

Ictal Activity

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KEY CONCEPTS

- The recording of ictal activity during stereoelectroencephalography (SEEG) investigation is an essential step to define the epileptogenic zone location and thus to plan future surgery.
- The classic notion of zones must now be replaced by the notion of epileptogenic networks.
- Several seizure onset patterns (SOPs) can be observed, a majority of them including fast low-voltage activity.
- Slower SOPs are however observed in 20% of the recordings.
- Quantitation methods based on spectral or connectivity methods are of great help to define and visualize the epileptogenic zone in the individual anatomy.

INTRODUCTION

SEEG in the context of epilepsy is based on the need to electrophysiologically locate the brain regions that cause seizures. When interpreting intracerebral EEG of patients with refractory focal epilepsy, the critical questions are: (a) where does the seizure start? (b) how does the seizure start? and (c) what is the spatio-temporal organization of seizure? As the complete resection of the areas generating the seizure is the best predictor of postsurgical outcome,¹ the exact analysis of ictal activity is crucial in SEEG.

Making use of the technique they had invented, Bancaud and Talairach observed that seizures could originate from regions far from the lesion itself or from the region of maximum interictal spiking,² and they called these regions the “epileptogenic zone” (EZ).³ The EZ is classically recognized as an entity distinct from the region of interictal spikes (irritative zone [IZ]) as well as from the region of structural anomalies if present (lesional zone [LZ]). These three regions may overlap to a greater or lesser degree.^{2,4} North American schools have proposed alternative definitions of EZ and “seizure onset zone” (SOZ).⁵ In this context, SOZ is “the area of the cortex from which clinical seizures are generated,” while the EZ is the area of cortical resection necessary to be removed to render patient seizure-free.⁵ Here we use the term “EZ” in its French definition, which can be considered as approximately equivalent to SOZ as defined from the SEEG recordings.^{6,7}

The characterization of the EZ requires the analysis of ictal activity over time in different structures (onset and early spread), with a direct comparison with the symptoms and clinical

signs (semiology) as they occur. This “anatomo-electrical-clinical correlation” process makes it possible to form a spatio-temporal vision of the organization of seizures in a given patient.^{6,8} The postictal period is also important to analyze. However, the emergence of clinical semiology during a seizure recorded by SEEG is a complex phenomenon, which depends largely on the involvement of various brain regions and networks, including subcortical regions,^{9,10} and is determined by both the spatial and temporal dynamics of the EZ and propagation patterns. Not only spontaneous ictal activity, but also seizures caused by stimulation studies, are crucial to analyze and provide a general picture of the role of different structures in seizure organization. Another important point concerning ictal activity is the analysis of the SOP. Moreover, as ictal activity could be complex to interpret because of widespread changes with limited delay of organization, several methods of quantitative analysis of ictal activity have been developed.

In the present chapter, we detail (a) the concept of network organization of ictal activity, (b) the SOPs, and (c) the quantitative analysis of ictal activity. We end with the description of an illustrative case

EPILEPTOGENIC NETWORKS

The classic image of the three zones, epileptogenic, irritative, and LZs (EZ, IZ, LZ), actually gives a rather misleading idea of reality. In the last 15 years, the notion of “epileptogenic networks” has become more and more popular in epileptology¹⁰ since its first description in the early 2000s.^{11,12} In relation to this concept, we have proposed to replace the scheme of zones with a model of “epileptogenic networks” in which there is a particular spatio-temporal dynamic of the genesis of ictal and interictal activities between a set of brain region more or less extended (Figure 27.1A). In this model, there is a hierarchy of brain regions according to their epileptogenicity: (a) EZ network, (b) propagation zone network (PZN), and (c) non-involved zone network. The MRI-visible lesion and the areas generating interictal paroxysm could, according to the patient, belong to one or more of the above ictal-defined networks.

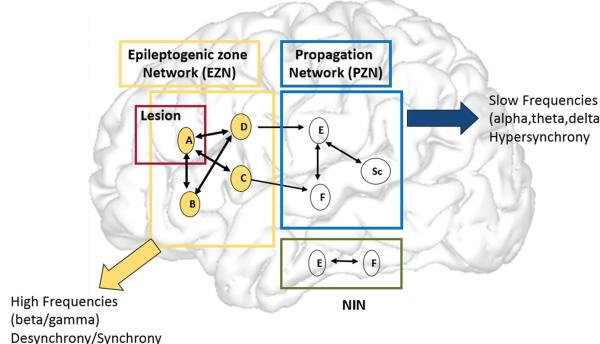
As we described in previous papers, regarding the spatial organization of the EZ, we can consider two schematically different situations when SEEG is used to record seizures (Figure 27.1B):¹⁰

1. In some cases, the EZ corresponds to a relatively restricted area of the cortex. Seizure genesis takes place in a unique “functional area,” a situation corresponding approximately to the classical notion of an epileptogenic focus. This kind of organization is the most classical description of the epileptogenic process, well summarized by the “zones” picture.⁵
2. However, in other cases the seizure onset is characterized by ictal discharges that rapidly involve several distinct brain regions, sometimes far apart. In this situation, the model of the EZ/focus is too simplistic and cannot accurately describe the spatial organization of the EZ. This kind of epileptogenic networks arises generally within physiological networks (e.g., mesial temporal lobe, motor-premotor, parieto-premotor, temporo-insular or occipito-temporal networks, etc.).

