Interpretation of the Intracranial Stereoelectroencephalography Signal

Vasileios Kokkinos, PhD

KEYWORDS

• Epilepsy • Epilepsy surgery • Intracranial EEG

KEY POINTS

- Understanding and recognizing the physiologic intracranial electroencephalogram (iEEG) is important for discriminating channels with normal activity from those with epileptic activity.
- The neurophysiologic changes the brain undergoes as a result of sleep are reflected in the iEEG.
- The interpretation of the ictal iEEG is tightly linked with the interpretation of the interictal background and its epileptic iEEG discharges.
- The correlation of spatial ictal iEEG spread to clinical semiology is the cornerstone of epileptic seizure comprehension.
- Unfortunately, criteria for the interpretation of iEEG have not yet been established and constitute work in progress.

INTRODUCTION

Stereoelectroencephalography (sEEG) was developed as a minimally invasive surgical investigative process that allows 3-dimensional, bilateral, and deep access to the brain for the purpose of testing a hypothesis regarding the location and extent of the epileptogenic zone.[1,2] First introduced by Talairach and Bancaud in the 1960s,[3–5] sEEG has successfully survived the test of time and has become an established approach for surgical investigations in epilepsy.[6,7] Its minimally invasive nature that avoids craniotomies and the complication risks that accompany them has rendered sEEG an attractive technique, particularly favorable in the treatment of pediatric populations.[7–10] Developed in the pre–magnetic resonance imaging (MRI) era, the sEEG implantation strategy grew as a concept independent from the presence of brain lesions, currently rendering sEEG particularly attractive in the investigation of nonlesional focal epilepsy cases.[11–14] More importantly, sEEG has revealed the dynamic character of focal epileptic syndromes,[13] thereby tremendously advancing understanding of this devastating episodic brain disorder.[14,15] Both the surgical and epileptologic advantages accompanying sEEG have contributed to its establishment as one of the dominant investigative approaches in epilepsy.[16]

As such, decision making in sEEG-guided epilepsy surgery heavily relies on the interpretation of the intracranial electroencephalogram (iEEG).[17–20] Despite the long history of intracranial recordings in epilepsy surgery, however, the interpretation of iEEG is still limited by 3 major barriers. The first is that, in contrast to the extracranial electroencephalogram (EEG), knowledge of what is normal brain activity in the intracranial realm under the various levels of human vigilance is limited.[21,22] The second is that the validity of interictal discharges as markers of epileptogenic localization remains questionable, given that their nature as

Department of Neurosurgery, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, 429A Thier, Boston, MA 02114, USA
E-mail address: vasileios.kokkinos@mgh.harvard.edu

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either reactive or paroxysmal elements is still debated, and they have been shown to spread fast through cortico-cortical connections.[23,24] The third is the lack of differentiation between a primary ictal onset pattern on iEEG that signifies successful localization of the epileptogenic zone and a secondary ictal onset pattern that represents secondary ictal recruitment of regions neighboring the epileptogenic zone.[25,26] This article discusses the current status of these barriers in iEEG interpretation, outlines what is understood so far, and suggests future steps.

PRINCIPLES

Surgical Planning

Surgical planning for sEEG is based on the development of a hypothesis regarding the location and extent of the epileptogenic zone and is established through the process of anatomo-electro-clinical correlation.[5,27,28] For that process, extracranial EEG, structural and functional imaging, clinical history, and ictal semiology data are evaluated. Data convergence is the main conceptual method used for the development of a primary hypothesis that delineates the areas of maximum probability of epileptogenicity and propagation of epileptic activity.[1] Alternative hypotheses also can be developed during that process, especially in the presence of data discordant to the primary hypothesis. All hypotheses should take under consideration the limitations imposed by the surgical approach as well as the anatomic and functional boundaries of cortical resection that preserve eloquent cortex.

Electrode Implantation

Following the formulation of the surgical hypotheses, sEEG is a less invasive intracranial investigative process that can be used to either confirm or reject them.[1,2] The number of electrodes used to achieve adequate coverage depends on the total suspected cerebral volume, which is defined by the surgical hypotheses. Although sEEG introduces a low risk of surgical complications, there is no consensus on the maximum number of sEEG electrodes implanted and the benefit-risk ratio always should be assessed.[29] The target and entry point of each electrode must be justified by hard data (clinical, neurophysiologic, and imaging) used in the hypothesis formulation process.[1,5,26,27] Depending on training and experience, electrode trajectories can be orthogonal,[30,31] oblique, or a combination of both.[32] Trajectories are influenced further by the local vasculature at the entry and target points,[33] where compromises regarding the ideal target have to be made for patient safety purposes.[34] Although there are no standard implantation templates corresponding to the various focal epilepsy syndromes, multicenter empirical implantation strategies have been proposed.[2]

Recording of Stereoelectroencephalography

The main goal of sEEG monitoring and recording is to capture at least 1 spontaneous typical seizure that reveals the spatial epileptogenic map and eventually evaluates the surgical hypothesis.[17,28] Reliability of recording is of utmost importance at this stage, because the ictal sEEG is a gold standard for surgical treatment decision making. A setting of 1-kHz sampling rate (providing a reliable sEEG signal in the 0.01–300 Hz range) and a greater than or equal to 16-bit analog-to-digital conversion is required to obtain the appropriate quality intracranial sEEG signal for diagnostic purposes.[1,19] High signal reliability, however, must be accompanied by respective video recording resolution that allows detection of even minute clinical manifestations and evaluation of the stereotypical character of recorded seizures.[35] A combination of a high-definition video recording documenting the clinical manifestation of the seizure and a high-quality intracranial sEEG signal documenting the neurophysiologic intracranial signature of the seizure is imperative for optimal surgical decision making.

INTERPRETATION OF INTRACRANIAL ELECTROENCEPHALOGRAM

Preparation for Review

The first step in interpretation of an iEEG is setting up a review environment that allows meaningful review of the record.[19,36] The main constituents of such an environment are the review montage and the electrode location map.

Creating a comfortable review montage entails 3 main tasks: (1) establishing meaningful electrode naming, (2) arranging electrodes in an anatomically meaningful order, and (3) creating electrode montages in both referential and bipolar configurations. Electrode naming in intracranial evaluations has not been broadly standardized; however, there currently are 2 main cultures that predominate: the alphabetical[1,2] and the anatomical[37,38] conventions. The alphabetical convention allocates letters of the alphabet to anatomic positions and uses the prime symbol to discriminate left from right hemispheric electrodes (eg, A', may represent an electrode implanted in the left amygdala and B in the right superior temporal gyrus); the latter uses abbreviations of anatomic terms that describe either the target or the entry point (eg, LAMY may represent an electrode implanted in the left amygdala

and RTS [or RST] may represent an electrode implanted in the right superior temporal gyrus). Epilepsy centers select their naming convention based on prior training and experience. It is important that iEEG reviewers adapt and become comfortable with both forms of electrode naming. Reliable anatomic assignment for each recording iEEG channel in either custom, however, is impossible without an electrode map.

