome in children with Rolandic epilepsy.

Methods

Clinical data

Between November 2015 and February 2019, we collected retrospective data from children with Rolandic epilepsy who underwent epilepsy surgery at the Paediatric Epilepsy Center of Peking University First Hospital. This study was approved by the Institutional Review Board of the Ethics Committee of Peking University First Hospital.

The inclusion criteria were as follows:

- children under 16 years old;
- drug-resistant epilepsy;
- surgical scope involving the Rolandic area (the Rolandic area was divided into four subgroups according to the anatomical location:
 - precentral gyrus;
 - postcentral gyrus;
 - paracentral lobule;
 - and central operculum);
- IONM was performed;
- and at least six months of follow-up data were available.

Presurgical evaluation

All children underwent presurgical evaluation including medical history, physical examination, semiology, aetiology, long-term scalp video-EEG (VEEG) including at least three habitual seizures, 3T epilepsy sequence magnetic resonance imaging (MRI), positron emission tomography (PET), and neuropsychological testing (including the Griffiths Mental Development Scales, Wechsler Intelligence Scale for Children and the Peabody Developmental Motor Scale). Coregistration of MRI and PET was analysed to help outline the lesion border. Genetic or immunological examinations should have been performed to exclude surgical contraindications. Some children underwent fMRI to determine the functional area of movement or language. Some underwent diffusion tensor imaging (DTI) tests to clarify the relationship between corticospinal projections and epileptogenic lesions. If the location of the EZ and eloquent cortex was uncertain and the patient showed sufficient cooperation, we implanted subdural strips and grids to record intracranial EEG and performed cortical electrical stimulation (CES) to locate the EZ and motor function cortex. All operations were performed by the same experienced functional neurosurgeon.

Intraoperative neurophysiological monitoring

The NIHON KOHDEN MEE-1200C neurophysiological monitoring system was used for IONM. The patients were under total intravenous anaesthesia (TIVA). Intravenous sufentanil at 0.1-0.2 mcg/kg, propofol at 3-4 mg/kg and rocuronium at 0.6 mg/kg were given for anaesthesia induction. The maintenance of anaesthesia consisted of TIVA using propofol at 4-12 mg/kg/h and remifentanil at 6-18 mcg/kg/h. No inhaled anaesthesia or muscle relaxants were used during IONM. After craniotomy, the central sulcus was determined by phase reversal of somatosensory evoked potential (SSEP). Then, motor evoked potential (MEP) was preceded by identification of the primary motor cortex. We used a monopolar (fast) short-train technique; stimulation was carried out using the first contact of a strip subdural electrode as a monopolar probe that delivered a train of 5-7 anodal pulses, 0.5-msec pulse width each, at a frequency of 500 Hz, which is equivalent to an interstimulus interval of 1.5 msec. MEPs were collected from paired subdermal needle electrodes placed in several muscles of interest: contralateral deltoids, biceps, triceps, extensor digitorum communis, abductor pollicis brevis, hypothenar muscles, quadriceps, tibialis anterior, gastrocnemius and plantar muscles. Due to the high threshold of stimulation current intensity in children, we routinely started at an intensity current of 20 mA for under six years of age and started at an intensity current of 15 mA beyond six years of age. Then, we adjusted the stimulation current intensity according to the reaction of compound muscle action potentials (CMAP). Generally, the maximum stimulation current intensity was 30 mA. Continuous MEP monitoring was achieved by repetitive stimulation every 1-5 sec during surgery. Once the amplitude of CMAP was attenuated or disappeared, the neurosurgeon was reminded promptly to trigger temporary cessation of surgical dissection and resection. Up to 2 minutes before the end of resection, CMAP was considered stable if the amplitude of CMAP did not reach 50% attenuation. CMAP was considered irreversibly changed if its amplitude attenuation exceeded 50% and did not return to baseline. In a few cases, CMAP was evoked by stimulation with a higher current intensity of more than 30 mA. In such situations, intermittent stimulation instead of continuous stimulation was performed to avoid brain cortical damage. If CMAP was not elicited by a stimulation current intensity of 45 mA, the stimulation current intensity would no longer be increased, and IONM was regarded as unsuccessful.