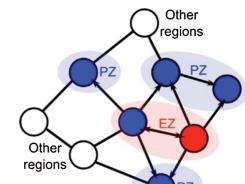
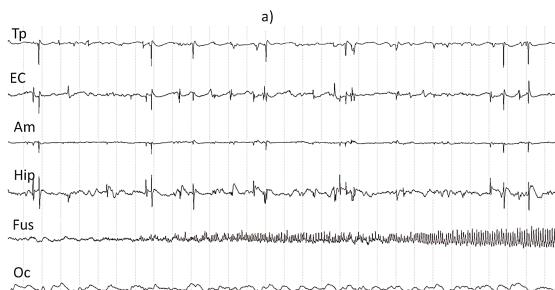
Noteworthy, in clinical practice the majority of patients have a network organization of their EZ. For example, in our series, about 60% of our patients had a network-organized EZ and the mean number of distinct structures involved during seizure was three.¹

Moreover, we have proposed that the EZ corresponds to a network (the “epileptogenic zone network” [EZN]) of hyperexcitable structures sharing at least two main spatio-temporal characteristics:¹⁰

1. The ability to generate fast oscillations, in the beta or/and the gamma range (low-voltage fast activity [LVFA]) and to suppress lower frequencies (However other modes of seizure onset are possible; see “Patterns of seizure onset” section.)

A**B**

Focal Mode of onset



Networked mode of onset

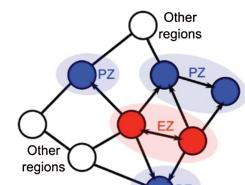
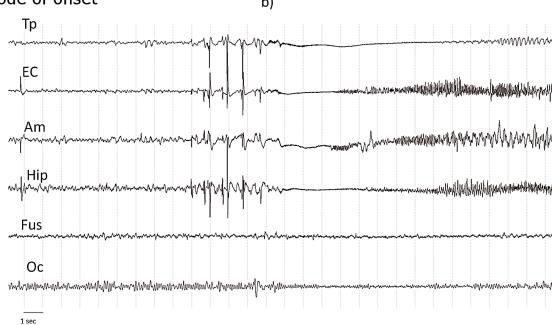


FIGURE 27.1 (A) The concept of epileptogenic networks in focal epilepsies is illustrated. The cerebral regions are represented by letters (A, B, etc.). The scheme proposes a hierarchical organization in terms of epileptogenicity in the epileptic brain. The EZ includes different brain regions that are able to generate seizures, in particular, fast activities, defining the EZN (labelled A, B, C, D). A represents a region with putative (visible or not) lesion. The EZN is also characterized by a pattern of synchrony-desynchrony. A second set of regions is less epileptogenic and is triggered in seizures by the EZ and is within the “propagation zone network” (E, F, Sc, H). Sc schematize the involvement of subcortical (e.g., thalamus) regions. Activity recorded in these regions are generally of lower frequency and more synchronized than in the EZ. Some regions are not involved during seizure propagation (noninvolved network, G, H). (B) Two types of seizure onset in the epileptogenic zone can be schematically observed in SEEG. A focal onset with a region generating the seizure before spreading and a more networked onset before secondary spread. Here, two seizures are illustrated in SEEG recordings. One generated focally in the fusiform cortex and the other showing a network involvement of the temporal mesial lobe.

Am, amygdala; EC, entorhinal cortex; EZ, epileptogenic zone; EZN, epileptogenic zone network; Fus, fusiform gyrus; Hip, hippocampus; NIN, noninvolved network; Oc, occipital cortex; PZ, propagation zone; PZN, propagation zone network; SEEG, stereoelectroencephalography; Tp, temporal pole.

Source: From Bartolomei F, Lagarde S, Wendling F, et al. Defining epileptogenic networks: contribution of SEEG and signal analysis. *Epilepsia*. 2017;58:1131-1147. doi:10.1111/epi.13791

2. The ability to synchronize their activity (after often an initial phase of desynchronization) at seizure onset and during the course of the seizure

Secondary delayed electrophysiological discharges are observed in regions outside the EZN and are consistent with the concept of propagation (“PZN”). However, the propagation of seizures is a complex process that does not correspond to the classical propagation of the nerve flux. Indeed, long delays of seizure propagation may occur from one region to the other. For example, ictal propagation varies between a mean of 13.7 plus or minus 2.2 seconds in case of temporal mesial, 7.6 plus or minus 1.4 seconds in temporal lateral and 3.8 plus or minus 1.0 seconds in frontal EZ.¹⁵ A larger cohort confirmed the wide range of ictal spread latency from 500 milliseconds to 102 seconds with a median time of 5.1 seconds.¹⁴ Such delays are probably linked to gradual changes in the biological properties of the regions of propagation.^{15–17} In addition and in a crucial way, the latency of the spread of the seizure depends on the location of the EZ. For example, frontal mesial discharges have shorter ipsilateral propagation than orbito-frontal and parietal regions which have shorter ipsilateral propagation than occipital EZ. Similarly, contralateral propagation is shorter from frontal mesial than from temporal mesial, temporal lateral, frontal orbital, or occipital EZ.¹⁵ Moreover, ictal spread is slower in temporal mesial than in temporal lateral or frontal EZ. It indicates that the ictal propagation depends fundamentally on the area of seizure onset and its anatomical connections.

