Original article

Epileptic Disord 2015; 17 (4): 425-35

Characterization of ictal slow waves in epileptic spasms

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Received July 03, 2015; Accepted October 25, 2015

ABSTRACT – We characterized the clinico-neurophysiological features of epileptic spasms, particularly focusing on high-voltage slow waves during ictal EEG. We studied 22 patients with epileptic spasms recorded during digital video-scalp EEG, including five individuals who still had persistent spasms after callosotomy. We analysed the duration, amplitude, latency to onset of electromyographic bursts, and distribution of the highest positive and negative peaks of slow waves in 352 spasms. High-voltage positive slow waves preceded the identifiable muscle contractions of spasms. The mean duration of these positive waves was 569±228 m, and the mean latency to electromyographic onset was 182±127 m. These parameters varied markedly even within a patient. The highest peak of the positive component was distributed in variable regions, which was not consistent with the location of lesions on MRI. The peak of the negative component following the positivity was distributed in the neighbouring or opposite areas of the positive peak distribution. No changes were evident in the pre- or post-surgical distributions of the positive peak, or in the interhemispheric delay between both hemispheres, in individuals with callosotomy. Our data imply that ictal positive slow waves are the most common EEG changes during spasms associated with a massive motor component. Plausible explanations for these widespread positive slow waves include the notion that EEG changes possibly reflect involvement of both cortical and subcortical structures.

Key words: epileptic spasms, high-voltage positive slow waves, scalp electroencephalography

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doi:10.1684/epd.2015.0783

Epileptic spasms are characterized by brief contractions, typically involving the axial muscles and proximal limb segments (Fusco and Vigevano, 1993). Motor phenomena are normally symmetric, but a variety of asymmetric or focal signs can be observed during events. Fragmentary motor phenomena such as eye movements, grimaces, motionless stare, or autonomic manifestations often accompany epileptic spasms (Kellaway *et al*., 1979; Fusco and

Vigevano, 1993; Watanabe *et al*., 2001), and sometimes these subtle seizures alone occur in series. In addition, other motor components such as sustained muscle contractions, motion arrest, and decreased consciousness, following the massive motor phenomena, may be observed. This variable semiology may make it difficult to identify spasms.

The pathological mechanisms giving rise to epileptic spasms remain largely unknown. The cortex and subcortical structures, including the brainstem, thalamus, and basal ganglia, have been implicated (Avanzini *et al*., 2002; Chugani, 2002). Previous studies have identified three patterns of ictal EEG during spasms:

– fast waves or high frequency oscillations (HFOs) preceding spasms;

– high-voltage slow waves;

– desynchronization of electrical activity (Fusco and Vigevano, 1993; Vigevano *et al*., 2001; Kellaway *et al*., 1979; Watanabe *et al*., 2001).

Emergence of fast waves or HFOs accompanying spasms suggests neocortical involvement in the genesis of the spasms, and that these have a localizing value since their distribution is correlated with the localization of the epileptogenic brain lesions (Kobayashi *et al*., 2004; Akiyama *et al*., 2005; Asano *et al*., 2005; Panzica *et al*., 2007; Nariai *et al*., 2011a). These electrical changes coincide with the initial minor components of the spasms, including eye deviation and grimaces. In subtle seizures with very slight motor phenomena such as only motionless stare, we only see these fast activities as ictal EEG changes. Desynchronization of the electrical activity can be seen at the end of a spasm, which is typically accompanied by periods of motion arrest after the massive motor phenomenon. On the other hand, the high-voltage slow waves coincide with the phasic motor component in almost 100% of spasms with massive muscle contractions (Fusco and Vigevano, 1993; Watanabe *et al*., 2001).

Given that the ictal slow waves are essential EEG changes in epileptic spasms with a motor component, characterization of their waveforms and origins is very important for understanding the pathophysiological mechanisms underlying the spasms. However, these issues have not been well delineated. Some studies have speculated that such ictal slow waves might be far-field potentials generated by the subcortical structures (Fusco and Vigevano, 1993), while others have suggested that these waves might be generated in the neocortex (Panzica *et al*., 1999; Kobayashi *et al*., 2005).

Furthermore, beneficial effects of callosotomy for epileptic spasms have been reported (Pinard *et al*., 1993; Suzuki *et al*., 2013). The authors of these studies postulated that the corticocortical pathway through the corpus callosum was important in the generalization of hypsarrhythmia, because the bilateral hypsarrhythmia before surgery was lateralized and the spasms became asymmetric after callosotomy. However, ictal EEG changes after callosotomy have not been described.

In this study, we investigated the clinico-neurophysiological features of epileptic spasms, particularly focusing on the high-voltage slow waves accompanying the spasms, with the aim of obtaining information about the pathophysiology of these spasms.