In contrast to the scalp EEG electrode positions, the localization of sEEG electrodes is not standardized, neither regarding the cortical entry and target points nor with respect to their interelectrode distance.[2] For that reason, a detailed electrode map is necessary for the iEEG reviewer so that interpretation is accompanied by anatomic references. Typically, this process involves the coregistration of a high-resolution preoperative MRI (T1 or fluid-attenuated inversion recovery sequence) with the postimplantation CT[39,40] (**Fig. 1**A). This fusion has the advantage that the CT electrode artifact is bright, which renders electrode mapping comfortable, but the preoperative MRI does not reflect the exact postimplantation state of the brain parenchyma. Another option, implemented by use of magnetic resonance (MR)-compatible electrodes, is a postimplantation high-resolution T1 MRI[41] (**Fig. 1**B). Although the electrode artifact appears dark on T1, this approach is more accurate in providing the actual electrode positions in the postimplanted brain and spares the patient from another CT exposure. At the end, the iEEG reviewer has to be able to navigate through the electrode map and comprehend the anatomic origin of the reviewed iEEG signals.

Normal Intracranial Electroencephalogram: Background and Distinctive Waveforms

Understanding and recognizing physiologic iEEG signals are important for discriminating channels with normal activity from those with epileptic activity.[21,22] The frequency bands corresponding to normal brain activity recorded on scalp EEG also can be recorded by iEEG, provided adequate sampling rate; however, waveforms tend to appear higher in amplitude and sharper in morphology. There are 2 reasons for that: (1) the iEEG is a recording closer to the generators of the scalp EEG entities, and (2) the sEEG recording corresponds to an order of magnitude less population of neurons compared with the extracranial EEG; normal synchronization among a smaller neuronal population may resemble the morphologic features of paroxysmal synchronization of a wider neuronal population. As such, the normal iEEG may well be interpreted as epileptic if scalp EEG criteria are used. Unfortunately, criteria for the interpretation of iEEG have not yet been established and constitute work in progress. This section outlines current knowledge on normal iEEG waveforms and regional background during the awake state.

The intracranial electroencephalogram correlate of the posterior dominant rhythm

The posterior dominant rhythm (PDR), or alpha rhythm, carries the historical weight of being the first recorded scalp EEG entity, by Berger.[42] The iEEG rhythm corresponding to PDR appears diffusely in the occipital lobe,[43,44] both its lateral[45] and mesial aspects,[46] and extends both toward the parietal lobe and the temporal lobe in the lateral posterior regions of each[45] (**Fig. 2**A). The occipital iEEG correlate of the PDR exhibits the expected reactivity to eye closure and eye opening.[47]

The intracranial electroencephalogram correlate of the mu rhythm

The mu rhythm has a known central distribution on scalp EEG and typical reactivity to contralateral motor activity.[48] sEEG recordings have described an iEEG entity carrying the same electrographic features across both the precentral[18,49] and postcentral[50,51] gyri, extending anteriorly toward the supplementary motor area and the premotor lateral region (**Fig. 2**C). The central iEEG correlate of the mu rhythm also is reactive to contralateral voluntary or passive movement.[49]

The intracranial electroencephalogram correlate of lambda waves

Lambda waves are sharp occipital transients seen on extracranial EEG when a patient is engaged in activities that include visual exploration.[52] iEEG correlates of lambda waves have been recorded in the calcarine fissure, the pericalcarine mesial occipital areas, and the lateral occipital lobe[43,53] (**Fig. 2**B). These intracranial entities share the same electrographic features with scalp lambdas and also are linked to visual scanning.

The hippocampal spindle

The hippocampus generates spindles[54–59] that are morphologically similar to the scalp sleep spindles,[60–63] following a waxing-waning oscillation profile (**Fig. 3**A), but the 2 entities are not temporally coincident.[64,65] Spindles have been recorded, however, in normal human hippocampal tissue, and their frequency of occurrence was found inversely proportional to the amount of interictal activity in the epileptic hippocampus.[66] These are the main arguments favoring the idea that the hippocampal spindle constitutes a normal iEEG graphoelement.

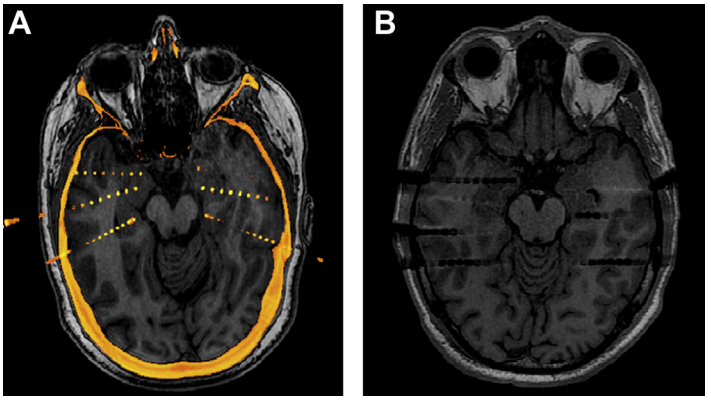

Fig. 1. Imaging of sEEG electrode implantation. (*A*) Fused postimplantation CT with preoperative MRI, when non–MR-compatible electrodes are used. (*B*) Postimplantation MRI when MR-compatible electrodes are used.

The intracranial electroencephalogram correlate of the 14 and 6 per second positive spikes variant

The 14 and 6/s positive spikes variant is a normal element of the scalp EEG, despite its spiky appearance that renders it epileptiform, with a posterior parietal-occipital distribution.[61,67,68] The iEEG correlate of this variant recently was identified in the hippocampus and consists of a waveform with sequential high-amplitude spikes of negative polarity, after a ramping up—often ramping down—profile.[69] This iEEG entity was named hippocampal barque[70] and, like the scalp 14 and 6/s positive variant, is considered normal, given their tight time-locked relationship (**Fig. 3**B).

Intracranial electroencephalogram beta rhythms

Beta-range oscillations normally are encountered on scalp EEG in the anterior frontal and central areas during the awake state.[71] iEEG rhythms in the beta range have been repeatedly recorded in the respective areas. In the precentral/postcentral complex,[49] iEEG beta oscillations are prominent, often interrupted by iEEG correlates of mu rhythm (see **Fig. 2**C). In the anterior frontal lobe,[72] beta often has a lateral distribution (**Fig. 3**D). Beta activity recently has been identified in regions whose activity typically is not represented on scalp EEG, such as the anterior insula and the middle cingulate.[21]

Intracranial electroencephalogram gamma activity

Gamma activity is difficult to identify by visual inspection of the scalp EEG but can be distinguished easily in iEEG recordings.[73] It makes regular spontaneous appearances in the frontal lobe, often coinciding with beta oscillations,[45,51,74] and becomes prominent in the postcentral gyrus

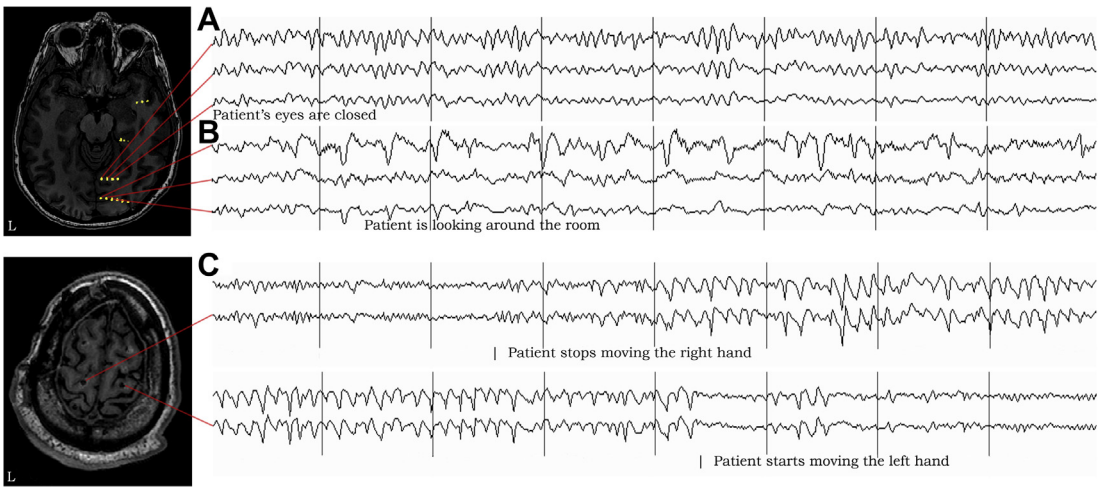

Fig. 2. Normal iEEG variants of wakefulness. (*A*) The intracranial correlate of PDR. (*B*) The intracranial correlate of lambda waves. (*C*) The intracranial correlate of the mu rhythm.