Noteworthy, the anatomical sites involved during seizure dynamics depend actually on the subjacent structural connectivity;^{18,19} with participation of both cortical and subcortical structures.^{20,21} Thus, propagation is determined by both local excitability as well as connectivity properties rather than passive conduction. In line with these data, it has been demonstrated that both MRI-derived structural and electrophysiological-derived functional interictal connectivity are higher within both epileptogenic and propagation networks.^{22,23} Modeling studies have also well demonstrated that in addition to excitability, connectivity is crucial in the determination of simulating ictal spread.^{16,17,24}

Finally, in terms of epileptogenicity, a hierarchical organization of epileptogenic networks has been proposed in focal epilepsies describing brain regions involved in seizure genesis and spread, from epileptogenic, to propagation, and noninvolved network. SEEG interpretation of ictal activity aims then to optimally define these three distinct networks.

PATTERNS OF SEIZURE ONSET

Another important question, when interpreting ictal activity, is how does the seizure start?

Indeed, SOPs are indicators that can point to a particular etiology or postsurgery prognosis. Several SOPs may be observed during intracerebral EEG recordings,^{1,14,25} most commonly in form of LVFA, a classical pattern in SEEG recordings (Figure 27.2). The LVFA may be preceded by EEG changes in the form of preictal epileptic spikes, burst of high-amplitude poly-spikes or slow-wave complexes/direct current (DC) shift.^{1,25} Frequencies involved in the LVFA range from beta/low gamma (15–30 Hz; e.g., in mesial temporal seizures)²⁶ to higher frequencies (gamma range, 30–100 Hz, generally observed in neocortical seizures).²⁷ Two subtypes of LVFA have recently been described: (a) large amplitude and abrupt slow-polarizing DC-like shifts with sharp on and off transients, superimposed on LVFA, which linearly decreased in frequency within 5 to 10 seconds (down chirp), and (b) LVFA with a slowly developing slow-polarizing DC-like shifts.²⁸ The first LVFA pattern was generated within neocortical structures of all brain lobes, whereas the second LVFA pattern was observed almost exclusively in the temporal lobe.

We demonstrated that SOPs may be linked to three main clinical features: (a) underlying histology, (b) spatial organization of the EZ, and (c) postsurgical seizure outcome. Associations between patterns and histopathology/etiology have been suggested from SEEG series.²⁵ For example, in focal cortical dysplasia (FCD) type I, LVFA (23.1%) and slow-wave/DC shift