Subjects and methods

Subjects

We enrolled 22 patients with epileptic spasms for this study, who were admitted to the Department of Child Neurology of the National Center of Neurology and Psychiatry (NCNP) or the Department of Pediatrics of Juntendo University Faculty of Medicine from 2006 to 2013, and underwent ictal EEG recording of epileptic spasms. We retrospectively collected clinical profiles from medical charts and reviewed the video-EEG recordings. This study was approved by the institutional review board of the NCNP.

EEG recordings and data analysis

Scalp EEG was recorded using Neurofax (Nihon-Kohden, Japan), with electrodes placed in the international 10-20 scalp-electrode position. Sampling rate was set at 200 Hz (Patient 4 and 22), 500 Hz (Patients 11, 12, and 21), and 1 kHz (Patients 1-3, 5-10, and 13-20). EEG and surface electromyography (EMG) were low-cut filtered at 0.53 Hz and 5.3 Hz, respectively. High-cut filter was set at 60, 120, 300 Hz, depending on the sampling rate. Surface EMG electrodes were placed on both deltoid muscles to identify the onset and duration of spasms. All subjects were examined with a digital video-EEG monitoring system to assess clinical manifestations. The present study targeted spasms that showed distinctive deltoid EMG bursts, and excluded those with non-negligible artefacts on EEG. Surface EMG essentially showed a characteristic crescendo-decrescendo pattern with a diamond-shaped configuration, as previously described by Fusco (Fusco and Vigevano, 1993). The ictal EEG recordings were visually examined using an expanded time scale and an appropriate amplitude display, in order to evaluate the EEG waveform preceding and/or following spasm onset more precisely.

We analysed characteristics of ictal EEG change, particularly focusing on the positive slow waves accompanying the epileptic spasms, including the duration (duration from the beginning of a positive component to the succeeding negative peak), amplitude, and delay of EMG onset (latency from the

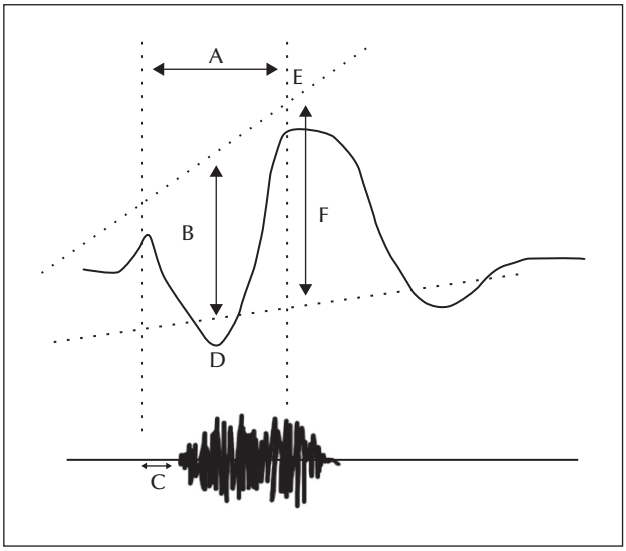

Figure 1. Parameters used for the analysis of ictal EEG waveforms. (A) Duration was defined as the interval between the beginning of a positive component and the succeeding negative peak. (B) Amplitude of positivity was defined as the height from the peak of a positive component to the tangential line between the negative peaks before and after the positivity. (C) Delay of electromyography (EMG) onset was measured from the beginning of a positive slow wave to the onset of EMG burst. (D) Positivity peak; (E) succeeding negativity peak. (F) Amplitude of negativity was measured by the vertical height of a negative peak from the tangential line between the positive peaks before and after the negativity.

onset/beginning of positive slow wave to the onset of EMG bursts) (*figure 1*). For quantitative analysis, 6-20 artefact-free tracings were randomly selected from each patient. Distribution of the highest peak of the positive and negative components was also analysed by using a topographic map of the potential field distribution of each slow wave with common average reference montages. Interhemispheric time delay was defined as the periods between the highest peaks of positivity in both hemispheres. We also analysed fast activity accompanying spasms in terms of frequency and distribution. The mean duration, amplitude, and interhemispheric time delay of positive slow waves, as well as the mean frequency of fast activity, were calculated for each patient using data from all the captured spasms. In 11 patients who exhibited a unilateral lesion on MRI (Patients 1-3, 5-9, 12, 15, and 16), we examined the difference in amplitude between the lesioned side and the non-lesioned side. Mann-Whitney U-tests were used for statistical analysis and $p<0.05$ was regarded as significant.

Five individuals (Patients 3, 5, 12, 21, and 22), who underwent callosotomy but still suffered from persistent spasms, were also analysed for changes in the aforementioned parameters of positive slow waves before and after the surgery.

