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What is the concordance between the seizure onset zone and the irritative zone? A SEEG quantified study

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HIGHLIGHTS

- A total of 539 brain regions from 32 patients were quantified both for spiking frequency (SI) and for seizure initiation (EI).
- A good concordance between regions with maximal EI and regions with maximal SI was found in 18/32 patients (56%).
- The proportion of patients with good concordance was ~75% in focal cortical dysplasia (FCD) group and only 33% in the non FCD group.

ABSTRACT

Objective: In focal epilepsies, the accurate delineation of the epileptogenic network is a fundamental step before surgery. For years, the relationship between the interictal epileptic spikes (defining the "irritative zone", IZ) and the sites of seizure initiation (SOZ) has been a matter of debate.
Methods: Our goal was to investigate from intracerebral recordings (stereoelectroencephalography, SEEG) the distribution of interictal epileptic spikes (based on a spike frequency index, SI) and the topography of the SOZ (based on the Epileptogenicity Index, EI) in patients having focal neocortical epilepsies. Thirty-one patients were studied. A total of 539 brain regions were quantified in term of both spike generation (SI) and seizure initiation (EI).
Results: We found a 56% (18/32) rate of agreement between maximal EI and maximal SI values. When considering separately patients with focal cortical dysplasia (FCD), the proportion of patients with good concordance was ~75% (15/20), whereas it was only 33% (4/12) in the non FCD group.
Conclusions: Our results show that a significant part of patients have some dissociation between regions showing pronounced spiking activity and those showing high epileptogenicity. e is clinically important.
Significance: For patients with these dissociations, other markers than spiking frequency remain to be investigated. In the FCD group, the good concordance between SI and EI confirms that the mapping of the irritative zone is clinically important.

1. Introduction

In focal epilepsies, the accurate delineation of the epileptogenic network is a fundamental step before surgery. For years, the relationship between the brain sites that generate interictal epileptic spikes (defining the so-called "irritative zone", IZ) and those involved in the initiation of seizures (seizure onset zone, SOZ)

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has been a subject of debate. The fact that interictal discharges can be seen in areas other than SOZ and in tissue distant from the lesional site has been described in the early works of Jasper and Penfield (Penfield and Jasper, 1954). They introduced the notion that not all spikes have the same pathological value and proposed the distinction between primary and propagated spikes suggesting that primary spikes were sharper and associated with structural lesions and/or abnormal background activity (Jasper et al., 1961). Since the beginning of intracerebral EEG investigations (especially stereoelectroencephalography, SEEG) it has also been observed that the IZ and SOZ may have complex relationships, as revealed by the possible dissociation between the topography of interictal epileptic spikes (IESs) and the seizure onset pattern, and it is generally recognized that the IZ is larger than the SOZ (Talairach and Bancaud, 1966). On this basis, most of the teams using SEEG have favored the analysis of seizures in order to identify the seizure onset zone and ultimately define the region(s) to be resected during surgery (Bancaud and Talairach, 1965; Talairach and Bancaud, 1966; Munari et al., 1994; Bartolomei et al., 2002; Kahane et al., 2006; Kahane and Landre, 2008).

On the other hand (somehow paradoxically) a large progress has been made in the development of non-invasive methods aimed at localizing the irritative zone, typically using high resolution EEG (Gavaret et al., 2006, 2009; Brodbeck et al., 2011; Pittau et al., 2014), MEG (Knowlton and Shih, 2004; Stefan et al., 2011) or using metabolic/bold changes associated with spiking activity (Hamandi et al., 2004; Laufs and Duncan, 2007; Gotman, 2008; Valentin et al., 2014).

Therefore, the relationships between SOZ and IZ are still an important research issue. Only few studies have specifically addressed this question in the past. In children with malformation of cortical development, in a study based on electrocorticographic recordings, Asano et al. (2003) found a good correlation between spiking frequency and amplitude and seizure onset. From electrocorticograms of 32 patients, Hufnagel et al., found a good concordance between seizure onset and the spikes disclosing the earliest peak, but a 53% concordance with the frequency of interictal spikes (Hufnagel et al., 2000). More recently Marsh et al., using corticographic recordings in children, found a good concordance between spike frequency and seizure onset zone in 60% of patients (Marsh et al., 2010). In patients with mesial temporal lobe epilepsy, our group has shown that the irritative zone encompasses not only mesial but also neocortical anterior temporal cortex and may form distinct networks independent from the SOZ (Bourien et al., 2005).

