Future of Neurology & Technology: Stereoelectroencephalography in Presurgical Epilepsy Evaluation

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Abstract

Stereoelectroencephalography (SEEG) is not only a sophisticated and highly technological investigation but a new and better way to conceptualize the spatial and temporal dynamics of epileptic activity. The first intracranial investigations with SEEG were performed in France in the mid-twentieth century; however, its use in North America is much more recent. Given its significantly lower risk of complications and its ability to sample both superficial and deep structures and both hemispheres simultaneously, SEEG has become the preferred method to conduct intracranial EEG monitoring in most comprehensive epilepsy centers in North America. SEEG is an invasive neurophysiologic methodology used for advanced presurgical workup in the 20% of drug-resistant patients with more complex focal epilepsy in whom noninvasive investigations do not allow to decide on surgical candidacy. SEEG uses stereotactically implanted depth electrodes to map the origin and propagation of epileptic seizures by creating a 3-dimensional representation of the abnormal electrical activity in the brain. SEEG analysis takes into account the background, interictal, and ictal activity, as well as the results of cortical electrical stimulation procedures, to reliably delineate the epileptogenic network. By means of a clinical vignette, this article will walk general neurologists, but especially neurology trainees through the immense potential of this methodology. In summary, SEEG enables to accurately identify the epileptogenic zone in patients with drug-resistant focal epilepsy who otherwise would be not amenable to surgical treatment. In this patient population, SEEG is the best way to improve seizure control and achieve seizure freedom.
At least 1 in 10 patients with epilepsy will fail 2 well-tolerated and appropriately chosen antiseizure medications, and this is even more common in focal epilepsy. Surgery revolutionized the management of patients with drug-resistant focal epilepsy and, for them, represents the best way to improve seizure control and sometimes even result in seizure freedom (SF). These patients should be timely referred to epilepsy centers to determine surgical amenability. Presurgical evaluation has the goal of identifying the epileptogenic zone (EZ, i.e., the minimum cortical area whose removal is necessary for SF).

A phase 1 (noninvasive) workup includes prolonged scalp video-EEG monitoring, structural and functional neuroimaging, and neuropsychological assessment. Magnetoencephalography, high-density EEG (HD-EEG), and combined EEG/MRI are additional auxiliary investigations. The exact combination of studies varies depending on the individual patient’s needs.

Some epilepsies are more complex than others and may therefore require invasive investigations (phase 2). This is the case in patients with inconclusive brain MRI, discordant findings in phase 1 workup, or close vicinity of the assumed EZ to eloquent cortex. In patients with such features, a phase 2 evaluation is needed to determine surgical candidacy. Phase 2 investigations are defined by their invasiveness and include electrocorticography, subdural electrodes (SDE, i.e., strips and grids), and stereoelectroencephalography (SEEG). Nowadays, SEEG has become the principal method for intracranial EEG monitoring in most epilepsy centers in North America. This article will introduce general neurologists, but especially neurology trainees to the potential of SEEG.

Clinical Vignette

A 25-year-old right-handed woman presented with sleep-related focal aware seizures characterized by an arousal due to a sensation involving her entire body, similar to a wave starting in the middle of the stomach and going up and down and then tactile hypersensitivity, restlessness, and anxiety. Sometimes, this evolved into left arm stiffening and, more rarely, to left leg shaking and then impaired awareness. These seizures started at age 12 years. Epilepsy risk factors were negative. She failed 4 antiseizure medications and was having 10 seizures per month. Her prolonged scalp video-EEG monitoring captured only late ictal EEG changes over the right central midline region. The interictal EEG was noncontributory. A 3-Tesla MRI showed a suspicious sulcus in the right posterior cingulate with subtle transmantle sign (Figure, A and B). An unusual sulcogyral morphology was also seen in the right anterior cingulate. The rest of the phase 1 investigations (i.e., neuropsychology, functional neuroimaging, magnetoencephalography, and HD-EEG) were noncontributory.