Results

Patient characteristics

The study included 13 boys and nine girls (*table 1*). The mean age at investigation was 37.5 months (range: 1-180), and the mean age at onset of spasms was 14.8 months (range: 0-102). Sixteen patients (72.7%) had onset before the age of 1 year, whereas three of the remaining six patients had a later onset, after the age of 3 years. Structural brain abnormalities were identified in 16 patients (seven with focal cortical dysplasia; two with hemimegalencephaly; two with lissencephaly; one with tuberous sclerosis complex; one with polymicrogyria; one with haemorrhage of hemangioma; one with hemiconvulsion-hemiplegia-epilepsy syndrome after meningitis; and one with dysembryoplastic neuroepithelial tumour). No abnormality was detected on MRI, and no genetic disorder or disorder of inborn errors of metabolism had been identified in the remaining six patients. At the period of ictal EEG recordings, the interictal background EEG activity in the patients included hypsarrhythmia (n=5), suppression-burst pattern (n=2), disorganized activity with focal or multifocal epileptic discharges (n=11), and diffuse spike-/polyspike-wave activity (n=4).

Clinical features of spasms

We analysed 344 spasms. These could be subdivided into five types by clinical manifestation and ictal EMG:

– symmetric spasms (n=118 in 13 patients);
– asymmetric spasms (n=168 in seven patients);
– spasms with atonic phase (n=29 in two patients);
– spasms followed by decreasing consciousness (n=6 in one patient);
– spasm-tonic seizure, spasm followed by sustained tonic contractions (n=23 in three patients).

Eleven patients had other types of seizures besides spasms (eight with tonic seizure; one with tonic and clonic seizure; one with myoclonic seizure; and one with complex partial seizure), and 10 of them had structural brain abnormalities.

Spasms occurred in clusters, but single spasms were observed in three elder patients (Cases 13, 16, and 22). Different types of spasms from the subdivided types described above were seen in 13 patients regardless of the presence of MRI lesions in their brain. Half of the patients with structural lesions, and five of six patients without lesions, had symmetric spasms. Asymmetric spasms were seen not only in patients with structural abnormalities but also in those without lesions.

Table 1. Patient characteristics.

Patient	Gender	Age (Months)	Age at onset (Months)	Aetiology	Interictal EEG	Cluster/ single	Type of spasms	Other seizure type
1	F	1	0	FCD	Focal discharges	Cluster	Asymmetric	Tonic
2	M	4	3	FCD	Focal discharges	Cluster	Symmetric/ asymmetric	Myoclonic
3	F	9	2	FCD	Focal discharges	Cluster	Symmetric/ asymmetric	None
4	M	12	2	FCD	Multifocal discharges	Cluster	Asymmetric	None
5	F	12	5	FCD	Focal discharges	Cluster	Symmetric/ asymmetric	None
6	M	40	14	FCD	Focal discharges	Cluster	Symmetric / atonic	None
7	M	24	4	FCD	Focal discharges	Cluster	Symmetric/ asymmetric	CPS
8	F	2	1	HME	Suppression-burst	Cluster	Spasm-tonic	Tonic, clonic
9	M	2	2	HME	Suppression-burst	Cluster	Symmetric / asymmetric	None
10	M	5	4	Lissen-cephaly	Multifocal discharges	Cluster	Asymmetric	Tonic
11	F	9	8	Lissen-cephaly	Multifocal discharges	Cluster	Asymmetric	Tonic
12	F	37	3	Polymi-crogyria	Hypsarrhy-thmia	Cluster	Symmetric / spasm-tonic	Tonic
13	M	180	7	TSC	Diffuse SWC	Single	Spasm-tonic	Tonic
14	F	90	51	Haemo-rrhage of heman-gioma	Diffuse SWC/PSW	Cluster	Symmetric	None
15	M	118	60	DNT	Focal discharges	Cluster	Asymmetric	Tonic
16	M	56	20	HHE	Multifocal discharges	Single	Asymmetric/ spasm-tonic	Tonic
17	M	4	1	Unknown	Hypsarrhy-thmia	Cluster	Symmetric/ asymmetric	None
18	M	11	4	Unknown	Hypsarrhy-thmia	Cluster	Symmetric/ asymmetric	None

Table 1. *(Continued).*

Patient	Gender	Age (Months)	Age at onset (Months)	Aetiology	Interictal EEG	Cluster/ single	Type of spasms	Other seizure type
19	F	12	8	Unknown	Hypsarrhythmia	Cluster	Symmetric/ asymmetric	None
20	F	12	4	Unknown	Hypsarrhythmia	Cluster	Symmetric/ asymmetric	None
21	M	36	21	Unknown	Diffuse SWC/PSW	Cluster	Symmetric / atonic	Tonic
22	M	148	102	Unknown	Diffuse SWC	Single	Followed by consciousness decreasing	None

DNT: dysembryoplastic neuroepithelial tumour; EEG: electroencephalography; FCD: focal cortical dysplasia; HHE: Hemiconvulsion-hemiplasia epilepsy syndrome; HME: hemimegalencephaly; PMG: polymicrogyria; PSW: polyspike and wave; SWC: spike and wave complex; TSC: tuberous sclerosis complex.

