Epileptogenic zone

The **epileptogenic zone (EZ)** refers to the area of the brain responsible for generating seizures in patients withepilepsy. Identifying the EZ is critical for diagnosing and treating epilepsy, particularly in patients who may benefit from surgical intervention.

Key Characteristics of the Epileptogenic Zone

1. **Definition:**

1. The EZ is the region of the brain that must be removed or treated to achieve seizure freedom in a patient.
2. It may not always correspond exactly to visible abnormalities on imaging or regions showing seizure activity during an EEG.

2. **Complex Nature:**

1. The EZ may overlap with other brain regions involved in seizure propagation (the “irritative zone,” “symptomatogenic zone,” or “seizure onset zone”).
2. It is often challenging to precisely define the boundaries of the EZ, requiring a multidisciplinary approach.

Diagnosis

1. **Electroencephalography (EEG):**

1. **Scalp EEG:** Detects electrical activity but has limited spatial resolution.

1. **Intracranial EEG (iEEG):** Electrodes are placed directly on the brain's surface or inserted into the brain to provide high-resolution data.

1. **Stereo-EEG (SEEG):** A minimally invasive technique that maps seizure networks in 3D.

2. **Neuroimaging:**

1. **MRI (Magnetic Resonance Imaging):**

1. Used to detect structural abnormalities such as cortical dysplasia, tumors, or hippocampal sclerosis.

1. **Functional Imaging:**

1. **PET (Positron Emission Tomography):** Identifies areas of altered metabolism, often hypometabolism in the interictal phase.

1. **SPECT (Single Photon Emission Computed Tomography):** Captures blood flow changes during a seizure (ictal SPECT).

1. **fMRI (Functional MRI):**

    1. Helps map eloquent brain regions to avoid functional deficits during surgery.

3. **Neuropsychological Testing:**

    1. Assesses cognitive function to correlate deficits with specific brain regions.

4. **Magnetoencephalography (MEG):**

    1. Measures magnetic fields produced by neural activity, offering high temporal and spatial resolution for localizing the EZ.

5. **Advanced Techniques:**

    1. **High-frequency Oscillations (HFOs):**
        1. Identified via EEG or iEEG, these are potential biomarkers of the EZ.
    2. **Artificial Intelligence (AI) and Machine Learning:**
        1. AI models analyze complex datasets from EEG, imaging, and patient history to pinpoint the EZ.

—

Epilepsy Surgery and the EZ - **Goal:** Surgical resection aims to remove the EZ while preserving critical brain functions. - **Common Procedures:**

1. **Temporal Lobectomy:** Effective for temporal lobe epilepsy, the most common focal epilepsy.
2. **Lesionectomy:** Targeted removal of structural lesions identified on imaging.
3. **Laser Interstitial Thermal Therapy (LITT):** A minimally invasive method to ablate the EZ.
4. **Responsive Neurostimulation (RNS):** Targets the EZ with electrical stimulation to prevent seizures.
5. **Deep Brain Stimulation (DBS):** Modulates seizure activity in networks involving the EZ.

—

Challenges in Localizing the EZ 1. **Complex Seizure Networks:**

1. The EZ is part of a larger epileptogenic network, complicating localization.

2. **Non-lesional Epilepsy:**

1. Patients without detectable structural abnormalities on MRI present a diagnostic challenge.

3. **Overlap with Functional Brain Areas:**

1. Surgery must balance seizure control with preserving critical functions like speech, memory, and motor skills.

—

Future Directions - **Multimodal Integration:** Combining data from EEG, imaging, and functional studies to improve EZ localization. - **AI and Big Data:** Enhancing diagnostic precision and predicting surgical outcomes. - **Non-invasive Methods:** Advancing technologies like transcranial magnetic stimulation (TMS) to map and potentially treat the EZ without surgery.

Understanding and accurately localizing the epileptogenic zone is vital for personalized epilepsy

treatment and achieving optimal patient outcomes.

Interictal high-frequency oscillations (HFOs) are a promising neurophysiological biomarker of the epileptogenic zone (EZ). However, the objective criteria for distinguishing pathological from physiological HFOs remains elusive, hindering clinical application. Zhang et al. investigated whether the distinct mechanisms underlying pathological and physiological HFOs are encapsulated in their signal morphology in intracranial EEG (iEEG) recordings and whether this mechanism-driven distinction could be simulated by a deep generative model.

In a retrospective cohort of 185 epilepsy patients who underwent iEEG monitoring, they analyzed 686,410 HFOs across 18,265 brain contacts. To learn morphological characteristics, each event was transformed into a time-frequency plot and input into a variational autoencoder. They characterized latent space clusters containing morphologically defined putative pathological HFOs (mpHFOs) using interpretability analysis, including latent space disentanglement and time-domain perturbation.

mpHFOs showed strong associations with expert-defined spikes and were predominantly located within the seizure onset zone (SOZ). Discovered novel pathological features included high power in the gamma (30-80 Hz) and ripple (>80 Hz) bands centered on the event. These characteristics were consistent across multiple variables, including institution, electrode type, and patient demographics. Predicting 12-month postoperative seizure outcomes using the resection ratio of mpHFOs outperformed unclassified HFOs (F1=0.72 vs. 0.68) and matched current clinical standards using SOZ resection (F1=0.74). Combining mpHFO data with demographic and SOZ resection status further improved prediction accuracy (F1=0.83).

The data-driven approach yielded a novel, explainable definition of pathological HFOs, which has the potential to further enhance the clinical use of HFOs for EZ delineation [1)]

1)
Zhang Y, Daida A, Liu L, Kuroda N, Ding Y, Oana S, Kanai S, Monsoor T, Duan C, Hussain SA, Qiao JX, Salamon N, Fallah A, Sim MS, Sankar R, Staba RJ, Engel J Jr, Asano E, Roychowdhury V, Nariai H. Self-Supervised Data-Driven Approach Defines Pathological High-Frequency Oscillations in Human. medRxiv [Preprint]. 2024 Nov 5:2024.07.10.24310189. doi: 10.1101/2024.07.10.24310189. PMID: 39040207; PMCID: PMC11261948.