Prognosis assessment

Motor function outcomes were dynamically observed within one week postoperatively. Children were evaluated at three and six months postoperatively and then yearly. The follow-up periods for all children were longer than six months. Seizure outcomes and motor function outcomes were evaluated at each follow-up visit. Seizure outcomes were assessed using the Engel classification [1]. Motor function outcomes were assessed by physical examination, using the Peabody Developmental Motor Scale and video recording. If a new motor function deficit occurred within one week post operation and returned to preoperative baseline level within three months, we referred to the deficit as postoperative transient motor injury. NPMD was defined as a new motor function deficit which was irreversible three months postoperatively.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 20.0. Continuous variables are expressed as medians and ranges. Categorical variables were summarized as frequencies and percentages. Chi-square and Fisher's exact tests were used to compare categorical variables, and the non-parametric Mann-Whitney U test was used to compare continuous variables. A *p* value <0.05 was regarded as statistically significant.

Results

Clinical data

• Demographics

Between November 2015 and February 2019, among 478 children with epilepsy who underwent resective epilepsy surgery in the Paediatric Epilepsy Center, Peking University First Hospital, 91 (19.0%) underwent Rolandic epilepsy surgery under IONM. These children included 53 (58.2%) males and 38 (41.8%) females. The median age at seizure onset was 1.3 years (0-12.3 years). The median age at surgery was 4.4 years (0.7-15.7 years). The median epilepsy duration was 2.8 years (0.3-12.2 years). According to the age at seizure onset, children were classified into two subgroups: 65 (71.4%) cases < three years old and 26 (28.6%) cases ≥ three years old.

• Semiological features

Semiological features originating from the Rolandic area were observed in 54 (59.3%) cases, such as myoclonic, clonic, tonic, and somatosensory features of the contralateral limbs. Spasms were observed in 27 (29.7%) children, who were all less than three years old. Seventy-six (83.5%) cases had seizure attacks every day. The relationship between seizure semiology and age at seizure onset is outlined in *table 1*.

• EEG features

On interictal EEG, 48 (52.7%) cases showed interictal epileptic discharges (IEDs) only in the Rolandic area unilaterally, 22 (24.2%) cases showed multifocal or generalized IEDs, and 10 (11%) cases showed IEDs in the Rolandic area with multifocal or generalized IEDs. Other types of IEDs were observed in 11 (12.1%) cases. On ictal EEG, ictal onset rhythms were observed in 90 children, 42 (46.2%) originated from Rolandic areas and 48 (52.7%) originated from other areas. One (1.1%) child had no ictal EEG because of the sparse seizure frequency.

• Neuroimaging features

Of the 91 children, the lesions of 86 (94.5%) cases were positive on MRI, which involved the Rolandic area. PET-CT was performed in 89 children, and 80 (89.9%) cases revealed hypometabolism lesions on PET-MRI coregistration.

• Genetic examination

Of the 91 children, 20 (22.0%) underwent genetic examination, six of whom had mutations in genes involved in mTOR signalling, including *DEPDC5* and *NPRL2* mutations in one, *DEPDC5* mutations in one, *TSC1* mutations in one, and *TSC2* mutations in three.

Seizure semiology	< 3 years group (n=65)	≥ 3 years group (n=26)	p value
Spasm			
Yes	27 (41.5%)	0 (0%)	<0.001
No	38 (58.5%)	26 (100%)	
Seizure type			
One type	35 (53.8%)	17 (65.4%)	0.315
Multiple types	30 (46.2%)	9 (34.6%)	
Seizure frequency			
Daily	58 (89.2%)	18 (69.2%)	0.044
Not daily	7 (10.8%)	8 (30.8%)	

Table 1. Correlation between seizure semiology and age at seizure onset.