Ictal EEG findings of spasms

In all spasm types, high-amplitude slow waves with positive polarity always accompanied the EMG bursts (*figure 2 and table 2*). These positive slow waves were widespread, but with localized fields on essentially all occasions. On bipolar montage, the positive potential appeared as an inverse phase reversal (Fusco and Vigevano, 1993) at the channel with the highest amplitude on referential recording (*figure 3*).

Regarding each seizure type, symmetric spasms were characterized by a diamond-shaped appearance in the EMG with bilateral synchrony (*figure 2A and 2B*), whereas asymmetric spasms had differences in the EMG amplitude between the bilateral deltoid muscles and were often asynchronous at onset of EMG (*figure 2C*). In spasms with atonic phase, patients lost muscle tone for a few hundred milliseconds after brief muscle contraction due to a spasm (*figure 2D*). In spasms followed by decreasing consciousness, positive slow waves on the EEG and diamond-shaped EMG were followed by a low-amplitude fast rhythm for 1-6 seconds with alterations in consciousness and ocular fluttering or head deviation (*figure 2E*). Spasm-tonic seizure was characterized by the evolution of recruiting rhythm corresponding to a longer tonic phase, lasting 2-10 seconds, after the positive slow waves and diamond-shaped EMG (*figure 2F*).

Electro-positive high-voltage slow waves coincided with all the spasms, in the form of positive-negative or negative-positive biphasic polarity, or negative-positive-negative triphasic polarity. The descending slope of the positive slow waves always preceded the onset of the EMG change. Considering the characteristics of these positive slow waves, the mean duration was 569±228 m and the mean amplitude was 297±214 μV. The mean delay of EMG onset was 182±127 m. The variation of latency was marked not only between patients, but also within each patient. The interhemispheric delay of the peak of the preceding side was not fixed in individual subjects. Although the amplitude often appeared higher on the lesion side than the non-lesion side in the patients with MRI lesion (the mean amplitude of the lesion side and non-lesion side was 382±215 μV and 301±130 μV, respectively), the interhemispheric difference was not statistically significant (p=0.130). Eighteen (12 symptomatic patients and six cryptogenic patients) of 22 patients showed fast activity preceding the positive slow wave (*figure 2C*), with a frequency of 19±2 Hz, the distribution of which was consistent with the hemisphere of the lesion side in the patients with MRI lesion, however, their distributions were not always consistent with those of the positive peak.

We also investigated the distribution of the peak of the positive component of the slow waves. The highest peak was distributed often in the fronto-central areas, however, posterior distribution was also observed in Patients 2, 3, 11, 12, 15, 20, and 21 (*figures 2B and 4*). Nevertheless, the positive polarity did not change wherever it appeared. *Figure 4* demonstrates the pattern of distribution of the positive and negative components of the slow waves. We could see the positive component on the midline region including Fz, Cz, and Pz in most cases. In addition, the positive peak distribution was not always consistent with the lesions

