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Lateralization of interictal spikes after corpus callosotomy

Masaki Iwasaki [a,*], Nobukazu Nakasato [b], Yosuke Kakisaka [c], Akitake Kanno [d], Mitsugu Uematsu [c], Kazuhiro Haginoya [e], Teiji Tominaga [a]

[a] *Department of Neurosurgery, Tohoku University School of Medicine, Sendai, Miyagi, Japan*
[b] *Department of Epileptology, Tohoku University School of Medicine, Sendai, Miyagi, Japan*
[c] *Department of Pediatrics, Tohoku University School of Medicine, Sendai, Miyagi, Japan*
[d] *Department of Functional Brain Imaging, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Miyagi, Japan*
[e] *Division of Pediatric Neurology, Takuto Rehabilitation Center for Children, Sendai, Miyagi, Japan*

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HIGHLIGHTS

- Interictal spikes are lateralized to the epileptogenic hemisphere in some patients after callosotomy.
- Lateralization can be expected in the presence of structural lesions and/or longer inter-hemispheric latency.
- Analysis of pre-operative EEG spikes may predict the primary epileptogenic hemisphere before corpus callosotomy.

ABSTRACT

Objective: Corpus callosotomy may limit secondary bilateral synchrony into the primary epileptogenic hemisphere. This study investigated whether pre-operative EEG can predict post-operative spike lateralization.
Methods: The subjects included 14 patients with medically intractable drop attacks who underwent total corpus callosotomy. Pre-operative patterns of inter-hemispheric propagation were quantified by peak-latency analysis with the template-based spike averaging technique.
Results: Postoperative lateralization of interictal spikes was observed in 5 of the 14 patients. Inter-hemispheric latency was significantly longer in these 5 patients (mean 14.0 ms, range from 0 to 78 ms, versus mean 5.2 ms, range from 0 to 29 ms, $p < 0.01$). The lateralization occurred in association with the presence of structural lesions ($p < 0.05$). The post-operative spikes were lateralized to the lesion side in 3 of 4 patients with unilateral epileptogenic lesion. Three patients presented one-way inter-hemispheric propagation pattern pre-operatively. The post-operative spikes were lateralized to the hemisphere of the leading spikes in two.
Conclusions: Interictal spikes are lateralized to the epileptogenic hemisphere in some patients after callosotomy. Lateralization can be expected in the presence of structural lesions and/or longer inter-hemispheric latency.
Significance: Analysis of pre-operative EEG spikes may predict the primary epileptogenic hemisphere before corpus callosotomy.
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1. Introduction

Corpus callosotomy is a palliative treatment for intractable epilepsy in patients with epileptic foci not removable by surgery. Corpus callosotomy is intended to disrupt inter-hemispheric generalization of epileptic activities, which is especially effective in reducing "drop attacks" due to sudden tonic or atonic seizures (Wyllie, 1988; Maehara and Shimizu, 2001; Turanli et al., 2006; Tanriverdi et al., 2009). Generalized epileptiform activities or epilepsy are occasionally caused by focal epileptogenic lesions, especially in younger patients, and are conventionally called "secondary bilateral synchrony." Removal of the primary epileptogenic lesion is a valid treatment option in such cases.

Corpus callosotomy often results in dramatic changes in interictal spikes, such as desynchronization or lateralization of bilateral

* Corresponding author. Address: 1-1 Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8574, Japan. Tel.: +81 22 717 7230; fax: +81 22 717 7233.
E-mail address: epinetmi@gmail.com (M. Iwasaki).

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spikes (Spencer et al., 1993; Oguni et al., 1994; Matsuo et al., 2003). Post-callosotomy lateralization of epileptiform discharges may reveal epileptic foci in one hemisphere, thus providing a secondary guide to subsequent surgery (Clarke et al., 2007; Nakayama et al., 2009). However, no systematic studies have evaluated the pre-operative EEG patterns associated with post-operative spike lateralization.

This study investigated whether inter-hemispheric latency of pre-operative epileptiform spikes is associated with post-operative spike lateralization.

2. Methods

2.1. Subjects

The study subjects included 14 consecutive patients with intractable epilepsy who underwent one-stage total corpus callosotomy for alleviation of "drop attacks." The patient characteristics are summarized in Table 1. The etiology was cryptogenic in 8 patients and symptomatic in 6 patients. All patients were diagnosed with West syndrome at the time of onset of epilepsy, and had epileptic seizures intractable to available medical therapies. Drop attacks due to sudden tonic or atonic seizures occurred as one of their main seizure types. Median post-operative follow up was 12 months, ranging from 6 to 28 months.