To our knowledge, there is no study using a quantification of both IZ and SOZ based on SEEG recordings. To this aim, in patients having focal neocortical epilepsies, we investigated and quantified the distribution of IESs (based on a spike frequency index, SI). We compared it to the topography of the SOZ (as characterized by the Epileptogenicity Index, EI (Bartolomei et al., 2008)).

2. Material and methods

2.1. Patients

Thirty-two consecutive adult patients with neocortical epilepsies (i.e.; starting outside the mesial temporal regions), investigated with SEEG were studied. Prior to selection for SEEG all patients underwent non-invasive assessment for drug resistant focal epilepsy including detailed clinical history, neurological examination, neuropsychological evaluation, long-term video-EEG recording and structural magnetic resonance imaging (MRI). SEEG recording was carried out during long term video-EEG monitoring in order to record several of the patient's habitual seizures, following complete or partial withdrawal of antiepileptic drugs. SEEG exploration was performed using intracerebral multiple contacts electrodes (Dixi Medical (France) or Alcis (France); 10–15 contacts, length: 2 mm, diameter: 0.8 mm, 1.5 mm apart) placed intracranially according to Talairach stereotactic method (Bancaud et al., 1970). The anatomical positioning of electrodes was established in each patient based upon available non-invasive data and hypotheses about the localization of the epileptogenic zone. Post-operative computerized scan (CT) was performed in order to verify the absence of bleeding and the position of each recording lead. After intracerebral electrodes removal, following a recording period of 1–3 weeks, cerebral MRI was performed, permitting the visualization of the trajectory of each electrode. Subsequently CT scan/MRI data fusion was performed in order to accurately identify and locate each contact along the electrode trajectory. Signals were recorded on a 128 channel system (Natus/Deltamed TM) sampled at 512 Hz and recorded on a hard disk (16 bits/sample) using no digital filter. DC offset and very slow of the baseline were suppressed by a built-in high-pass hardware filter (cut-off frequency equal to 0.16 Hz at −3 dB).

2.2. Detection and analysis of intracerebral interictal spikes (IESs)

In order to detect IESs, we used a previously described algorithm (Bourien et al., 2004, 2005). This method stems from the fact that IESs are characterized by a sharp component corresponding to a transient wave of high amplitude and short duration compared to background activity. This component is typically associated with an increase of energy in the beta-gamma frequency band (ranging from 20 to 40 Hz) perfectly visible in the time–frequency plane. Based on this observation, the monovariate detection method used in this study included two main steps. In the first stage, SEEG signals are decomposed on a wavelet filter bank. The value $q(t)$ of the squared modulus of filter outputs averaged over a short-duration sliding window (0.5 s) was computed at each sample time. By construction, the quantity $q(t)$ exhibits high values during IESs and low values during background EEG. Thus, in the second stage, the CUSUM algorithm was used to automatically estimate time instants corresponding to abrupt changes of $q(t)$, each abrupt change corresponding to the occurrence of an IES in the SEEG signal (Basseville and Nikiforov, 1993).

For each patient, we performed intracerebral IES detection on user-selected SEEG signals recorded from bipolar contacts of each depth electrode. For each patient, 8–22 bipolar traces representative of different brain regions were analyzed. A 15 min period of continuous interictal SEEG was selected taking into account seizure occurrence, state of vigilance of the patient, residual effect of anaesthesia and anti-epileptic drug withdrawal. Typically, the analyzed SEEG periods were thus selected during the second day of SEEG exploration (same time following anaesthesia for all patients and beginning of anti-epileptic drug withdrawal), when the patient was awake. All selected periods were temporally distant from seizure episodes (at least two hours).

Finally, for each patient, and for each bipolar signal (representative of the activity of a brain region), a normalized "Spike Index (SI)" was computed. This SI was simply obtained by dividing the number of intracerebral IESs detected in one region by the total number of spikes detected from all analyzed brain regions. This ratio, indicative of the amount of IESs per region, ranges from 0 (no spike) to 1 (maximal spiking activity). For each patient, the bipolar traces were selected in order to give a good sampling of the SEEG explored regions.

2.3. Seizure onset zone quantification with the Epileptogenicity Index (EI)

For each patient, the Epileptogenicity Index (EI) values were computed for each selected bipolar trace (8–22, the same as those