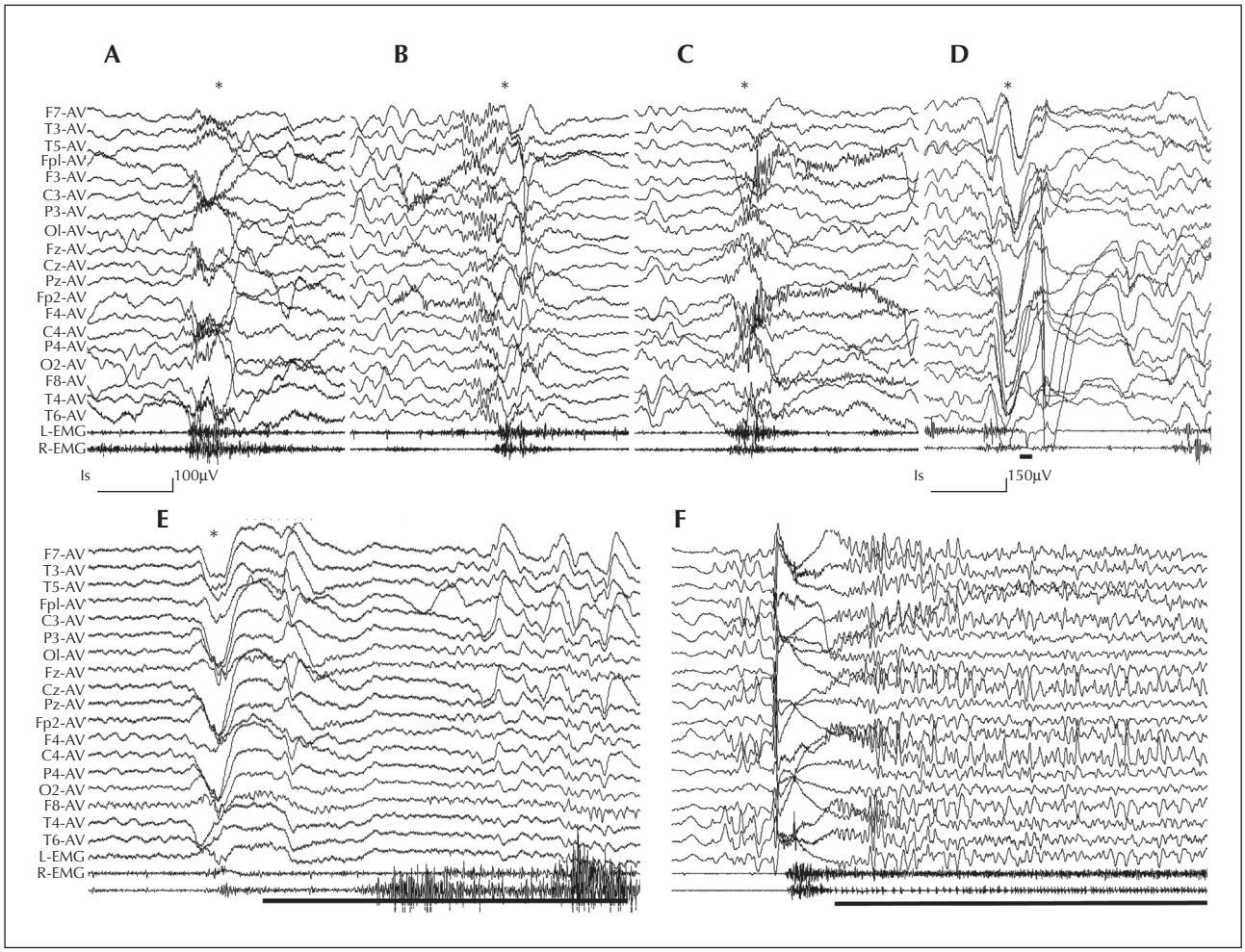

Figure 2. Ictal EEG patterns for each type of spasm using common average reference montages. Asterisks indicate the point of the peak of positive slow waves. (A and B) Symmetric spasm ([A] Patient 5; [B] Patient 20); symmetric and synchronous electromyography (EMG) bursts are seen bilaterally on these tracings. The positive slow waves with the highest amplitude are distributed at the bifrontal areas in (A), and at T4/T6 in (B). (C) Asymmetric spasm (Patient 5); deltoid EMG burst is predominant on the left side. Note that the fast activity preceding the spasm distributes over the right hemisphere, and the positivity of the ictal slow waves is most prominent at the Fp2 electrode. (D) Spasm with atonic phase (Patient 21); the lower bar shows the period of atonic phase. Muscle tone is attenuated for about 200 milliseconds immediately after the brief muscle contraction. (E) Spasm followed by decreasing consciousness (Patient 22); the lower bar shows the period of decreased consciousness confirmed on video monitoring. (F) Spasm-tonic seizure (Patient 13); spasm followed by sustained muscle contraction.

on the MRI in the patients with structural abnormalities. Interestingly, the peak of the negative component following the positive peak was distributed in the surrounding area or even in the opposite area of the positive peak distribution.

Five patients underwent callosotomy, but unfortunately suffered from persistent refractory spasms (*table 3*). Two of them had anterior callosotomy and the others had total callosotomy. After callosotomy, the distribution of the peak of the positive slow waves did not significantly change or lateralize. In addition, interhemispheric delay between the hemispheres did not change significantly (p=0.305).

Discussion

Clinical manifestation of epileptic spasms is either monophasic, with simple muscle contraction, or biphasic, accompanied by components such as tonic phase, atonic phase, and decreasing consciousness. However, in ictal EEG, high-voltage positive slow waves are common to all types of spasms accompanying EMG change. The ictal EEG activities associated with the spasms have been described as complex and variable waveforms, consisting of fast activity, slow wave, and decremental pattern with background attenuation. Among these patterns, previous studies have

Table 2. Ictal EEG findings.