2.2. EEG recording

Routine interictal EEG in the wakeful and sleeping states were recorded for approximately 60 min before and after corpus callosotomy. Post-operative EEG was performed within 30 days after surgery in 10 patients (mean 12.3 days, range from 7 to 21 days). Cases 3 and 4 underwent post-operative EEG at 350 and 190 days after surgery, respectively. Scalp electrodes were placed according to the international 10–20 system. The EEG was digitized at 500 Hz and stored for offline analysis (Nihon-Kohden Co., Tokyo, Japan).

2.3. Inter-hemispheric latency analysis

Inter-hemispheric latency was measured using averaged interictal spikes in the pre-operative EEG. The process of averaging is schematically shown in Fig. 1. Longitudinal bipolar montage was used to review the EEG. Template-based searching and averaging of spikes were performed using commercially available software (BESA 5.2.2; BESA GmbH, Gräfelfing, Germany). In the analysis, 4 or 5 representative spikes were first identified by visual inspection as "templates." If different types of spike topographies were observed in a patient, at least one representative spike of each type was included in these templates. For each template, the EEG epoch of 80 ms before and 50 ms after the spike peak was marked in the channel with highest amplitude. This single-channel epoch was used for subsequent pattern search through the entire EEG recording. For this search, both the template and the EEG were band-pass filtered between 2 and 35 Hz and the correlation between the template and the EEG was calculated at each peak in the marked channel with highest amplitude. At peaks with a correlation >85%, tags were set for fast inspection of the aligned detected segments. This allowed for easy visual scanning and rejection of rarely occurring highly correlated artifacts prior to averaging. Thus, for each patient 4 or 5 artifact-free averaged spikes were generated. The details of the method were described in previous studies (Scherg et al., 2002; Bast et al., 2004). Lastly, inter-hemispheric latency was calculated as the peak time difference of the averaged spike between the left and right hemispheres. The peak was determined on the channel used for template and on the contralaterally homologous channel. The inter-hemispheric latency and side of the leading hemisphere were correlated with the post-operative EEG findings. The Mann–Whitney *U* test was used to compare non-parametric continuous variables.

3. Results

3.1. Pre-operative EEG

Pre-operative EEG was characterized by the presence of generalized or bilaterally synchronized spikes in 11, multifocal spikes of

Table 1
Pre- and post-operative EEG findings, and seizure outcome.

Case	Age/Sex	Etiology	Pre-op EEG spikes*	Post-op EEG spikes*	Seizure outcome	
					Drop attacks	Other seizure types
1	7/F	Cryptogenic	Multifocal (Rt T–O, Lt P–O, Lt F)	Lt hemisphere	Seizure free	50% reduction
2	1/F	Tuberous sclerosis (Bilateral multiple tubers)	Multifocal and generalized	Rt P–O	Seizure free	50% reduction
3	14/M	Infantile hemiplegia (Lt hemisphere infarct)	Lt F–T	Lt F–T	Seizure free	Seizure free
4	8/F	Tuberous sclerosis (Rt frontal tuber)	Lt F–T	Rt F	90% reduction	No improvement
5	7/M	Traumatic lesion (Lt occipital lobe)	Generalized spike wave complex	Lt hemisphere	Seizure free	>90% reduction
6	15/F	Sturge-Weber syndrome (Lt occipital angioma)	Generalized	Rt O, Lt F–C	>50% reduction	No improvement
7	7/F	Smith-Magenis syndrome (normal MRI)	Generalized	Lt P–O, Rt P–O	Seizure free	>90% reduction
8	20/M	Cryptogenic	Generalized	Rt FC, Rt P–O, Lt F, Lt C–P	Seizure free	<50% reduction
9	5/M	Cryptogenic	Generalized maximum C–P	Lt P, Rt P	Seizure free	>90% reduction
10	14/F	Cryptogenic	Generalized and Lt hemisphere	Lt hemisphere, Rt hemisphere	Seizure free	<50% reduction
11	10/M	Cryptogenic	Multifocal and generalized	Multifocal and generalized	No improvement	No improvement
12	6/M	Cryptogenic	Generalized slow spike wave complex	Lt P–O, Rt P–O	Seizure free	Seizure free
13	4/F	Cryptogenic	Generalized slow spike wave complex	Lt hemisphere, Rt F–C	Seizure free	Seizure free
14	4/F	Cryptogenic	Generalized slow spike wave complex	Lt F–C, Lt C–P, Rt F–C	Seizure free	Seizure free

F: frontal, T: temporal, C: central, P: parietal.
* Region of maximum amplitude of epileptiform spikes. Not described when the areas of maximum cannot be specified.

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