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# Cortical involvement in focal epilepsies with epileptic spasms

Sabine de la Vaissière[a,b], Mathieu Milh[e], Didier Scavarda[c], Romain Carron[d], Anne Lépine[a], Agnes Trébuchon[f], Martine Gavaret[f], Russell Hewett[f], Virginie Laguitton[a], Géraldine Daquin[a], Nathalie Villeneuve[a,e], Fabrice Bartolomei[a,f,*]

[a] *Hôpital Henri Gastaut, Marseille, France*
[b] *Service de Pédiatrie, Clocheville Hospital, CHRU Tours F-37000, France*
[c] *Service de Neurochirurgie Pédiatrique, Assistance Publique des Hôpitaux de Marseille, Marseille F-13005, France*
[d] *Service de Neurochirurgie fonctionnelle et Stéréotaxie, Assistance Publique des Hôpitaux de Marseille, Marseille F-13005, France*
[e] *Service de Neuropédiatrie, Assistance Publique des Hôpitaux de Marseille, Marseille F-13005, France*
[f] *Service de Neurophysiologie Clinique, Assistance Publique des Hôpitaux de Marseille, Marseille F-13005, France*

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**Summary** The pathophysiological mechanisms of epileptic spasms are still poorly understood. The role of subcortical structures has been suggested on the basis of non-localized EEG features and from experimental data. The description of asymmetric spasms associated with lateralized EEG patterns has challenged this view and raises the possibility of a cortical origin. This study investigated the cortical organization of partial seizures associated with epileptic spasms in children undergoing intracerebral EEG recordings for presurgical evaluation. Eleven children with drug resistant epileptic spasms and for whom depth electrode recordings were performed were retrospectively studied. In all children several features suggested a focal origin. Cortical involvement was studied using the ''Epileptogenicity Index'' (EI). A focal origin was finally demonstrated in 10/11 patients. Seven patients demonstrated pre-ictal changes in the seizure onset zone area. EI analysis showed maximal values in the temporal ($n = 5$), parietal ($n = 1$) or frontal ($n = 5$) cortices. EEG changes were also observed in the premotor cortex during spasms

* Corresponding author at: Service de Neurophysiologie Clinique, CHU Timone-264 Rue st Pierre, 13005 Marseille, France. Tel.: +33 491385833; fax: +33 491385826.
*E-mail address:* fabrice.bartolomei@ap-hm.fr (F. Bartolomei).

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in patients with frontal or parietal seizures and in 3/5 patients with temporal lobe seizures. Good surgical outcome (class I or II) was obtained in 7/10 patients.
Seizures associated with epileptic spasms may originate from various cortical regions. Premotor/motor cortices are probably involved in determining ictal clinical changes.


## Introduction

Since the most recent classification proposed by the ILEA, the clinical entity of epileptic spasms (ES) has been separated from West syndrome and constitutes a distinct type of seizure (Berg et al., 2010). However their pathophysiology remain unknown such that at present it has been difficult to class them as either generalized or partial seizures.

The following clinical description is commonly recognized: an axial contraction, more often flexion than extension, brief and sudden, lasting from 0.2 to 2 s, occasionally recurring in short clusters separated by periods lasting between 5 and 20 s (Holmes and Vigevano, 1997). They occur typically in infancy (6—12 months) but they may occur at a later stage of life (Gobbi et al., 1987). In addition, some patients with ES may have other types of epileptic seizures, most commonly partial seizures (Kubota et al., 1999; Pachatz et al., 2003). In these cases surgical treatment may lead to seizure remission and neurocognitive improvement (Jonas et al., 2005; Ricard-Mousnier et al., 2012)

Epileptic spasms were initially considered as originating sub-cortically (Gastaut et al., 1964), but a cortical origin of the spams has alternatively been suggested, in particular from the results of cortical surgery (Asano et al., 2001). Furthermore, more recent animal models also support the hypothesis of cortical involvement in the genesis of ES (Scantlebury et al., 2010).

Few studies have analyzed intracerebral EEG recordings in this context (Asano et al., 2005; Ricard-Mousnier et al., 2012). A corticographic study of 62 spasms from patients suffering from tuberous sclerosis suggested that spasms were elicited by a cortical onset (Asano et al., 2005). Two patterns of discharges were described in this study, a first type with a localized spike followed by fast activity or a second type without a focal spike.

Our objective was to study the cortical organization of partial seizures associated with ES in children undergoing intracerebral EEG recordings for presurgical evaluation. We have analyzed the ictal IcEEG characteristics in children with pharmacoresistant ES, for whom intracerebral EEG recordings were proposed due to a suspected focal onset.

## Material and methods

### Patients and EEG recordings

This retrospective study analyzed the IcEEG of children with pharmacoresistant ES recorded at the hospital La Timone in Marseilles, France. They were selected from 280 intracerebral investigations between 2002 and 2012. All the patients with ongoing ES that had IcEEG were included in this retrospective study.

Non-invasive pre-surgical recordings (pre-surgical assessment Phase 1) were performed at the hospitals Henri Gastaut or La Timone in Marseilles. The EEG trace was performed using 20 scalp electrodes, following the international 10—20 system. Additional polygraphic recordings were composed of EMG of both deltoids and ECG.

Pre-surgical assessment phase 2 consisted of IcEEG recordings over a number of days. It is performed following discussion by a multidisciplinary team, utilizing the clinical and imaging data, and the results from phase 1. The number and position of the implanted electrodes were also discussed.

The implantation of the intracerebral electrodes was performed in the neurosurgery departments. The adequate localization of the electrodes in the cerebral space was checked using 1.5 MRI or using a fusion of preimplatation MRI and CT scan with electrodes in place. ICEEG recordings were performed using intracerebral multiple contact electrodes (10—15 contacts: 2 mm diameter; 0.8 mm and 1.5 mm apart). The anatomical targeting and number of necessary electrodes was established in each patient according to the hypotheses for localization of the epileptogenic zone determined by the clinical data and EEG recordings from phase 1. Each electrode comprised of multiple contact points numbered 1 to 15.

The signals were recorded on a 196 channels Deltamed™ system. They were sampled at 512 Hz or 1024 Hz and recorded on hard disk (16bits/sample) using no digital filter. The only filter present in the acquisition process was a high-pass analog filter (cut-off frequency equal to 0.16 Hz) used to remove very slow non-physiological variations that sometimes contaminate the baseline. The video-EEG recordings were prolonged as long as necessary to capture several of the patient's habitual seizures.

### Intracerebral EEG signal analysis: determination of the Epileptogenicity Index (EI)

For each seizure, the corresponding IcEEG trace was studied and the Epileptogenic Index (EI) was calculated. The objective was to better characterize the regions involved at seizure onset.

This quantification has been proposed in order to characterize the propensity of a given brain structure to generate a 'rapid discharge' (the high frequency oscillations observed during the transition between ictal and interictal activity) and takes into account the delay of appearance of this discharge with respect to seizure onset (Bartolomei et al., 2008, 2010, 2011). The purpose of this index is to provide quantified information about the behavior of brain structures recorded from signals they generate during the seizure process. This index summarizes two pieces of information