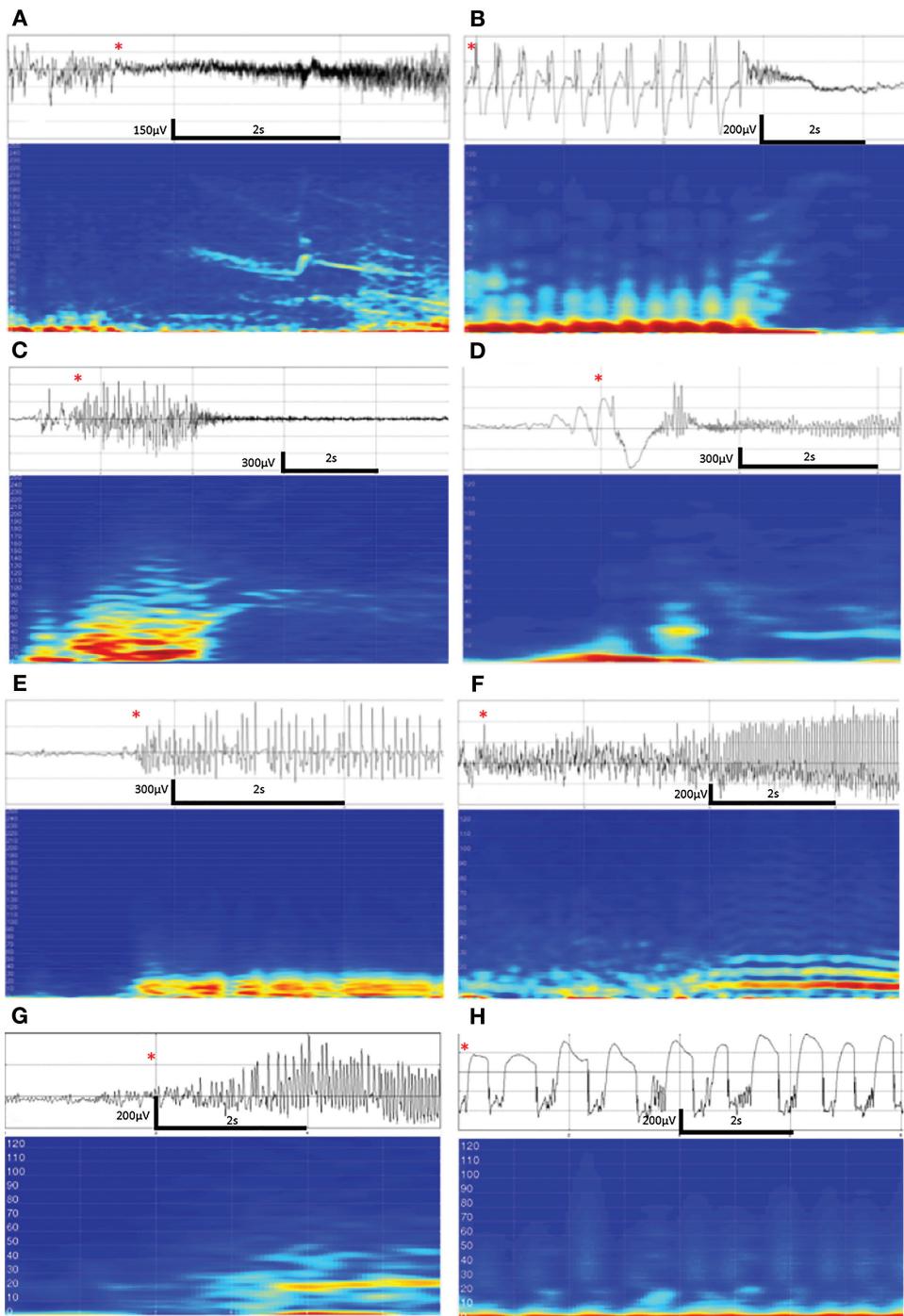


FIGURE 27.2 Eight seizure-onset patterns according to the time frequency representation from SEEG traces. **(A)** LVFA, **(B)** preictal spiking followed by LVFA, **(C)** burst of polyspikes followed by LVFA, **(D)** slow-wave or baseline shift followed by LVFA, **(E)** rhythmic slow spikes, **(F)** theta/alpha sharp activity, **(G)** beta sharp activity, and **(H)** delta-brush. The red asterisks mark the seizure onset. LVFA, low-voltage fast activity; SEEG, stereoelectroencephalography.

Source: From Lagarde S, Buzori S, Trebuchon A, et al. The repertoire of seizure onset patterns in human focal epilepsies: determinants and prognostic values. *Epilepsia*. 2019;60:85–95. doi:10.1111/epi.14604

followed by LVFA (15.4%) were found to be the most prevalent SOP, while in FCD type II, burst of polyspikes followed by LVFA (31%), LVFA (27.6%), and preictal spiking followed by LVFA (27.6%) were the most frequent SOPs.^{1,25,29,30} In MRI-negative cases, strong correlation between SOP and histology was demonstrated for: (a) slow-wave/DC-shift followed by LVFA, associated with normal/nonspecific histology, and (b) bursts of polyspikes followed by LVFA, exclusively observed in FCD, suggesting that this specific SOP may help to detect an MRI-invisible FCD.³⁰

In studies investigating temporal lobe epilepsies, six out of 11 found an association between mesial temporal sclerosis and low-frequency repetitive spikes and three out of 11 found that this SOP was significantly associated with more severe mesial temporal sclerosis as compared to LVFA.³¹ Another study found that low-frequency repetitive spikes were a pattern associated with mesial temporal atrophy (on MRI), whereas LVFA was associated with MRI-negative forms.³² LVFA was also over-represented in patients with malformation of cortical development such as polymicrogyria,^{1,29} poststroke, and “cryptogenic” epilepsies.¹

Concerning spatial organization of the EZ, the presence of a DC shift/slow wave prior to LVFA was more frequently associated with a network EZ organization of the EZ.¹ However, in about 20% of cases, slower patterns of onset may be observed.¹ These patterns include rhythmic spikes or spike-waves, and theta/alpha sharp activity with progressively increasing amplitude. These slower patterns tend to be more frequent in some etiologies (FCD type I, neurodevelopmental tumors) and associated with a networked seizure onset.¹

Finally, it has been shown that SOPs including LVFA are associated with the better surgical outcome and conversely a poorer prognosis is observed in patients with slower SOPs (with rhythmic slow spikes or sharp theta/alpha).^{1,23,31} However, this association was not confirmed in a recent study by our group focusing on MRI-negative epilepsy, where surgical outcome depended essentially on the complete removal of the EZ, regardless of electrophysiological features.³⁰ These data argue against the traditional assumption that SOPs without LVFA would be only a propagation pattern. Consequently, patients with such patterns should not be excluded from potential resective surgery if the EZ is well defined.

QUANTIFICATION OF ICTAL NETWORKS

In clinical practice, a challenging issue is the ability to evaluate the epileptogenicity of structures in case of widespread seizure onset, in order to define the minimal but sufficient target to resect. Moreover, the distinction between ictal pattern arising from EZ and from propagation zone (PZ) could be challenging, especially because seizure onset and propagated pattern could share common features.¹⁴ Therefore, sharp activity below 13 Hz, LVFA, rhythmic spike-wave and low-frequency periodic spikes could be observed as propagation patterns.¹⁴ Noteworthy, some patterns are not detected in regions of spread, especially burst of polyspikes followed by LVFA. The finding that LVFA was detected in regions of spread proves that LVFA is not a perfect biomarker of the structures belonging to the EZ. Because SEEG sampling is necessarily limited and because of overlap in the intracerebral EEG onset and spread pattern, in some case it is worthwhile to ask if the seizure onset is really recorded and not solely propagation activity. The appearance of intracerebral EEG ictal activity before clinical signs may bring some confidence in the correct localization of the EZ. However, other neurophysiologic markers have been described as well which can help in those situations. Signal features appear with different properties between EZ and PZ. For example, decrease in variance, skewness, and kurtosis indicate that ictal activity in the PZ is more likely to have “simpler” morphology and greater normality than within the EZ.³³ The concept of timing of involvement of brain regions is another way to increase the specificity for detecting the SOZ.⁸

The issues just mentioned, combined with sometimes widespread seizure onset involving often distant and functionally distinct brain sites almost simultaneously, challenge the sole visual analysis of ictal activity. Therefore, several methods have been developed over the last 10 years to help define the EZ and to quantitatively analyze ictal activity.^{8,34–37} The first works and with the largest evidence come from the use of the Epileptogenicity Index (EI) method. From SEEG signals, the EI combines analysis of both spectral and temporal features, respectively related to the propensity of a brain area to generate fast discharges (>12 Hz) with or without depression of background slower frequencies; and to the earliness of involvement of this area in the seizure.⁸ Results may be shown in a three-dimensional representation of the patient's MRI using adapted software for automatic registration and depth electrode localization (Figure 27.3).³⁸ Another approach has been proposed to quantify epileptogenicity from SEEG recordings by adopting a neuroimaging approach, in order to generate statistical parametric maps of high-frequency oscillations (HFOs) at seizure onset, called "epileptogenicity maps" (EMs).³⁴ Another study suggests good performance of a method combining three biomarkers: the capability to generate ictal, LVFA and slow transient polarizing shift, and postictal voltage depression (flattening).³⁵ Following initial EI studies,⁸ recent works have combined quantification of power increase in higher frequency with a decrease in lower frequency power to localize the EZ.³⁷