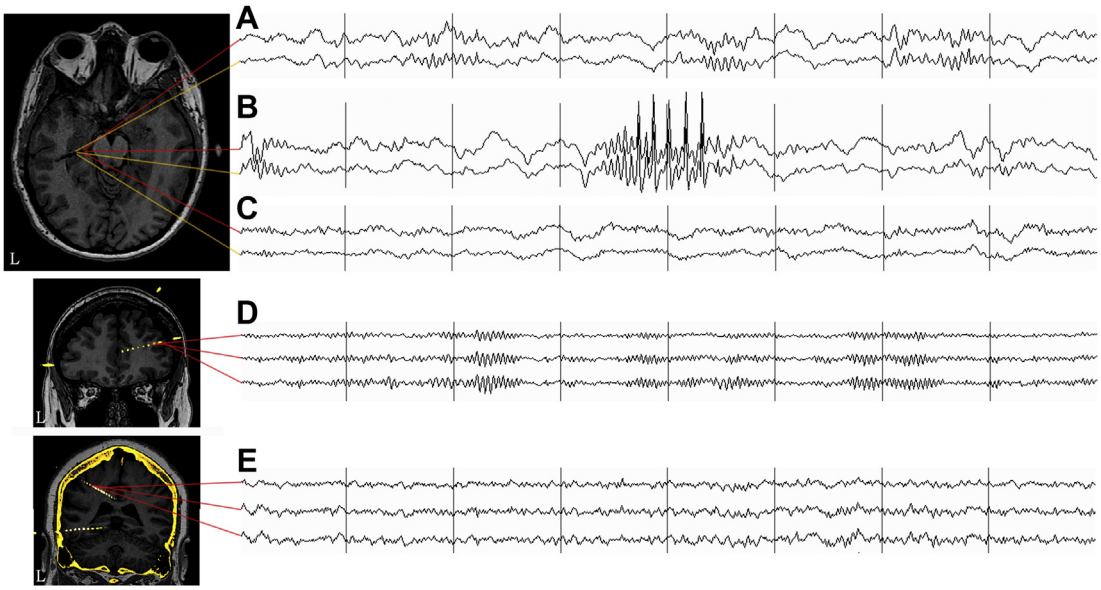

Fig. 3. Normal iEEG variants of the hippocampus. (*A*) The hippocampal spindle. (*B*) The hippocampal barque. (*C*) The hippocampal delta background during wakefulness. (*D*) Samples of beta and (*E*) gamma iEEG activity.

during contralateral voluntary motor activity[49] (Fig. 3E).

Intracranial electroencephalogram delta waves

Although the presence of delta waves on scalp EEG outside the realm of non–rapid eye movement (NREM) sleep is a marker of brain pathology,[75–77] their presence in iEEG does not necessarily denote an underlying lesion.[21] A typical example of that is the normal human hippocampus, which exhibits frequent spontaneous sequences of delta waves, even during wakefulness (Fig. 3C). The entorhinal cortex also generates delta activity, which is out of phase with respect to that originating from the hippocampus.[78] Less frequent delta waves have been shown to appear in the middle temporal gyrus, the angular gyrus, the inferior occipital gyrus, the occipital pole, the mesial frontal, and the orbital areas.

The intracranial electroencephalogram background per lobe

The background of the temporal lobe is characterized in general by high theta and alpha frequencies, and the lateral neocortex often presents with additional delta activity.[21] The occipital lobe background is rich in alpha activity. The parietal lobe iEEG background consists of a combination of alpha and beta activity. On the other hand, the frontal lobe is rich in beta and gamma background activity.

Normal Intracranial Electroencephalogram: The Effect of Sleep

An average of 35% of every iEEG recording represents the state of sleep. As in scalp EEG, the neurophysiologic changes the brain undergoes as a result of sleep are reflected in the iEEG.[22] This section outlines current knowledge on normal iEEG waveforms and regional background during the sleep state and its separate stages.

Sleep spindles

The sleep spindle is one of the hallmarks of NREM II that manifests on scalp EEG in 2 types: the fast type (14–17 Hz), with a central-parietal distribution, and the low type (11–13 Hz), with anterior frontal distribution.[61,70] Sleep spindles in the iEEG manifest the same frequency categorization (Fig. 4A, B) but their spatial distribution and temporal behavior are markedly distinct because they appear widespread in various cortical areas[79]—although higher in the centro-parietal regions and lower in the frontal lobes[80]—and exhibit a low level of synchrony both between intracranial areas and with respect to their extracranial counterpart.[64] The rate of spindle occurrence is lower in the mesial occipital regions.[22]

Non–rapid eye movement delta waves

Although delta waves predominate diffusely during the deepest stage of NREM sleep, their rate of appearance varies across the brain[22] (Fig. 4C). The mesial part of the precentral gyrus and the parietal operculum exhibit the highest rate of delta

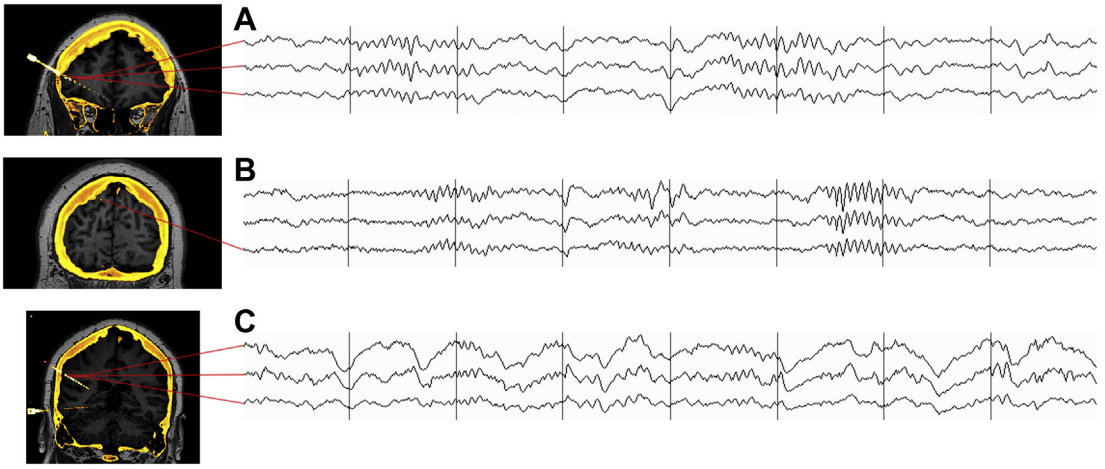

Fig. 4. Normal iEEG variants of sleep. (*A*) Frontal slow sleep spindles. (*B*). Parietal fast sleep spindles. (*C*) Parietal delta waves of NREM III.

waves during NREM III. On the other hand, areas, such as the lateral part of the precentral gyrus, the transverse temporal gyrus, the cuneus, and the calcarine fissure, manifest the lowest rates of NREM III delta activity. And, although the baseline background of the hippocampus during the awake state is already rich in delta activity, this activity increases even further during NREM II and NREM III stages. In addition, hippocampus-generated and amygdala-generated delta activity persists during rapid eye movement (REM) sleep.