Preoperative and intraoperative motor function assessment and prognosis

Thirty-three (36.3%) cases had contralateral presurgical motor deficits based on motor function evaluation. Functional MRI and DTI were performed in 14 children, and eight (8/14, 57.1%) of them showed motor and language functional reorganization. Eleven (11/14, 78.6%) cases showed that there were overlaps between the EZ and corticospinal tract projection. Overall, subdural grid electrodes (15 cases) and stereoelectroencephalography (SEEG) (13 cases) were used in 28 children to locate the EZ and the eloquent cortex. Successful IONM was performed in 88 (96.7%) cases. The following are the results analysed based on these 88 cases. The hand function area was determined by MEP within the precentral gyrus in 73 (83.0%) cases, the postcentral gyrus in 13 (14.8%) cases, and both the precentral and postcentral gyri in two (2.2%) cases. Intraoperatively, stable CMAPs were found in 79 (89.8%) cases (figure 1), and irreversible disappearance of CMAPs was found in nine (10.2%) cases. Compared to the baseline, postoperative transient motor injury was observed in 30 (34.1%) cases, and most of them recovered within one to two weeks. NPMD was observed in 13 (14.8%) cases, including the unilateral upper limbs in four cases, unilateral lower limbs in two

cases, and unilateral limbs in seven cases. Of these 13 children, 10 were seizure-free, and one was classified each as Engel Class II, Engel Class III, and Engel Class IV. The specificity of stable CMAP to predict non-NPMD was 96%, the sensitivity was 46.2%, and the prediction accuracy was 88.6%. The relationship between CMAP and NPMD is illustrated in *table 2*.

In this cohort, there were overlaps between the EZ and the motor eloquent cortex in five cases. All of these patients had no preoperative contralateral motor deficits. There was no NPMD after the first surgery under IONM, but all of these cases suffered frequent seizure attacks postoperatively. A second extended resection was performed at least six months after the first operation. Four cases were seizure-free, but NPMD was observed. Only one patient still suffered with seizure attacks, without NPMD. This study only included data for the first IONM and the postoperative follow-up.

Surgical site and seizure outcome

The surgical resection sites were the central operculum in 52 (57.1%) cases, the postcentral gyrus in 19 (20.9%), the precentral gyrus in nine (9.9%), and the paracentral lobules in four (4.4%). In addition, several children underwent combined subregional resection or bottom of the central sulcus resection

СМАР	NPMD			p value
	No	Yes	Total	
Stable	72 (81.8%)	7 (8.0%)	79 (89.8%)	
Irreversible disappearance	3 (3.4%)	6 (6.8%)	9 (10.2%)	<0.001
Total	75 (85.2%)	13 (14.8%)	88 (100%)	

▼ Table 2. Correlation between CMAP and NPMD.