Patient	MRI lesion	No. of analysed spasms	Positive slow wave				Fast activity	
			Duration (ms)	Amplitude (μV)	Delay of EMG onset after positivity onset (ms)	Interhemispheric delay of positivity peak (ms)	Frequency (Hz)	Distribution
1	Lt. TPO	15	778 ± 175	314 ± 74	186 ± 167	110 ± 104	25 ± 3	Lt FC
2	Lt. Fp	10	652 ± 216	193 ± 48	223 ± 204	126 ± 117	15 ± 3	Lt CP
3	Lt. TPO	20	523 ± 232	231 ± 60	277 ± 114	99 ± 89	17 ± 2	Lt CPT
4	Both frontal	20	704 ± 313	482 ± 207	133 ± 78	48 ± 19	18 ± 2	Rt CP
5	Rt. Fp	20	730 ± 169	179 ± 86	108 ± 48	67 ± 44	18 ± 3	Rt FCP
6	Rt. T	20	443 ± 129	231 ± 105	171 ± 100	48 ± 20	20 ± 2	Rt T
7	Lt. P	10	449 ±103	120 ± 104	97 ± 46	40 ± 21	None	None
8	Lt. hemisphere	5	522 ± 67	411 ± 183	191 ± 33	17 ± 1	22 ± 5	Lt. hemisphere
9	Rt. hemisphere	20	502 ± 161	165 ± 84	153 ± 98	60 ± 30	20 ± 3	Rt FC
10	Both hemisphere	20	323 ± 171	673 ± 232	333 ± 132	36 ± 37	16 ± 6	Rt P
11	Both hemisphere	20	492 ±278	417 ± 344	228 ± 95	56 ± 35	None	None
12	Lt. FCPT	10	529 ± 244	202 ± 103	151 ± 87	36 ± 16	14 ± 3	Lt FC
13	Multiple	7	512 ± 43	318 ± 67	159 ± 27	77 ± 48	None	None
14	Both FTP	11	535 ± 69	217 ± 147	202 ± 147	39 ± 21	18 ± 1	Diffuse
15	Rt. P	20	628 ± 136	628 ± 179	144 ± 189	46 ± 9	18 ± 2	Diffuse
16	Lt. hemisphere	10	460 ± 251	145 ± 49	43 ± 20	153 ± 70	None	None
17	No lesion	20	423 ± 74	106 ± 34	116 ± 64	83 ± 62	18 ± 1	Diffuse
18	No lesion	20	569 ± 63	290 ± 95	198 ± 63	43 ± 26	19 ± 1	Diffuse
19	No lesion	20	703 ± 361	107 ± 47	109 ± 58	61 ± 14	16 ± 2	Diffuse
20	No lesion	20	414 ± 76	145 ± 30	86 ± 40	32 ± 6	25 ± 3	Diffuse
21	No lesion	20	541 ± 66	549 ± 52	299 ± 239	34 ± 19	25 ± 2	Diffuse
22	No lesion	6	798 ± 17	620 ± 29	42 ± 3	44 ± 12	18 ± 2	Rt CP

CP: centro-parietal; CPT: centro-parieto-temporal; EEG: electroencephalography; EMG: electromyography; FCP: fronto-centro-parietal; FCPT: fronto-centro-parieto-temporal; Fp: frontal pole; Lt: left; MRI: magnetic resonance imaging; P: parietal; Rt: right; T: temporal; TPO: temporo-parieto-occipital.

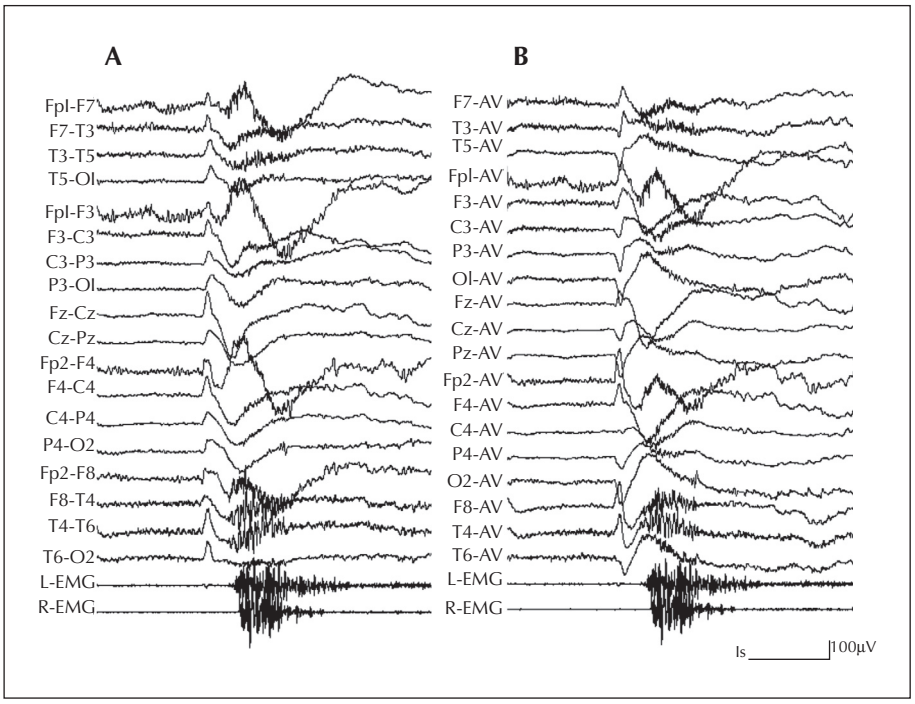

Figure 3. Ictal EEG in Patient 15. (A) Bipolar montage; inverse phase reversals are seen at F3 and F4 channels. (B) Referential recording using common average reference; ictal positive waves are more prominent in F3 and F4 channels than in Fp1 and Fp2.

regarded the slow waves as the most essential component (Fusco and Vigevano, 1993; Gaily *et al*., 1995; Kobayashi *et al*., 2005; Vigevano *et al*., 2001; Watanabe *et al*., 2001). Although the fast activity alone may be the only ictal EEG change, the associated clinical manifestation was a motionless stare (Vigevano *et al*., 2001), thus it seems to be the EEG equivalent of the "subtle spasms". Consistent with these assumptions, the positive slow waves were present in all the spasms that were strong enough to manifest as deltoid EMG changes in our series. This means that the positive slow waves could be of the highest diagnostic value for the spasms with apparent motor components.