Recently, studies have investigated the idea of using connectivity analysis during ictal activity to define the EZ. Functional connectivity between two regions could be estimated statistically using SEEG signals. Actually, the functional connectivity changes dramatically during seizure.¹⁰ Then, several studies using diverse methods of connectivity analysis have tried to define the regions (nodes) with the highest outgoing connectivity during the ictal period. These studies demonstrated that electrode contacts with the highest total outgoing connectivity corresponded well with the epileptogenic region.^{39,40} This approach seems promising especially in case of the SOP without high-frequency activity, in which the methods mapping the SOZ such as EI⁸ or gamma map³⁴ are less successful.

Studies using EI have shown that the EZ in drug-resistant epilepsies is generally formed by at least two distinct epileptogenic areas. For example, in temporal lobe epilepsy (TLE), the most complex networks are observed in mesio-lateral or "temporal plus" (perisylvian) subtypes, where a large set of regions is epileptogenic.⁴¹ Bitemporal epilepsies are characterized by an EZ that preferentially involves subcortical regions⁴² while larger networks have been observed in patients with normal MRI as opposed to hippocampal sclerosis in TLE.⁸ Complex patterns of epileptogenicity have been also described in parietal lobe epilepsies,⁴³ frontal motor seizures,⁴⁴ and occipital lobe epilepsies.⁴⁵ EMs have been used to quantify the EZ in patients with startle seizures⁴⁶ and to quantify the insular involvement in temporal lobe seizures.⁴⁷ Surgical prognosis has been found to correlate with the number of epileptogenic regions in TLEs.^{8,41} Recently, seizure outcome was found to correlate with the resection ratio for fast activity (as detected using the EM method) which was significantly higher in seizure-free (Engel's class Ia) than in nonseizure-free patients (class Ic-IV; $p = .048$).⁴⁸

In the context of surgery, the role of the epileptogenic lesion(s) in the network of regions generating seizures is a crucial issue. A study dealing with the estimation of epileptogenicity of FCD and sites remote from the lesion found that high epileptogenicity values could be found in remote sites in 60% of patients and that surgical outcome was better in patients with a focal pattern.⁴⁹ In epilepsy related to cavernomas, an EZ network largely extending outside the limits of the lesion was observed in the majority of cases.⁵⁰ Similarly, poststroke epilepsies often exhibited extended epileptogenic networks, involving both the edge of the vascular lesion and distant structures.⁴⁵ A recent study investigated the roles of heterotopic and normotopic cortex in the epileptogenic networks in patients with periventricular nodular heterotopia using quantitative signal analysis on SEEG.⁵¹ According to EI values, seizures were mostly normotopic