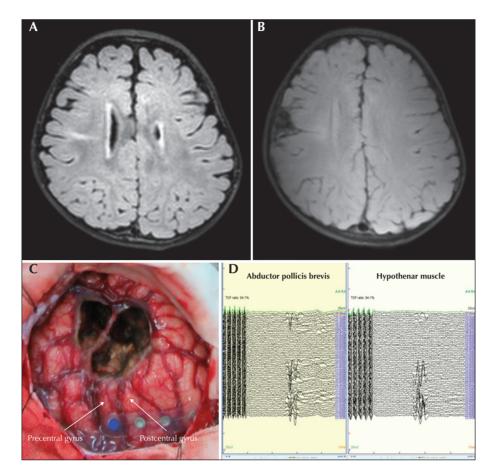


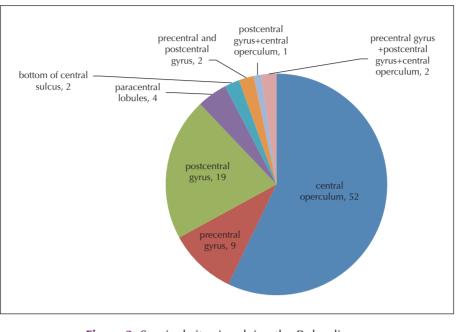
Figure 1. Female, age two years and 10 months, with FCD of the right precentral gyrus and seizure onset at 10 months. The girl's muscle strength was normal preoperatively. (A) Presurgical MRI, T2 FLAIR showing a lesion with typical "transmantle sign" indicated by the arrow. (B) Postsurgical MRI, T2 FLAIR, showing a tailored resection of the lesion; the pathology was FCDIIb. (C) The area of surgery; the blue dot shows the MEP stimulation electrode. (D) Intraoperative MEP monitoring of the abductor pollicis brevis, hypothenar muscles and extensor digitorum communis. The CMAP exhibited transient disappearance twice, and the longest duration was 20 seconds. The amplitude was swiftly reversed by cessation of surgery. There was no hemiparesis postoperatively. The girl had normal motor function and was seizure-free at the last follow-up visit (after more than three years).

(*figure 2*). Pathological results were obtained in 87 cases (*supplementary table 1*). Focal cortical dysplasia (FCD) was the most common pathology (77%).

In this cohort, the follow-up time was 6-36 months. Postoperative follow-up cases and seizure-free rates are shown in *supplementary table 2*. The relationship between follow-up time and seizure-free rate is shown in *figure 3*. Six patients who had mTOR pathway-related mutations were all seizure-free. The relationship between seizure outcome and prognostic factors is shown in *table 3*. The only significant factor associated with seizure outcome was IEDs of the Rolandic area (p=0.016).

Discussion

Generally, focal-onset epilepsy originating from the primary sensorimotor cortex exhibits typical seizure semiology and EEG features, and electrical-clinical manifestations can provide reliable localization information. For the surgical treatment of drug-resistant epilepsy involving the Rolandic area, the major challenge is to remove the EZ while protecting the eloquent cortex. To the best of our knowledge, few articles have reported on the prognosis of surgery in children with Rolandic epilepsy, and the sample sizes were too small. A single-centre study of 48 cases had the largest sample





size, with 13 years of experience [2-5]. Our study is the largest sample size thus far with a three-year timespan, and the same neurosurgeon was included throughout the study. Additionally, it is homogeneous with regards to presurgical evaluation and IONM.

Typical seizure semiology of the primary sensorimotor cortex could provide reliable localization information. However, in our cohort, 43% of children had multiple types of seizures. Spasm was observed in 30% of children, and 53% had ictal EEG onset outside the Rolandic area. All these ictal EEG findings demonstrate that electroclinical features are complex in paediatric Rolandic epilepsy, and localization is poor, especially in young children with spasms. In this situation, localization of the EZ relied on lesions on MRI (95%), hypometabolism on PET (90%), and IEDs in the Rolandic region (64%).

With the development of presurgical evaluation techniques for epilepsy, a variety of techniques could be used to determine the motor function cortex, including some non-invasive techniques (e.g., fMRI, MEG, transcranial magnetic stimulation motor evoked potential [TMS-MEP]). Invasive techniques include subdural grid electrodes, SEEG, CES and intraoperative procedures during wakefulness [6]. For children, especially young children, there were limitations in presurgical evaluation techniques. The most common problem was poor cooperation in young children



Figure 3. Correlation between follow-up time and surgical outcome.

Table 3. Surgical prognostic factors.