The intracranial electroencephalogram background features during sleep

The iEEG activity becomes diffusely homogeneous during NREM III.[22] Slow wave activity is characterized by a semirhythmic alternation between activated and deactivated states that aggregates high-frequency physiologic rhythms (beta and gamma) to the slow wave activated state. During REM sleep, the iEEG background amplitude assumes a level similar to that of wakefulness.

Epileptic Intracranial Electroencephalogram: Interictal Activity

Interictal epileptic iEEG discharges associated with epileptogenic cortex are important to identify, because it has been well established that their inclusion in surgical resection maximizes chances of postoperative improved seizure control.[81–83] Discriminating interictal iEEG activity generated in epileptogenic tissue from activity in nonepileptogenic tissue, however, is a challenging task.[17,84] Moreover, the importance of addressing interictal activity has gained more attention in the context of breakthrough seizures after years of postoperative seizure freedom.[85,86] The hypothesis that this recurrence is the result of latent or dormant epileptogenic tissue that was not clinically and electrographically relevant to the epileptogenic zone at the time of intracranial evaluation renders the interpretation of interictal iEEG patterns a core task.[86,87] This section discusses the features of iEEG interictal activity and their relationship with underlying epileptogenic pathologies.

The main morphology of interictal iEEG activity resembles that of the extracranial EEG and is composed of a high-amplitude spike often immediately followed by a slow wave[88,89] (**Fig. 5**A). The specificity of the spike-wave iEEG interictal discharges to epileptogenicity has been linked through 4 main features: (1) frequency of occurrence: continuous or frequent or semicontinuous interictal activity appearing consistent in terms of morphology and localization is more specific to epileptogenic tissue than isolated, infrequent, rare discharges[90–92]; (2) spatiotemporal relation: leading spikes, that is, discharges that consistently precede iEEG interictal spikes in other locations, have higher specificity to epileptogenic tissue than the spikes that follow[93,94]; (3) iEEG background: interictal discharges appearing over an abnormal iEEG background, such as one with continuous slow wave activity or diffuse attenuation, more likely are markers of epileptogenicity than discharges appearing over a normal iEEG background[82,95]; and (4) persistence throughout the invasive recording: spikes attenuating in frequency and/or amplitude after the first or second day of recording, potentially disappearing entirely afterward, are more specific to neural tissue irritated by the implantation process than

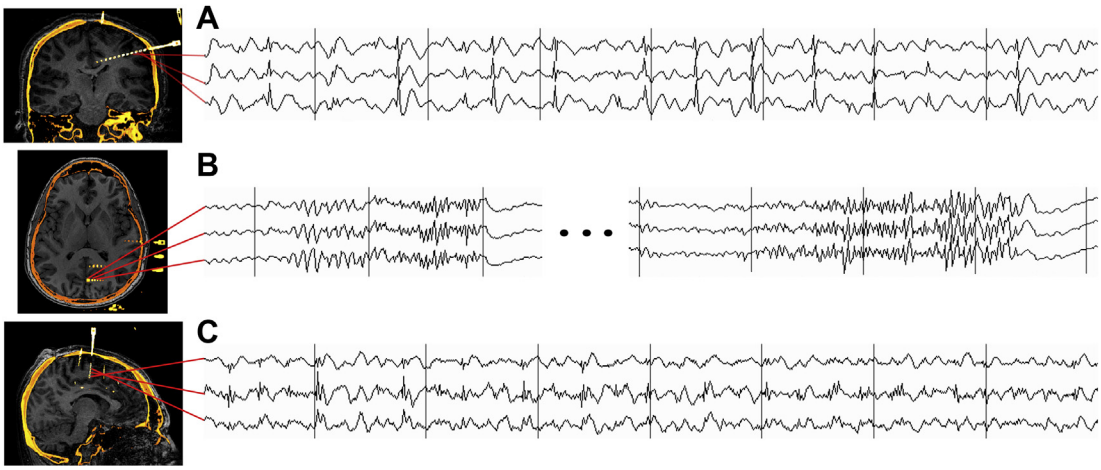

Fig. 5. Focal interictal iEEG patterns. (*A*) Spike-wave discharges. (*B*) Intermittent bursts of high-frequency activity. (*C*) Mixed pattern of spike-waves and fast intermittent bursts.

epileptogenicity.[19] Other features of the interictal iEEG spike pattern, whose importance and relevance are still under investigation, are morphology and rhythmicity.[94,96–98]

A less often met but equally robust form of interictal iEEG activity is intermittent paroxysmal fast activity[96,99–101] (**Fig. 5**B). This type of iEEG interictal activity can appear independent over the iEEG background or can coincide with spike-wave discharges, and its presence has been reliably shown to be specific for epileptogenic tissue. In particular, fast ripples are considered reliable markers of epileptogenicity and their morphology has been suggested to provide prognostic information.[102]

Of particular interest are the interictal iEEG patterns associated with focal cortical dysplasia (FCD) type II.[103–105] Three distinct interictal patterns have been confirmed: (1) a remarkable pattern of continuous spiking and repetitive bursting of polyspikes, with more than 75% specificity for FCD type II[91,106] (**Fig. 5**C); (2) a combination of paroxysmal fast activity with semicontinuous spikes, which is considered a highly localizing iEEG interictal pattern for FCD[14,107] (see **Fig. 5**B); and (3) a less impressive pattern of discontinuous, less frequent, interictal spikes over an abnormal background.[91,108] These patterns appear well localized during wakefulness and very well localized during REM sleep[109] but less localized during NREM sleep where synchronization is increased.[110–112] The exclusion of brain tissue manifesting these interictal iEEG patterns from resection has been associated with seizure recurrence and less favorable postoperative seizure control.[14,102,107]

On the contrary, no specific interictal iEEG patterns have been associated with FCD type I.[104,105] What often is described in these cases is an abundance of slow wave and spiking activity accompanied by diffuse changes in normal iEEG background in both awake and asleep states.[113] This is not surprising given the spatially extended and often multilobar distribution of this condition that renders both electrode implantation planning and localization of the epileptogenic zone challenging.[114,115]

Epileptic Intracranial Electroencephalogram: Ictal Onset Patterns

The interpretation of the ictal iEEG is tightly linked with the interpretation of the interictal background and its epileptic iEEG discharges. This is because the border between the 2 can be defined by the following rule of thumb: the iEEG becomes ictal the moment it stops being interictal. The reliable detection of the first electrographic change in time, where the interictal iEEG pattern disappears and a distinctive ictal pattern appears, is central in the clinical evaluation of iEEG seizures. For that reason, the iEEG reviewer has to be very familiar with the background and interictal features of each electrode separately, in both wakefulness and sleep states, before reviewing the ictal onset iEEG.