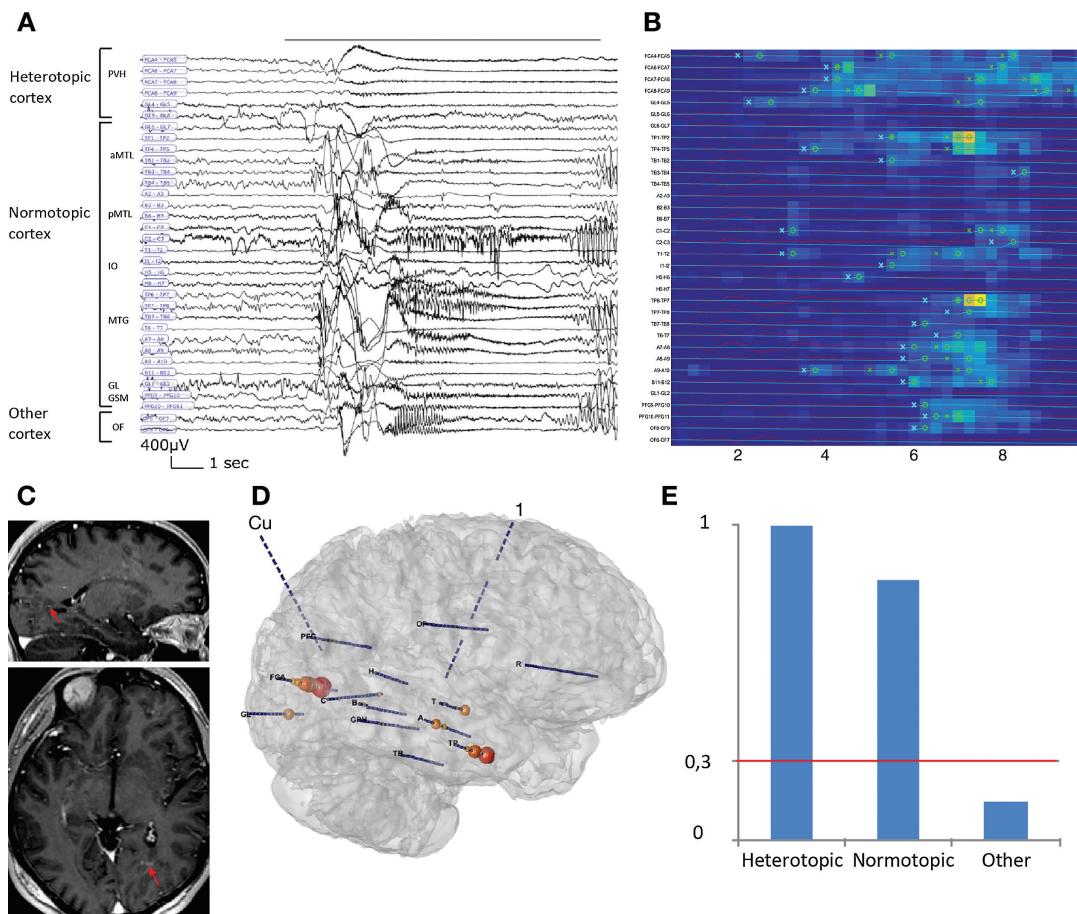


FIGURE 27.3 Quantification of ictal activity using the EI method in a patient with periventricular nodular heterotopia. **(A)** SEEG recording from the heterotopic cortex, local neocortex, and distant neocortex. The heterotopic cortex is explored in the posterior periventricular region. Local neocortex is shown in the anterior mesial temporal lobe, posterior mesial temporal region, insulo-opercular region, middle temporal gyrus, GL, and gyrus supramarginalis. Distant neocortex is showed in the fronto-opercular region. The black line on the top identifies the SEEG segment analyzed in the EI map **(B)**. The EI map showed increase in energy ratio (in blue to yellow scale) and time of detection (circle: alarm time and cross-detection time³⁰) in each SEEG channel selected. The epileptogenicity is high in both local neocortex and heterotopic cortex. **(C)** MRI (three-dimensional [3D] T1): CT data fusion 1, 2. Electrode FCA placed inside the heterotopic cortex. The red arrow indicates contact 4. **(D)** 3D representation of the SEEG exploration; the balloons indicate the EI detections. Balloon color (from yellow to red) and dimension correspond to the EI value. To note the diffuse epileptogenicity involving both local neocortex (electrodes TP, A and T) and heterotopic cortex (mesial contacts of GL and median contacts of FCA). **(E)** EI maximal values obtained in each group of contacts in this seizure. The red line marks the 0.3 value considered as a threshold to define a region as epileptogenic. Both local neocortex and heterotopic cortex showed a high degree of epileptogenicity, identifying this seizure as a normo-heterotopic seizure.

aMT, anterior mesial temporal; EI, Epileptogenicity Index; FCA, electrode reaching the heterotopic cortex; GL, gyrus lingualis; GSM, gyrus supra-marginalis; IO, insulo-opercular; MTG, middle temporal gyrus; OF, fronto-opercular; pMTL, posterior mesial temporal; PVH, posterior periventricular; SEEG, stereoelectroencephalography.

Source: From Pizzo F, Roehri N, Catenoix H, et al. Epileptogenic networks in nodular heterotopia: a stereoelectroencephalography study. *Epilepsia*. 2017;58:2112-2123. doi:10.1111/epi.13919

(48.5%) or normo-heterotopic (45.5%); only 6% were purely heterotopic illustrating the complexity of the epileptogenic networks in this etiology. An example of normo-heterotopic seizure is illustrated in Figure 27.3. These approaches have also added information about the possible evolution of the network size with time. A positive correlation between the duration of the epilepsy and the number of epileptogenic regions (defined by a high EI value) has been found in temporal lobe epilepsies⁸ and in frontal epilepsies.⁴⁴ These results advocate for a secondary epileptogenesis process in human focal epilepsies, at least in some anatomical localizations and some etiologies.

ILLUSTRATIVE CASE

This 25-year-old, right-handed woman, with normal development and no family history of epilepsy, started experiencing recurrent paroxysmal episodes with behavioral modification and alteration of consciousness at the age of 10. Her previous history was uneventful, with the exception of a fall from a horse a few weeks before epilepsy onset. Focal, and occasionally secondary generalized seizures, occurred in clusters twice per month, precipitated by stress or fatigue. Her habitual seizure semiology at the time of presurgical evaluation comprised two distinct types of subjective initial signs: the first consisted of nonlateralized auditory illusions, with feeling of “resonance in the head” and amplification of environmental sounds, rapidly followed by the impairment of comprehension; the second started with a sudden feeling of anxiety or an intense fear, and an impression of a frightening presence behind her. Both types were then followed by loss of consciousness, with behavioral arrest, fearful face expression, head deviation to the left, and a dystonic posture of the right hand. Sustained postictal language difficulties, including comprehension aphasia and anomia, were observed. Neuropsychological evaluation showed cognitive scores within the average–low range, with a significant visual–verbal performances dissociation due to the impairment of the latter (Total IQ 81, Verbal 71, Performance 99), as well as immediate verbal memory and working memory deficits. Language-functional MRI confirmed the left hemispheric dominance. Scalp video-EEG recordings demonstrated bilateral temporal interictal epileptiform abnormalities, activated during sleep, predominant over the left temporal anterior and temporo-basal regions. Ictal patterns were bilateral, predominant over the left temporal region. 3 T and 7 T MRI scans showed as the only abnormality a left amygdala enlargement without hyperintense signal whereas fluorodeoxyglucose-PET demonstrated a prominent left temporal lateral and polar hypometabolism. The clinical hypothesis based on the noninvasive findings was that of a left temporo-perisylvian epileptogenic network.