Prognostic factors	Engel Class I	Engel Class II-IV	p value
Sex			
Male	42 (79.2%)	11 (20.8%)	0.368
Female	27 (71.1%)	11 (28.9%)	
Mean age at seizure onset (y)	1.4(0-12.3)	0.8(0-7.0)	0.161
Age at seizure onset			
< 3 y	46 (70.8%)	19 (29.2%)	0.075
≥ 3 y	23 (88.5%)	3 (11.5%)	
Mean age at surgery (y)	5.0(1.1-15.7)	3.7(0.7-13.1)	0.127
Duration of epilepsy (y)	2.9(0.3-12.2)	2.3(0.3-11.1)	0.288
Family history			
Yes	7 (70%)	3 (30%)	0.949
No	62 (76.5%)	19 (23.5%)	
Seizure type			
One type	39 (75%)	13 (25%)	0.832
Multiple types	30 (76.9%)	9 (23.1%)	
Semiology of Rolandic area			
Yes	44 (81.5%)	10 (18.5%)	0.128
No	25 (67.6%)	12 (32.4%)	
Spasm			
Yes	17 (63%)	10 (37%)	0.063
No	52 (81.2%)	12 (18.8%)	
Seizure frequency			
Daily	57 (75%)	19 (25%)	
Not daily	12 (80%)	3 (20%)	
Interictal EEG			
Rolandic area	41 (85.4%)	7 (14.6%)	0.016
Generalized or multifocal	12 (54.5%)	10 (45.5%)	
Rolandic area with other area	9 (90%)	1 (10%)	
Ictal EEG			
Rolandic area	35 (83.3%)	7 (16.7%)	0.162
Non-Rolandic area	34 (70.8%)	14 (29.2%)	
Surgical laterality			
Left	30 (78.9%)	8 (21.1%)	0.556
Right	39 (73.6%)	14 (26.4%)	
Surgical site	0 (00 00()	4 (44 40/)	0.646
Precentral gyrus	8 (88.9%)	1 (11.1%)	0.619
Postcentral gyrus Central operculum	16 (84.2%) 37 (71.2%)	3 (15.8%) 15 (28.8%)	
Paracentral lobule	3 (75%)	13 (25%)	
Pathology	0 (10 /0)		
FCD type II	44 (75.9%)	14 (24.1%)	0.369
Other congenital malformations	13 (65%)	7 (35%)	0.303
Acquired causes	8 (88.9%)	1 (11.1%)	

(fMRI, intraoperative monitoring during wakefulness). In addition, non-invasive techniques were not accurate. At the same time, it was difficult to implant electrodes in young children. In our cohort, only 14 (15%) patients underwent fMRI, and more than half of them showed motor function reorganization. However, most of the patients could not complete fMRI successfully, and the relationship between the EZ and the eloquent cortex was not accurately reflected by fMRI. Intracranial EEG monitoring and CES were performed in 28 (31%) cases. Due to the poor cooperation with some children, the results of functional mapping were not reliable. In our study, intraoperative SEP-MEP and continuous MEP monitoring were performed to locate the primary motor cortex. IONM did not require cooperation with the patients. Real-time motor function monitoring could precisely locate and protect the primary motor cortex [7]. Although a previous study reported that IONM was unsuccessfully performed in children who were under seven years old [8], we improved the monitoring technology to achieve a success rate of 98.9%, and the minimum age was only eight months.

In previous reports, 58% of patients with Rolandic epilepsy had motor function injury immediately after surgery. In addition, 22.7%-66.7% of patients had NPMD postoperatively. In our cohort, 34.1% of children had transient motor function injury, which might be related to cortical oedema in the Rolandic area [9, 10]. In addition, NPMD was observed in 14.3% cases. We analysed the relationship between intraoperative MEP and postoperative permanent motor function outcomes in 88 patients from this cohort. The results showed that the specificity of stable CMAP for predicting non-NPMD was 96.0%, and the accuracy was 88.6%. Irreversible disappearance of CMAP occurred in nine cases, and six of them had NPMD. Because there was an overlap between the planned resection area of the EZ and the eloquent cortex, resection of the PMA and NPMD was inevitable. The other three cases had no NPMD. We suspected that the stimulation site might not be located in the most sensitive area of the motor function cortex. For example, when the central operculum was the planned resection area, motor representative areas of the upper and lower limbs in the precentral gyrus were difficult to expose. Another explanation was that motor function might be partially reorganized, and it was difficult to localize the PMA precisely. In a previous report of epilepsy surgery involving the Rolandic area in adults, NPMD was more likely to occur when the upper limb representative area of the precentral gyrus was resected, or extended resection was performed [11]. In our cohort, extended resection was performed in five cases; while the resection area involved the precentral gyrus in one case, NPMD was documented in