Although there is significant variety in ictal onset patterns recorded by sEEG,[116] 2 main patterns stand out in the literature: (1) the abrupt recruitment of fast discharging spikes, that may or may not resemble the interictal ones, over a slow depolarizing shift[117] (**Fig. 6**A), and (2) the appearance of low-voltage high-frequency activity, sometimes

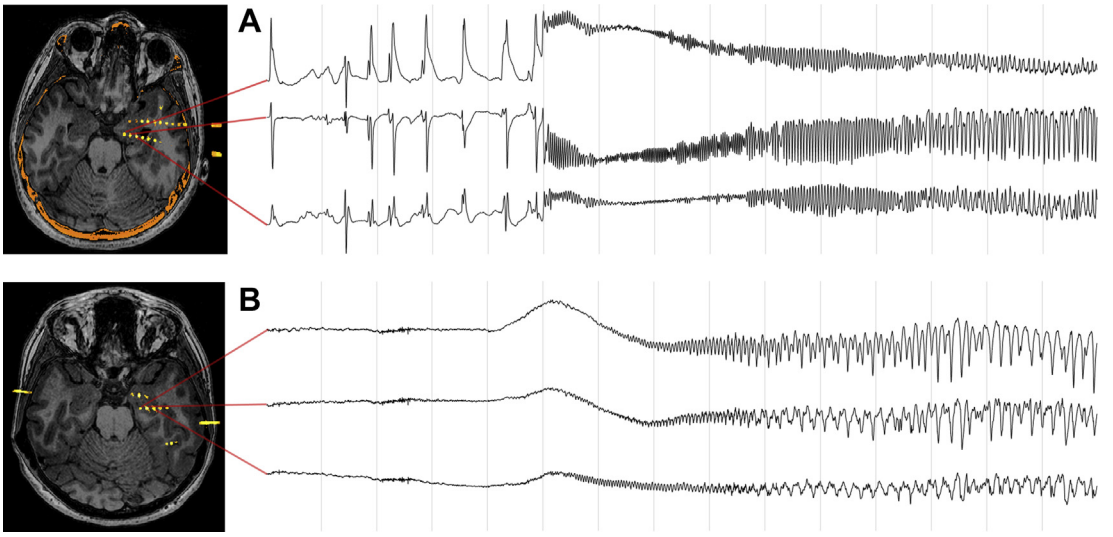

Fig. 6. Focal ictal onset iEEG patterns in the hippocampus. (*A*) Recruitment of fast discharging spikes followed by high-frequency synchronization and progression to high-amplitude sharp ictal discharges. (*B*) Low-amplitude high-frequency ictal onset, progressing to high-amplitude sharp ictal discharges.

over a slow depolarizing shift[118,119]; this pattern can appear out of the interictal background but also often is observed following the first pattern (**Fig. 6**B). For both patterns to be considered genuine ictal onsets, they are expected to follow an evolving progression to highly synchronized paroxysmal iEEG. Reproducibility of the ictal onset and progression pattern across several seizures is desirable in order to increase the reliability of ictal iEEG interpretation.[19]

The appearance of low-voltage high-frequency activity at the ictal onset is highly specific for the localization of epileptogenic tissue. The combination of the previous patterns, that is, increased paroxysmal spikes that cease abruptly on the appearance of low-voltage fast activity, is highly specific for underlying FCD.[114,115,120] In addition, the epileptogenic neuronal substrate seems to have specific windows of paroxysmal oscillation: in the hippocampal 3-layered archicortex, low-voltage fast ictal onsets occur in the 15-Hz to 30-Hz range,[121] whereas in the 6-layered neocortex, they occupy the gamma range (30–100 Hz and more).[26]

In addition to analyzing the ictal onset pattern, there are 3 important factors for the iEEG reviewers to consider: (1) the time interval between the first ictal change and the first clinical change on video: confidence of seizure-onset localization is high when the electrographic changes precede the clinical ones, whereas in the opposite scenario, localization confidence is low; (2) the spatial pattern of propagation to other monitored regions: a comprehensive description of the seizure-onset pattern should include areas of early epileptic activity spread as well as the level of synchrony between those regions; and (3) the temporal evolution characteristics of the ictal iEEG activity in each electrode separately: rapid synchronization into high-amplitude rhythmic spikes denotes regions primarily involved in organization and recruitment of the epileptic ictal discharge, whereas the presence of slow wave rhythmic or semirhythmic activity most likely represents a secondary reaction of nonepileptogenic tissue to the occurrence of the seizure.

Finally, the correlation of spatial ictal spread to clinical semiology is the cornerstone of epileptic seizure comprehension[122,123] (the role and significance of semiology in surgical planning are described in more detail by McGonigal in this issue). As the clinical seizure manifests and evolves, subjective (aura and percepts) and objective (elementary motor and complex behavior) symptoms become the constituents of the semiological picture, reflecting the ictal recruitment of anatomically and functionally interconnected cortical and subcortical regions that form the epileptic network. The process of localization of the ictal iEEG discharge at onset and subsequent propagation and its temporal correlation with the appearance of discrete semiology features on video constitute the anatomo-electro-clinical correlation of sEEG that provides a strong link between neurophysiology and clinical phenomenology.[35]

DISCLOSURE

The author has nothing to disclose.