As a limitation of common average reference for data analysis, we cannot rule out the possibility that large signal deflections at a few channels may have altered the voltage of reference and resulted in noticeable alteration of ictal EEG waves at the remaining channels on some occasions. However, the onset of slow waves before the EMG change suggested that these electrographic changes were not artefacts, presumed to be generated by the brain. In addition, these slow EEG components were different artefacts or electrode pops in that these slow waves were predominant in areas other than Fp1/Fp2 channels on most occasions, and were often localized but distributed in more than one electrode (*figures 2 and 3*).

Our finding that the distribution of the slow wave peaks was not consistent with the structural brain lesions and extended widely, including the midline region, implies that these slow waves do not represent the epilepsy focus triggering the spasms. Further, we found that the distribution of positive slow waves was not concordant with that of preceding fast activity, which is assumed to be involved in the neocortical genesis of the spasms. This fact implies that these slow waves do not represent the trigger activity of epileptic spasms. Akiyama *et al*. analysed the slow EEG components and fast activity using intracranial EEG and found that the slow EEG components were concordant temporally but not spatially with fast activity (Akiyama *et al*., 2015), which supported our results. They suggested that the slow waves were unlikely to reflect the inhibitory process within the local cortex generating the fast components, and hypothesized that this might not be the cortical response arising from the surrounding area of the epileptogenic site.

In our series, the morphology of slow waves and the latency to the onset of EMG change were not fixed even within the same patient. Distribution of the slow waves varied among patients, involving the frontal, central, temporal, or parietal areas. Although it is reasonable to suppose that these slow waves represent the electrical change associated with motor components of spasms, the intra- and interpersonal variations in the clinical patterns of the motor phenomenon may be related to the variations in the parameters of the slow waves.

Kobayashi *et al*. described that the positive and negative slow waves were prominent over the fronto-temporal and posterior regions, respectively