the postcentral gyrus and central operculum postoperatively. The other four cases had no NPMD. This reflected the possible stronger plasticity in the developing brain [12, 13]. Our study also showed that seven (8%) patients had NPMD postoperatively, while CMAP was stable intraoperatively. We speculate that this phenomenon was related to ischaemic injury due to angiospasm. In general, the stability of intraoperative CMAP was highly consistent with permanent motor function outcome (p<0.001).

In a previous study, it was mentioned that patients with EZ located in the precentral gyrus and central operculum had better surgical outcomes than those with EZ located in the postcentral gyrus [11]. In our study, surgical resection involved the central operculum in 57.1% of cases. The postoperative seizure-free rate following surgical resection involving the precentral gyrus and postcentral gyrus was slightly higher than that involving the central operculum and paracentral lobule. However, there was no statistical significance between groups. Investigation of the prognostic factors for seizure outcome showed that age at seizure onset, duration of epilepsy, seizure type and frequency, resection area, and pathology were not associated with seizure outcome. Interictal EEG was the only factor associated with seizure outcome. Patients with IEDs in the Rolandic area had a higher seizure-free rate than those with other types of IEDs (p=0.016). This result indicates that multifocal or generalized IEDs, in the absence of IEDs outside the Rolandic area, would affect surgical outcome. In our study, at two years after surgery, 83.7% of children were seizure-free, and at three years after surgery, 76.4% were seizure-free. These results are more favourable than the 42.9%-64.0% of patients in previous studies [2-5], which may be attributed to the following. Almost 95% of cases had obvious lesions on neuroimaging, making the EZ accurate; on the other hand, IONM helped to protect the motor function area, thus the EZ could be removed as completely as possible, improving the seizure-free rate [8].

There were several limitations in our study. The follow-up period for some cases was short, and long-term follow-up should be carried out. In this cohort, 77% of children had FCD based on pathology. However, only 20% of children underwent genetic examination. In the future, with the increasing use of next-generation sequencing technology, genetic examination should be emphasised, which may be important regarding surgical indications and improvement in surgical outcomes. To the best of our knowledge, this is the largest single-centre study of surgical treatment of children with Rolandic epilepsy. The results show that ictal electroclinical features may make it difficult to precisely locate the EZ in children with epilepsy involving the Rolandic area. Local structural and functional abnormalities are present on MRI and PET, however, IEDs in Rolandic areas are the main prognostic factor affecting surgical outcome. IONM can effectively protect motor function with the removal of the EZ as precisely as possible and can markedly improve the seizure-free rate.

Supplementary data.

Summary didactic slides and supplementary tables are available on the www.epilepticdisorders.com website.

Disclosures.

None of the authors have any conflict of interest to declare.

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TEST YOURSELF

(1) In the study, intraoperative neurophysiological monitoring included:

- A. somatosensory evoked potential (SSEP)
- B. motor evoked potential (MEP)
- C. both

(2) Which statement is correct according to this study?

- A. Once the amplitude of CMAP was attenuated or disappeared, the neurosurgeon was reminded promptly to trigger temporary cessation of surgical dissection and resection.
- B. CMAP was considered stable if the amplitude of CMAP did not reach 75% attenuation.
- C. CMAP was considered to irreversibly disappear if the amplitude of CMAP exceeded 75% attenuation and did not recover to baseline constantly.

(3) Which of the following holds true?

- A. Intraoperative neurophysiological monitoring can effectively protect motor function.
- B. Intraoperative neurophysiological monitoring is often unsuccessfully performed in young children.
- C. Intraoperative neurophysiological monitoring is affected by age, intelligence or consciousness.

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".