A bilateral SEEG was performed, with an extensive left side exploration, sampling temporal, perisylvian, frontal and parietal regions, and a right exploration comprising several temporal lobe sentinels (Figure 27.4). Interictal activities (spikes, HFO) were expressed mostly by the left temporal structures, with mesio-lateral distribution. The maximal spike rates were found within the amygdala and the maximal HFO rates—within the superior temporal gyrus (STG); some independent spikes were observed within the left posterior insula as well as the right temporal neocortex and hippocampus. Spatio-temporal organization of typical spontaneous seizures with initial auditory signs is illustrated in Figure 27.4B. Seizure started from the left STG with a delta-brush SOP followed by low-voltage rapid discharges (LVRD) in low-gamma band that affected simultaneously both its anterior and posterior aspects including the Heschl gyrus and the planum temporale, shortly before the emergence of an auditory illusion (resonance). The principal regions of the PZ network (the left temporal pole and ipsilateral mesial temporal structures) were involved with a latency of several seconds, while the modality of ictal discharge changed from tonic gamma to rhythmic polyspike activity in

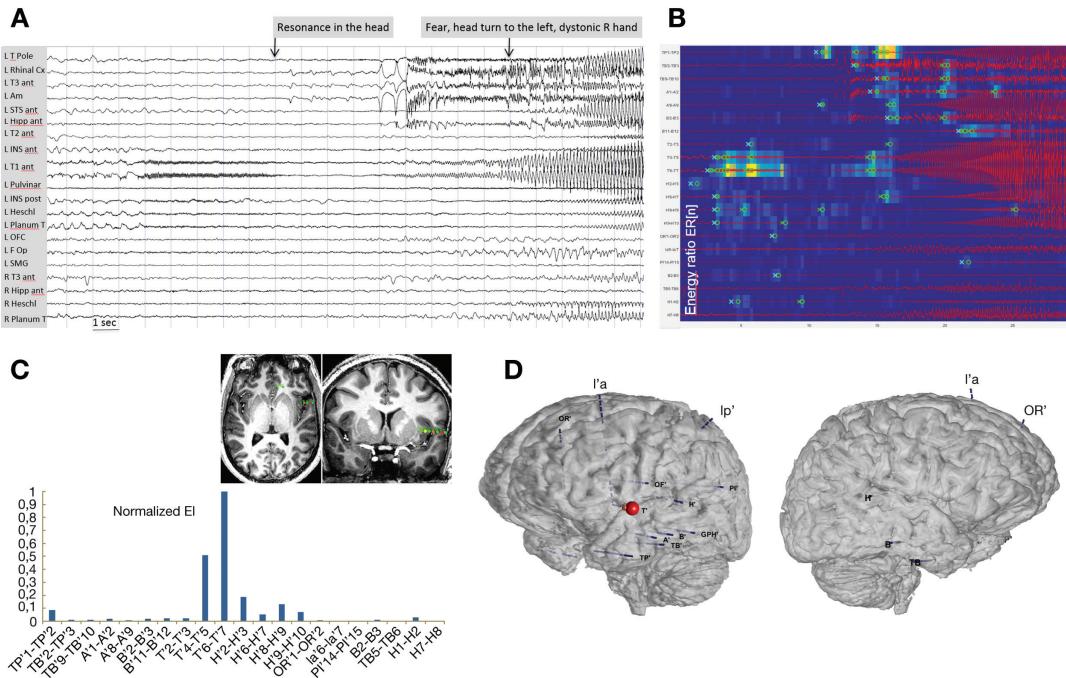


FIGURE 27.4 (A) SEEG recordings of a habitual seizure that starts from the left superior temporal gyrus and rapidly involves left mesial temporal structures. Note a well-distinguishable delta-brush seizure-onset pattern followed by low-voltage fast discharge in gamma band on the external contacts of electrode T', exploring anterior aspect of T1, as confirmed by time-frequency analysis (shown in a separate window). Its posterior aspects (Heschl gyrus and planum temporale) are affected simultaneously as a part of the EZ network, however with a less-sustained rapid discharge. The left temporal pole, as well as amygdala, entorhinal cortex, and anterior hippocampus are involved with a latency of 6 and 8 sec respectively, thus belonging to the PZ network. Interestingly, there is a change from tonic, to slow, synchronizing discharge within the EZ network structures, concomitant with the left mesial temporal involvement. Some left extratemporal regions (insula, frontal operculum) as well as some right T1 subregions (Heschl, planum temporale) are subsequently involved in the propagation zone network, whereas the left supramarginal gyrus and the right hippocampus are spared. (B) (Bottom): changes in energy ratio (ER) of high frequencies (ER[n]) in the previously mentioned SEEG signals are disclosed with a color scale. Early increase in ER is seen in the left anterior T1, Heschl and planum temporale, as well as in the ipsilateral pulvinar, whereas the ER changes in the left temporal pole and mesial temporal structures follow with the latency of 8 sec. (C) Maximal normalized EI values obtained in each recorded structure in two spontaneous seizures, demonstrating maximal epileptogenicity in the left anterior T1, followed by the ipsilateral pulvinar, Heschl gyrus, planum temporale, and the temporal pole. (Top): Axial and coronal planes of the patient's 7 T MP2RAGE image showing the contacts of electrode T', with maximal normalized EI values represented by 'hot' color map for values above the settled threshold. (D) Patient's three-dimensional cortical surface rendering (left and right hemisphere) with implanted SEEG electrodes. Reconstructed electrode images (blue) correspond to real trajectories and entry points (EpiTools software suite).³⁸ Left hemisphere: electrode TP' sampled the mesial and lateral aspects of the temporal pole; electrode TB' explored the entorhinal cortex, anterior aspect of the occipito-temporal sulcus, and anterior aspect of the inferior temporal gyrus; electrode A' explored the amygdala, anterior aspect of the superior temporal sulcus, and the anterior aspect of the middle temporal gyrus; electrode B' explored the anterior hippocampus and the anterior T2; electrode GPH' sampled the posterior hippocampus and the posterior T2; electrode T' recorded the anterior insula and anterior aspect of the superior temporal gyrus; electrode H' recorded the pulvinar thalamus, the posterior insula, the Heschl gyrus, and the planum temporale; electrode PI' explored the posterior cingulate cortex and posterior aspect of the supramarginal gyrus; electrode l'a' sampled the anterior insula, pars opercularis of the inferior frontal gyrus, and the caudal aspect