REFERENCES

1. Isnard J, Taussig D, Bartolomei F, et al. French guidelines on stereoelectroencephalography (SEEG). Neurophysiol Clin 2018;48(1):5–13.
2. Chassoux F, Navarro V, Catenoix H, et al. Planning and management of SEEG. Neurophysiol Clin 2018;48(1):25–37.
3. Talairach J, Bancaud J, Bonis A, et al. Functional stereotaxic exploration of epilepsy. Confin Neurol 1962;22:328–31.
4. Bancaud J, Angelergues R, Bernouilli C, et al. Functional stereotaxic exploration (SEEG) of epilepsy. Electroencephalogr Clin Neurophysiol 1970;28(1):85–6.
5. Munari C, Bancaud J. The role of stereoelectroencephalography (SEEG) in the evaluation of partial epileptic patients. In: Porter RJ, Morselli PL, editors. The epilepsies. London: Butterworths; 1987. p. 267–306.
6. Gonzalez-Martinez J, Bulacio J, Alexopoulos A, et al. Stereoelectroencephalography in the "difficult to localize" refractory focal epilepsy: early experience from a North American epilepsy center. Epilepsia 2013;54(2):323–30.
7. Tomlinson SB, Buch VP, Armstrong D, et al. Stereoelectroencephalography in pediatric epilepsy surgery. J Korean Neurosurg Soc 2019;62(3):302–12.
8. Karsy M, Guan J, Ducis K, et al. Emerging surgical therapies in the treatment of pediatric epilepsy. Transl Pediatr 2016;5(2):67–78.
9. Gadgil N, LoPresti MA, Muir M, et al. An update on pediatric surgical epilepsy: Part I. Surg Neurol Int 2019;10:257.
10. Gadgil N, Muir M, Lopresti MA, et al. An update on pediatric surgical epilepsy: Part II. Surg Neurol Int 2019;10:258.
11. McGonigal A, Bartolomei F, Régis J, et al. Stereoelectroencephalography in presurgical assessment of MRI-negative epilepsy. Brain 2007;130:3169–83.
12. Nobili L, Francione S, Mai R, et al. Surgical treatment of drug-resistant nocturnal frontal lobe epilepsy. Brain 2007;130:561–73.
13. Besson P, Andermann F, Dubeau F, et al. Small focal cortical dysplasia lesions are located at the bottom of a deep sulcus. Brain 2008;131:3246–55.
14. Chassoux F, Devaux B, Landré E, et al. Stereoelectroencephalography in focal cortical dysplasia A 3D approach to delineating the dysplastic cortex. Brain 2000;123:1733–51.
15. Katz JS, Abel TJ. Stereoelectroencephalography versus subdural electrodes for localization of the epileptogenic zone: what is the evidence? Neurotherapeutics 2019;16(1):59–66.
16. Jehi L, Friedman D, Carlson C, et al. The evolution of epilepsy surgery between 1991 and 2011 in nine major epilepsy centers across the United States, Germany, and Australia. Epilepsia 2015;56:1526–33.
17. Rosenow F, Luders H. Presurgical evaluation of epilepsy. Brain 2001;124:1683–700.
18. Graf M, Niedermeyer E, Schiemann J, et al. Electrocorticography: information derived from intraoperative recordings during seizure surgery. Clin Electroencephalogr 1984;15:83–91.
19. Bulacio JC, Chauvel P, McGonigal A. Stereoelectroencephalography: interpretation. J Clin Neurophysiol 2016;33(6):503–10.
20. Bartolomei F, Nica A, Valenti-Hirsch MP, et al. Interpretation of SEEG recordings. Neurophysiol Clin 2018 Feb;48(1):53–7.
21. Frauscher B, von Ellenrieder N, Zelmann R, et al. Atlas of the normal intracranial electroencephalogram: neurophysiological awake activity in different cortical areas. Brain 2018;141(4):1130–44.
22. von Ellenrieder N, Gotman J, Zelmann R, et al. How the human brain sleeps: direct cortical recordings of normal brain activity. Ann Neurol 2019;87(2):289–301.
23. Bourien J, Bartolomei F, Bellanger JJ, et al. A method to identify reproducible subsets of coactivated structures during interictal spikes. Application to intracerebral EEG in temporal lobe epilepsy. Clin Neurophysiol 2005;116:443–55.
24. Dahal P, Ghani N, Flinker A, et al. Interictal epileptiform discharges shape large-scale intercortical communication. Brain 2019;142(11):3502–13.
25. Kahane P, Landré E, Minotti L, et al. The Bancaud and Talairach view on the epileptogenic zone: a working hypothesis. Epileptic Disord 2006;8(Suppl 2):S16–26.
26. Grinenko O, Li J, Mosher JC, et al. A fingerprint of the epileptogenic zone in human epilepsies. Brain 2018;141(1):117–31.
27. Bancaud J. Surgery of epilepsy based on stereotactic investigations — the plan of the SEEG investigation. Acta Neurochir Suppl 1980;30:25—34.
28. Talairach J, Bancaud J, Szikla G, et al. Approche nouvelle de la neurochirurgie de l'épilepsie. Méthodologie stéréotaxique et résultats thérapeutiques. Neurochirurgie 1974;20(suppl 1):1—249.
29. Mullin J, Shriver M, Alomar S, et al. Is SEEG safe? A systematic review and meta-analysis of stereoelectroencephalography-related complications. Epilepsia 2016;57:386—401.
30. Musolino A, Tournoux P, Missir O, et al. Methodology of "in vivo" anatomical study and stereoelectroencephalographic exploration in brain surgery for epilepsy. J Neuroradiol 1990;17(2):67–102.
31. Guenot M, Isnard J, Ryvlin P, et al. Neurophysiological monitoring for epilepsy surgery: the Talairach SEEG method. StereoElectroEncephaloGraphy. Indications, results, complications and therapeutic

applications in a series of 100 consecutive cases. Stereotact Funct Neurosurg 2001;77(1–4):29–32.
32. Bourdillon P, Châtillon CE, Moles A, et al. Effective accuracy of stereoelectroencephalography: robotic 3D versus Talairach orthogonal approaches. J Neurosurg 2018;131(6):1938–46.
33. Li K, Vakharia VN, Sparks R, et al. Stereoelectroencephalography electrode placement: detection of blood vessel conflicts. Epilepsia 2019;60(9): 1942–8.
34. Bottan JS, Rubino PA, Lau JC, et al. Robot-assisted insular depth electrode implantation through oblique trajectories: 3-dimensional anatomical nuances, technique, accuracy, and safety. Oper Neurosurg (Hagerstown) 2019;18(3):278–83.
35. Chauvel P, McGonigal A. Emergence of semiology in epileptic seizures. Epilepsy Behav 2014;38: 94–103.
36. Chauvel P, Vignal J, Biraben A, et al. Stereoelectroencephalography. In: Pawlik G, Stefan H, editors. Multimethodological assessment of the epileptic forms. New York: Springer Verlag; 1996. p. 270.
37. Abramovici S, Antony A, Baldwin ME, et al. Features of simultaneous scalp and intracranial EEG that predict localization of ictal onset zone. Clin EEG Neurosci 2018;49(3):206–12.
38. Kalamangalam GP, Tandon N. Stereo-EEG implantation strategy. J Clin Neurophysiol 2016;33(6): 483–9.
39. Qin C, Tan Z, Pan Y, et al. Automatic and precise localization and cortical labeling of subdural and depth intracranial electrodes. Front Neuroinform 2017;11:10.
40. Medina Villalon S, Paz R, Roehri N, et al. EpiTools, A software suite for presurgical brain mapping in epilepsy: Intracerebral EEG. J Neurosci Methods 2018;303:7–15.
41. Hinds WA, Misra A, Sperling MR, et al. Enhanced co-registration methods to improve intracranial electrode contact localization. Neuroimage Clin 2018;20:398–406.
42. Berger H. Über das Elektrenkephalogramm des Menschen. Arch Psychiatr Nervenkr 1929;87: 527–70.
43. Perez-Borja C, Chatrian GE, Tyce FA, et al. Electrographic patterns of the occipital lobe in man: a topographic study based on use of implanted electrodes. Electroencephalogr Clin Neurophysiol 1962;14:171–82.
44. Gastaut H. Enregistrement sous-cortical de l'activité électrique spontanée et provoquée du lobe occipital humain. Electroencephalogr Clin Neurophysiol 1949;1(2):205–21.
45. Sem-Jacobsen CW, Petersen MC, Dodge HW Jr, et al. Electroencephalographic rhythms from the depths of the parietal, occipital and temporal lobes in man. Electroencephalogr Clin Neurophysiol 1956;8(2):263–78.
46. Chatrian GE, Bickford RG, Uihlein A. Depth electrographic study of a fast rhythm evoked from the human calcarine region by steady illumination. Electroencephalogr Clin Neurophysiol 1960;12: 167–76.
47. Sem-Jacobsen CW, Bickford RG, Petersen MC, et al. Depth distribution of normal electroencephalographic rhythms. Proc Staff Meet Mayo Clin 1953; 28(6):156–61.
48. Gastaut H, Terzian H, Gastaut Y. Etude d'une activite electroencephalographique meconnue: le rhythme rolandique en arceau. Mars Med 1952; 89(6):296–310.
49. Jasper H, Penfield W. Electrocorticograms in man: effect of voluntary movement upon the electrical activity of the pre-central gyrus. Arch Psychiatr Nervenkr 1949;183:163–74.
50. Szurhaj W, Derambure P, Labyt E, et al. Basic mechanisms of central rhythms reactivity to preparation and execution of a voluntary movement: a stereoelectroencephalographic study. Clin Neurophysiol 2003;114(1):107–19.
51. Szurhaj W, Derambure P. Intracerebral study of gamma oscillations in the human sensorimotor cortex. Prog Brain Res 2006;159:297–310.
52. Chatrian GE. The lambda waves. In: Remond A, editor. Handbook of electroencephalography and clinical neurophysiology, vol. 6A. Amsterdam: Elsevier; 1976. p. 123–49.
53. Chatrian GE, Bickford RG, Petersen MC, et al. Lambda waves with depth electrodes in humans. In: Ramey ER, O'Doherty DS, editors. Electrical studies on the unanesthetized brain. New York: PB Hoeber; 1960. p. 291–310.
54. Brazier MA. Regional activities within the hippocampus and hippocampal gyrus. Exp Neurol 1970;26:354–68.
55. Brazier MA. Interactions of deep structures during seizures in man. In: Petche U, MA Brazier, editors. Mechanisms of synchronization in epileptic seizures. Vienna (Austria): Springer-Verlang; 1972. p. 409–24.
56. Crowne DP, Radcliffe D. Some characteristics and functional relations of the electrical activity of the primate hippocampus and hypothesis of hippocampal function. In: Isaaacson RL, Pribram KH, editors. The hippocampus. New York: Plenum Press; 1974. p. 185–207.
57. Moiseeva NI, Aleksanyan ZA. Activity of neuronal populations of human subcortical structures during sleep. Electroencephalogr Clin Neurophysiol 1976; 41:467–75.
58. Da Silva L. Physiology of the hippocampus and related structures. Annu Rev Physiol 1978;40: 185–216.

