

Functional Connectivity of Gamma Activity Quantifies Brain Epileptogenicity in Children with Refractory Epilepsy

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Introduction

- **Drug resistant epilepsy (DRE)** disrupts structural and functional connections within a large-scale neuronal network causing seizures.
- The alterations of this network is crucial for identifying epileptogenic nodes that may help us to delineate the epileptogenic zone (EZ).
- The **objective** of this study is to characterize alterations in functional connectivity (FC) of epileptogenic brain networks based on **interictal and ictal intracranial EEG (icEEG)** recordings.
- We **hypothesize** that: (i) FC increases in epileptogenic nodes of the network compared to non-epileptogenic nodes; and (ii) FC discriminates between inter-ictal, pre-ictal, ictal, and post-ictal states.

Methods

- **Patients:** Thirty-one children (mean age: 11.41 ± 5.94 years; 11 females) who underwent epilepsy surgery at Boston Children's Hospital.
- **icEEG recordings:** We identified one-minute of data containing: (i) interictal activity without frequent spikes ("No Spikes"); (ii) interictal activity with frequent spikes ("Spikes"); (iii) pre-ictal activity before the onset of a clinical seizure ("Pre-ictal"); (iv) ictal activity during a clinical seizure ("Ictal"); and (v) post-ictal activity after the end of a clinical seizure ("Post-ictal").
- **Connectivity Measures:** We estimated the Amplitude Envelope Correlation (AEC), Correlation (Corr), and Phase locked Value (PLV) in low (30-60 Hz) and high gamma (60-90 Hz) bands, which characterize synchronization of neural populations before and during seizures.

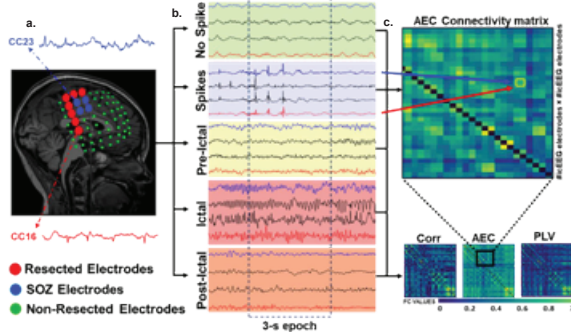


Fig. 1: Functional connectivity measures for icEEG recordings. (a) The MRI shows resected (red), non-resected (green), and SOZ (blue) electrodes. (b) Interictal and ictal data containing different neuronal conditions. (c) AEC, PLV and Corr matrices generated from each 3-second epoch computed for all data. AEC matrix shows the FC value of the neural activity recorded from CC16 and CC23 electrodes.

- **Resection & Outcome:** Resection zone was determined by coregistering the patient's preoperational and postoperational MRIs. Surgical outcome was evaluated using the Engel scale and dichotomized into **good (Engel 1)** and **poor (Engel 2)**.
- **Wilcoxon Signed-rank test:** We tested differences in mean connectivity between the icEEG electrodes **inside and outside the Seizure Onset Zone** defined by the epileptologists. We also compared FC values between **resected and non-resected areas** for good and poor outcome patients.
- **Nodal strength** was computed as the average connection strength of all functional connections of a particular node. **Global Connectivity** was calculated as average nodal strength of all electrodes in all interictal and ictal data segment.
- Also, **Predictive values** was estimated from FC values based on all interictal and ictal data segments.

Results

- We observed higher mean FC values ($p < 0.05$) for the nodes inside compared to outside resection in good outcome patients for the following metrics: (i) AEC (low and high gamma) for all conditions (Fig. 2a); (ii) PLV (low and high gamma) for "Post-ictal"; and (iii) CORR (low gamma) for "Spikes" and "Ictal". Similar findings yield the analysis for the clinically defined SOZ (Fig. 2b).
- For poor outcome patients, FC values between nodes inside vs. outside resection and SOZ did not reveal significant findings.

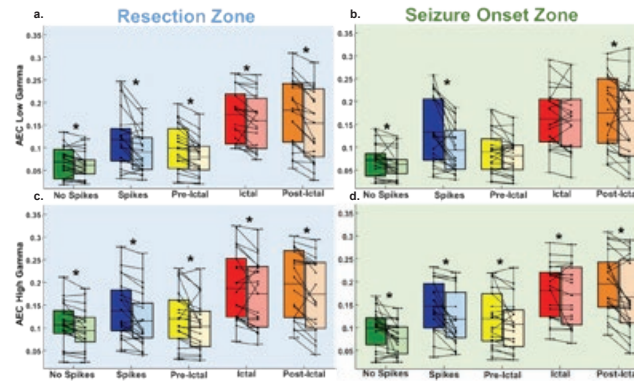


Fig. 2: AEC based FC measure for interictal and ictal segments in good outcome patients. (a, c) AEC in both low gamma and high gamma showed significant increase of FC inside resection compared to outside of the resection zone. (c, d)

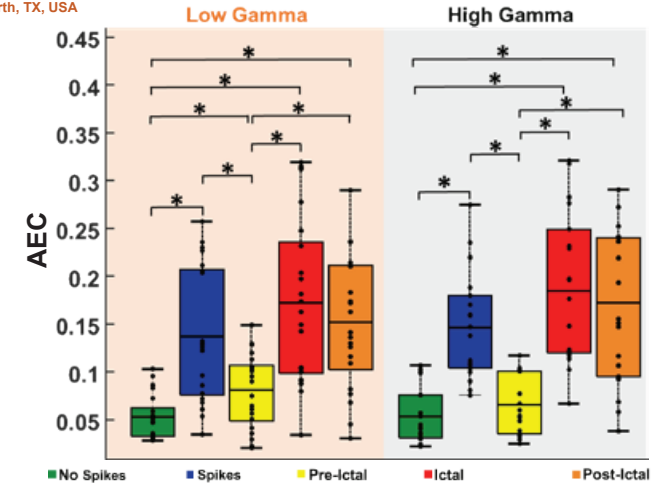


Fig. 3: Global Connectivity of good surgical outcome. AEC values of "No Spikes" were lower compared to all other conditions in both frequency bands ($p < 0.05$). Similarly, AEC values were lower in "Pre-ictal" compared to "Spikes", "Ictal", and "Post-ictal" ($p < 0.05$).

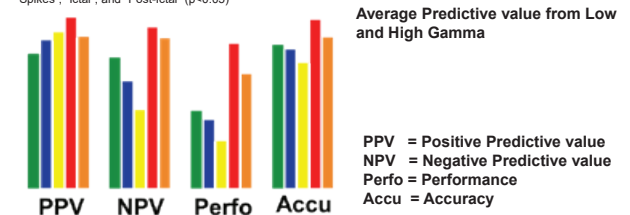


Fig. 4: Surgical predictive measure. AEC measure in low and high gamma was predictive of the surgical outcome.

Conclusions

- Our findings indicate that FC of gamma activity can quantify the epileptogenicity of brain network nodes. Thus, it can be used as an indirect biomarker for identifying critical epileptogenic nodes.
- Such a biomarker can predict surgical outcome by identifying the EZ without necessitating long-term icEEG recordings for capturing stereotyped seizures.

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