the alpha-theta band. This “slow” synchronizing discharge then rapidly spread to the left insulo-opercular and the right temporal lateral regions and correlated clinically with facial expression of fear, loss of consciousness, and other objective ictal signs just described. A quantitative ictal SEEG signal analysis using the EI (Figure 27.4B–D) confirmed the leading role of the left STG, which showed the highest epileptogenicity, with the maximal EI values in the anterior part, followed by the left temporal pole and the ipsilateral pulvinar. Interestingly, the latter was not clearly identified by visual analysis probably due to very low signal amplitude within this structure.

Stimulations of the left mesial temporal pole, amygdala, and entorhinal cortex reproduced the ictal fear sensation, whereas habitual auditory signs were elicited by stimulations of the left Heschl gyrus. Fifty Hz stimulations of the left hippocampus reproduced the electro-clinical pattern of the central phase of spontaneous seizures. Temporal language area determined by functional mapping overlapped with the posterior part of the EZ network.

Based on these findings, a tailored resection of the left STG and temporal pole with amygdala disconnection has been performed, with the posterior resection limit determined by perioperative language mapping. Histopathological examination revealed FCD type I. The patient remains completely seizure-free 6 months after surgery.

In conclusion, this case illustrates the hierarchic temporo-spatial organization of ictal discharge that initiated within the superior temporal, auditory- and language-processing network, and secondarily involved the limbic, emotional network. However, the notion of fear as initial sign in some habitual seizures suggests the dynamic relationships between these two systems, with possible implication of limbic structures—in particular the amygdala as a part of the EZ network.

CONCLUSION

The recording of intracerebral EEG activity has significantly expanded over the last 15 years. Signal analysis methods have also made it possible to better describe the phenomenology of the genesis of focal seizures in the human brain. A very “focal” view of these epilepsies has gradually been replaced by that of distributed epileptogenic networks, corroborated by neuroimaging data. This network concept is now being used to develop methods combining neuroanatomy, electrophysiology, and large-scale computational modeling,^{17–19,52} which will probably enable us to better understand the complex phenomena underlying ictogenesis and propagation of seizures and to better predict the results of epilepsy surgery.

FIGURE 27.4 (Continued). of the middle frontal gyrus (F2); electrode Ip' recorded the posterior insula, the parietal operculum, the postcentral sulcus, and the superior parietal lobule; electrode OR' sampled the OFC and rostral aspect of the F2; electrode OF' recorded the caudate nucleus and the central operculum. Right hemisphere: electrode TB explored the rhinal cortex, anterior aspect of the occipito-temporal sulcus, and the anterior T3; electrode B sampled the anterior hippocampus and the anterior T2; electrode H recorded the Heschl gyrus and the planum temporale. The maximal EI values are represented as spheres on the respective contacts of electrode T' according to a color map from yellow to red.

Am, amygdala; EI, Epileptogenicity Index; ER, energy ratio; EZ, epileptogenic zone; F Op, pars opercularis of the inferior frontal gyrus; Hipp ant, anterior hippocampus; INS ant, anterior insula; INS post, posterior insula; MP2RAGE, magnetization prepared 2 rapid acquisition gradient echoes; OFC, orbitofrontal cortex; planum T, planum temporale; SEEG, stereoelectroencephalography; STS ant, anterior aspect of the superior temporal sulcus; T1 ant, anterior aspect of the superior temporal gyrus; T2 ant, anterior aspect of the middle temporal gyrus; T3 ant, anterior aspect of the inferior temporal gyrus.

KEY REFERENCES

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1. Lagarde S, Buzori S, Trebuchon A, et al. The repertoire of seizure onset patterns in human focal epilepsies: determinants and prognostic values. *Epilepsia*. 2019;60:85–95. doi:10.1111/epi.14604
8. Bartolomei F, Chauvel P, Wendling F. Epileptogenicity of brain structures in human temporal lobe epilepsy: a quantified study from intracerebral EEG. *Brain*. 2008;131:1818–1830. doi:10.1093/brain/awn111
10. Bartolomei F, Lagarde S, Wendling F, et al. Defining epileptogenic networks: contribution of SEEG and signal analysis. *Epilepsia*. 2017;58:1131–1147. doi:10.1111/epi.13791
28. Gnatkovsky V, Pelliccia V, de Curtis M, Tassi L. Two main focal seizure patterns revealed by intra-cerebral electroencephalographic biomarker analysis. *Epilepsia*. 2019;60:96–106. doi:10.1111/epi.14610
35. Gnatkovsky V, de Curtis M, Pastori C, et al. Biomarkers of epileptogenic zone defined by quantified stereo-EEG analysis. *Epilepsia*. 2014;55:296–305. doi:10.1111/epi.12507