59. Halgren E, Walter RD, Cherlow DG, et al. Mental phenomena evoked by electrical stimulation of the human hippocampal formation and amygdala. Brain 1978;101:83–117.
60. Loomis AL, Harvey EN, Hobart G. Potential rhythms of the cerebral cortex during sleep. Science 1935; 81:597–8.
61. Gibbs FA, Gibbs EL. In: Reading A, editor. Atlas of electroencephalography, vol. 1. Reading (MA): Addison-Wesley; 1964. p. 90–6.
62. De Gennaro L, Ferrara M. Sleep spindles: an overview. Sleep Med Rev 2003;7:423–40.
63. Steriade M. Grouping of brain rhythms in corticothalamic systems. Neuroscience 2006;137: 1087–106.
64. Frauscher B, von Ellenrieder N, Dubeau F, et al. Scalp spindles are associated with widespread intracranial activity with unexpectedly low synchrony. Neuroimage 2015;105:1–12.
65. Dehghani N, Cash SS, Halgren E. Emergence of synchronous EEG spindles from asynchronous MEG spindles. Hum Brain Mapp 2011;32:2217–27.
66. Frauscher B, Bernasconi N, Caldairou B, et al. Interictal hippocampal spiking influences the occurrence of hippocampal sleep spindles. Sleep 2015;38(12):1927–33.
67. Lombroso CT, Schwartz IH, Clark DM, et al. Ctenoids in healthy youth: controlled study of 14- and 6-per-second positive spiking. Neurology 1966;16:1152–8.
68. Schwartz IH, Lombroso CT. 14 and 6/second positive spiking (ctenoids) in the electroencephalograms of primary school pupils. J Pediatr 1968; 72(5):678–82.
69. Kokkinos V, Zaher N, Antony A, et al. The intracranial correlate of the 14&6/sec positive spikes normal scalp EEG variant. Clin Neurophysiol 2019;130(9):1570–80.
70. Kokkinos V, Richardson MR, Urban A. The hippocampal barque: an epileptiform but non-epileptic ECoG hippocampal entity. Front Hum Neurosci 2020;14:92.
71. Chang BS, Schomer DL, Niedermeyer E. Normal EEG and sleep: adults and elderly. In: Schomer DL, Lopes da Silva FH, editors. Niedermeyer's encephalography. 6th edition. Philadelphia: Lippincott Williams & Wilkins; 2011. p. 183–215.
72. Sem-Jacobsen CW, Petersen MC, Lazarte JA, et al. Electroencephalographic rhythms from the depths of the frontal lobe in 60 psychotic patients. Electroencephalogr Clin Neurophysiol 1955;7(2):193–210.
73. Singer W. Synchronization of cortical activity and its putative role in information processing and learning. Annu Rev Physiol 1993;55:349–74.
74. Pfurtscheller G, Lopes da Silva FH. Event-related EEG/MEG synchronization and desynchronization: basic principles. Clin Neurophysiol 1999;110(11): 1842–57.
75. Niedermeyer E. Abnormal EEG patterns: epileptic and paroxysmal. In: Niedermeyer E, Lopes da Silva FH, editors. Electroencephalography: Basic principles, clinical applications and related fields. 5th edition. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 255–80.
76. Fischer-Williams M, Dike GL. Brain tumors and other space-occupying lesions. In: Niedermeyer E, Lopes da Silva FH, editors. Electroencephalography: Basic principles, clinical applications and related fields. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 305–22.
77. Bauer G. Coma and brain death. In: Niedermeyer E, Lopes da Silva FH, editors. Electroencephalography: Basic principles, clinical applications and related fields. 5th edition. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 471–88.
78. Mormann F, Osterhage H, Andrzejak RG, et al. Independent delta/theta rhythms in the human hippocampus and entorhinal cortex. Front Hum Neurosci 2008;2:3.
79. Andrillon T, Nir Y, Cirelli C, et al. Single-neuron activity and eye movements during human REM sleep and awake vision. Nat Commun 2015;6:7884.
80. Peter-Derex L, Comte JC, Mauguière F, et al. Density and frequency caudo-rostral gradients of sleep spindles recorded in the human cortex. Sleep 2012;35(1):69–79.
81. Wyllie E, Luders H, Morris HH III, et al. Clinical outcome after complete or partial cortical resection for intractable epilepsy. Neurology 1987;37: 1634–41.
82. Paolicchi JM, Jayakar P, Dean P, et al. Predictors of outcome in pediatric epilepsy surgery. Neurology 2000;54:642–7.
83. Krsek P, Maton B, Jayakar P, et al. Incomplete resection of focal cortical dysplasia is the main predictor of poor postsurgical outcome. Neurology 2009;72:217–23.
84. Palmini A. The concept of the epileptogenic zone: a modern look at Penfield and Jasper's views on the role of interictal spikes. Epileptic Disord 2006; 8(Suppl 2):S10–5.
85. Hemb M, Palmini A, Paglioli E, et al. An 18-year follow-up of seizure outcome after surgery for temporal lobe epilepsy and hippocampal sclerosis. J Neurol Neurosurg Psychiatry 2013;84(7):800–5.
86. Najm I, Jehi L, Palmini A, et al. Temporal patterns and mechanisms of epilepsy surgery failure. Epilepsia 2013;54(5):772–82.
87. Hemb M, Paglioli E, Dubeau F, et al. Mirror EPC": epilepsia partialis continua shifting sides after rolandic resection in dysplasia. Neurology 2014; 83(16):1439–43.