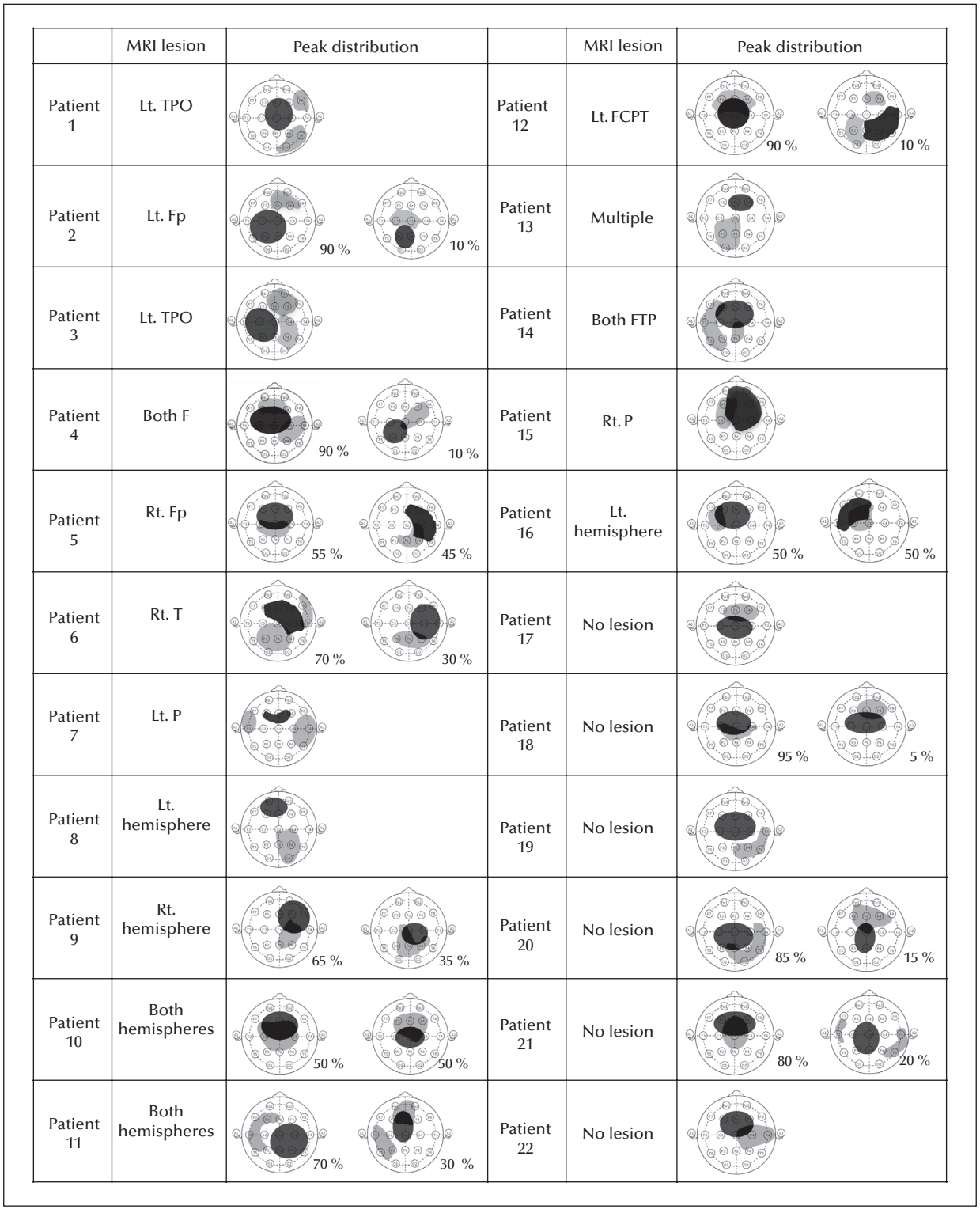

Figure 4. The distribution of the positive and negative components of the ictal slow waves during spasms. Dark grey areas represent the distribution of the positive component with highest amplitude, and light grey areas represent the distribution of the successive negative component with highest amplitude. Different distribution patterns among the total ictal records were identified in 12 individual patients, and the proportion of these patterns are shown in individual cases.
CP: centoro-parietal; CPT: centro-parieto-temporal; F: frontal; FCP: fronto-centro-parietal; FCPT: fronto-centro-parieto-temporal; Fp: frontal pole; Lt: left; P: parietal; Rt: right; T: temporal; TPO: temporo-parieto-occipital.

Table 3. Characteristics of patients who underwent callosotomy

Patient	Before callosotomy				After callosotomy		
	Age (months)	Lesion	Distribution of positivity peak	Interhemispheric delay between hemispheres	Time after callosotomy (months)	Distribution of positivity peak	Interhemispheric delay between hemispheres
3	5	Lt TPO	C3/T3/P3/Cz	99 ± 89 ms	2	F3 or Cz	93 ± 18 ms
5	12	Rt Fp	Fz/Cz/C or Fz/F4/C4/T4/T6	67 ± 44 ms	4	Fz/Cz	43 ± 19 ms
12	37	Lt FCPT	Fz/Cz/C	36 ± 16 ms	9	C3/Cz	71 ± 5 ms
21	26	Unknown	F/Fz or Cz/Pz	34 ± 19 ms	4	Fz/Cz	49 ± 21 ms
22	148	Unknown	F/Fz/Cz	44 ± 12 ms	8	Fz	39 ± 5 ms

Fp: frontal pole; FCPT: fronto-centro-parieto-temporal; Lt: left; Rt: right; TPO: temporo-parieto-occipital.

(Kobayashi *et al*., 2005). In the present study, despite the wide distribution of slow waves, they were observed most frequently in midline areas propagating frontal, central, and parietal areas. These correspond to the primary motor cortex, supplementary motor area, premotor cortex, and parietal lobe that are strongly connected with the premotor cortex. The ictal slow waves may represent the involvement of the motor association cortex in the motor manifestation of spasms. On the contrary, after callosotomy, there were no significant changes in the bilateral distribution or any parameters of the slow waves, which indicate that these slow waves did not originate from the cortico-cortical pathway via the corpus callosum, but rather from the cortico-subcortico-cortical pathway. Hence, subcortical structures may also play a role in the generation of slow waves as well as cortical responses.

Furthermore, we should note that the peak of the negative component following the positive component of slow waves was distributed in the surrounding or opposite area to the positive peak. The negative component may be representative of a response from the adjacent cortex to the positivity.

The generator of the primary motor component of spasms is still controversial. It has been hypothesized to be located in the brainstem (Chugani *et al*., 1992; Haginoya *et al*., 1999; Bisulli *et al*., 2002), and also in the cortex (Asano *et al*., 2005; Nariai *et al*., 2011b; de la Vaissiere *et al*., 2014). The widespread positive slow waves associated with spasms might reflect a spasm-related activity in both cortex and subcortical structures, however, the positive waves may not be epileptogenic, but represent an epiphenomenon accompanying spasms. In addition, we analysed EMG using only deltoid muscle electrodes in this series. Considering the variability of motor manifestation of spasms, analysis of more muscles and the influence of posture during spasms is needed. Furthermore, studies using electrocorticograms or deep brain electrodes are needed to prove that both the cortex and subcortical areas are involved. □

Disclosures.
None of the authors have any conflicts of interest to disclose.

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TEST YOURSELF

(1) Provide a brief description of the clinical presentation of epileptic spasms.

(2) What are the polymyographic features of epileptic spasms?

(3) What are the characteristics of ictal EEG of epileptic spasms?

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".