SEEG was proposed. The main hypothesis was a right hemispheric, midline close, deep seated EZ in the parietal lobe in keeping with the potential MRI lesion. Alternatively, a mesiofrontal generator and an anterior insula generator with rapid mesiofrontal propagation were considered. To test these hypotheses, 16 depth electrodes were implanted over the right hemisphere (Figure, C). Ictal recordings demonstrated that all seizures originated from the right midline parietal region (i.e., the presumed focal cortical dysplasia [FCD] seen on MRI) with rapid spread to the ipsilateral supplementary motor area (Figure, main panel and B). This patient underwent a selective right posterior cingulate cortical resection, and histopathology revealed FCD type 2a. No seizure recurrence has occurred since surgery 3 years ago.

SEEG: The What and the How

SEEG is an advanced invasive neurophysiologic methodology that uses multicontact intracerebral depth electrodes to...
consideration of the whole armamentarium obtained during the presurgical workup. It also allows for not only tailoring resection to the minimum amount needed to achieve SF, but it can also be used to conduct (or guide) therapeutic procedures such as radiofrequency thermocoagulation, thermoablation, and responsive neurostimulation.

Interdisciplinary collaboration is a critical component of SEEG, and neurologists with subspecialization in epileptology or clinical neurophysiology play a key role during the entire process, including implantation planning, interpretation, and finally resection planning. Human SEEG recordings are already used in experimental neuroscience, and in the very near future, SEEG clinical applications will likely expand and impact on medical domains outside of epileptology such as neuropsychiatry and cognitive neurology. SEEG is considered to be the safest intracranial EEG recording modality with complication rates of 0.6%–2%, including asymptomatic—and considerably less frequent symptomatic—intracerebral hemorrhages and transient postsurgical nonhemorrhagic neurologic deficits. Admissions for SEEG exceeding 4 weeks are not recommended due to patient-related factors and a higher risk of infectious complications. In addition, SEEG is the only intracranial EEG option to sample deep regions, delineate epileptogenic networks, and also safely conduct bilateral explorations, as in suspected bitemporal epilepsy.

Until very recently, SDE was the mainstay of intracranial EEG monitoring in North America. Although SDE spatial coverage is often thought to be superior in the neocortex, this is only true for gyri, but not sulci. Regarding surgical outcomes, SEEG is at least noninferior to SDE: slightly lower surgical resections (76.9 vs 81.6%) are outbalanced by better SF outcomes (61.0 vs 56.4%). In contrast to SDE, SEEG is better tolerated and also associated with lower morbidity (4.8 vs 15.5%) and mortality (0.2 vs 0.4%).

Training Opportunities
SEEG training is recommended for the whole team involved in this procedure. For neurologists, some authors have suggested either a minimum of a 6-month training or participation in at least 10 SEEGs in a center with a minimum of 5 years of experience. At present, there are no clinical fellowship programs specifically focused on SEEG. However, this training is available at some epilepsy centers in North America as a part of epilepsy or clinical neurophysiology fellowships, especially for second-year or advanced fellows.

The Grenoble-Lyon-Milan alliance and Cleveland Clinic offer introductory courses on SEEG. Although these courses do not intend to replace a formal training in an experienced center, they are a great starting point. An additional educational initiative is the Montreal Neurological Institute (MNI) Open Intracranial EEG Atlas, a freely available online resource illustrating brain activity during both wakefulness and sleep across 38 different cortical regions.

Research Opportunities
SEEG is a flourishing field for epilepsy research and research on experimental neurophysiology. Within epilepsy, new computerized approaches for EZ localization based on ictal or interictal data are currently in development. The aim of these algorithms is to improve localization accuracy, reduce functional deficits and the time needed for presurgical evaluation, and predict reliably the probability of SF after surgery. Hopefully, in the near future, these new techniques will inform clinical decisions during presurgical epilepsy workup. Human SEEG-derived data are also increasingly used by neuroscientists. For instance, the Functional Brain Tractography international project aims to improve our knowledge on large-scale human brain connectivity using low-frequency CES
in patients with epilepsy who are surgical candidates. SEEG-derived data have also contributed extensively to elucidate the local aspects of human sleep. These findings may soon have a clinical translation to different fields including neuropsychiatry, cognitive neurology, and sleep medicine.

Conclusions
In summary, SEEG is an invasive neurophysiologic methodology originally proposed to map the SOZ, and it is currently used for advanced presurgical workup in patients with complex focal epilepsies. Research opportunities in this area are multiple and not only related to epilepsy. For neurologists, SEEG provides a unique possibility for subspecialization given the rise of SEEG procedures in North America.

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References

Appendix Authors

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