88. Jasper HH. Electrocorticography. In: Penfield W, Erickson TC, editors. Epilepsy and cortical localization. Springfield (IL): Charles C Thomas; 1941. p. 380–454.
89. Jasper HH, Arfel-Capdeville G, Rasmussen T. Evaluation of EEG and cortical electrographic studies for prognosis of seizures following surgical excision of epileptogenic lesions. Epilepsia 1961;2: 130–7.
90. Rasmussen T. Characteristics of a pure culture of frontal lobe epilepsy. Epilepsia 1983;24(4):482–93.
91. Palmini A, Gambardella A, Andermann F, et al. Intrinsic epileptogenicity of human dysplastic cortex as suggested by corticography and surgical results. Ann Neurol 1995;37(4):476–87.
92. Guerreiro MM, Quesney LF, Salanova V, et al. Continuous electrocorticogram epileptiform discharges due to brain gliosis. J Clin Neurophysiol 2003;20(4):239–42.
93. Alarcon G, Garcia Seoane JJ, Binnie CD, et al. Origin and propagation of interictal discharges in the acute electrocorticogram. Implications for pathophysiology and surgical treatment of temporal lobe epilepsy. Brain 1997;120(Pt 12):2259–82.
94. Asano E, Muzik O, Shah A, et al. Quantitative interictal subdural EEG analyses in children with neocortical epilepsy. Epilepsia 2003;44(3):425–34.
95. Holthausen HH, Teixera V, Tuxhorn I, et al. Epilepsy surgery in children and adolescents with focal cortical dysplasias. In: Tuxhorn I, Holthausen H, Boenigk H, editors. Paediatric epilepsy syndromes and their surgical treatment. London: John Libbey; 1997. p. 199–215.
96. Crépon B, Navarro V, Hasboun D, et al. Mapping interictal oscillations greater than 200 Hz recorded with intracranial macroelectrodes in human epilepsy. Brain 2010;133:33–45.
97. Spencer SS, Goncharova II, Duckrow RB, et al. Interictal spikes on intracranial recording: behavior, physiology, and implications. Epilepsia 2008;49: 1881–92.
98. Widdess-Walsh P, Jeha L, Nair D, et al. Subdural electrode analysis in focal cortical dysplasia: predictors of surgical outcome. Neurology 2007;69: 660–7.
99. Jacobs J, Zijlmans M, Zelmann R, et al. High-frequency electroencephalographic oscillations correlate with outcome of epilepsy surgery. Ann Neurol 2010;67:209–20.
100. Urrestarazu E, Chander R, Dubeau F, et al. Interictal high-frequency oscillations (100–500 Hz) in the intracerebral EEG of epileptic patients. Brain 2007;130:2354–66.
101. Wendling F, Bartolomei F, Bellanger JJ, et al. Epileptic fast intracerebral EEG activity: evidence for spatial decorrelation at seizure onset. Brain 2003;126:1449–59.
102. Kerber K, Dumpelmann M, Schelter B, et al. Differentiation of specific ripple patterns helps to identify epileptogenic areas for surgical procedures. Clin Neurophysiol 2014;125:1339–45.
103. Taylor DC, Falconer MA, Bruton CJ, et al. Focal dysplasia of the cerebral cortex in epilepsy. J Neurol Neurosurg Psychiatry 1971;34:369–87.
104. Palmini A, Najm I, Avanzini G, et al. Terminology and classification of the cortical dysplasias. Neurology 2004;62:S2–8.
105. Blümcke I, Thom M, Aronica E, et al. The clinicopathologic spectrum of focal cortical dysplasias: a consensus classification proposed by an ad hoc Task Force of the ILAE Diagnostic Methods Commission. Epilepsia 2011;52(1):158–74.
106. Ferrier CH, Alarcon G, Engelsman J, et al. Relevance of residual histologic and electrocorticographic abnormalities for surgical outcome in frontal lobe epilepsy. Epilepsia 2001;42(3):363–71.
107. Tassi L, Colombo N, Garbelli R, et al. Focal cortical dysplasia: neuropathological subtypes, EEG, neuroimaging and surgical outcome. Brain 2002;125: 1719–32.
108. Binnie CD, Polkey CE, Alarcon G. Electrocorticography. In: Luders H, Comair Y, editors. Epilepsy surgery. 2nd edition. Philadelphia: Lippincott Williams & Wilkins; 2000. p. 637–41.
109. Frauscher B, von Ellenrieder N, Dubeau F, et al. EEG desynchronization during phasic REM sleep suppresses interictal epileptic activity in humans. Epilepsia 2016;57(6):879–88.
110. Sammaritano M, Gigli GL, Gotman J. Interictal spiking during wakefulness and sleep and the localization of foci in temporal lobe epilepsy. Neurology 1991;41(2 Pt 1):290–7.
111. Menezes Cordeiro I, von Ellenrieder N, Zazubovits N, et al. Sleep influences the intracerebral EEG pattern of focal cortical dysplasia. Epilepsy Res 2015;113:132–9.
112. Klimes P, Cimbalnik J, Brazdil M, et al. NREM sleep is the state of vigilance that best identifies the epileptogenic zone in the interictal electroencephalogram. Epilepsia 2019;60(12):2404–15.
113. Holthausen H, Pieper T, Winkler P, et al. Electroclinical-pathological correlations in focal cortical dysplasia (FCD) at young ages. Childs Nerv Syst 2014;30(12):2015–26.
114. Buoni S, Zannolli R, Miracco C, et al. Focal cortical dysplasia type 1b as a cause of severe epilepsy with multiple independent spike foci. Brain Dev 2008;30(1):53–8.
115. Krsek P, Pieper T, Karlmeier A, et al. Different presurgical characteristics and seizure outcomes in children with focal cortical dysplasia type I or II. Epilepsia 2009;50(1):125–37.
116. Chauvel P, Buser P, Badier JM, et al. The "epileptogenic zone" in humans: representation of

intercritical events by spatio-temporal maps [French]. Rev Neurol (Paris) 1987;143:443–50.
117. Chabard_es S, Kahane P, Minotti L, et al. The temporopolar cortex plays a pivotal role in temporal lobe seizures. Brain 2005;128:1818–31.
118. Arroyo S, Uematsu S. High-frequency EEG activity at the start of seizures. J Clin Neurophysiol 1992;9:441–8.
119. Lee SA, Spencer DD, Spencer SS. Intracranial EEG seizure-onset patterns in neocortical epilepsy. Epilepsia 2000;41:297–307.
120. Lagarde S, Bonini F, McGonigal A, et al. Seizure-onset patterns in focal cortical dysplasia and neurodevelopmental tumors: Relationship with surgical prognosis and neuropathologic subtypes. Epilepsia 2016;57(9):1426–35.
121. Bartolomei F, Wendling F, Régis J, et al. Pre-ictal synchronicity in limbic networks of mesial temporal lobe epilepsy. Epilepsy Res 2004;61:89–104.
122. Bonini F, McGonigal A, Trébuchon A, et al. Frontal lobe seizures: from clinical semiology to localization. Epilepsia 2014;55(2):264–77.
123. Gibbs SA, Proserpio P, Francione S, et al. Clinical features of sleep-related hypermotor epilepsy in relation to the seizure-onset zone: A review of 135 surgically treated cases. Epilepsia 2019;60(4):707–17.