Functional Connectome-based Biomarkers of Epileptogenesis in Drug-Resistant Human Epilepsy

Farid Hamzei-Sichani MD, PhD; Stefan Fuertinger PhD; Kristina Simonyan MD, PhD
Department of Neurological Surgery, University of Massachusetts Medical School, Worcester, MA, USA

assfn American Society for Stereotactic and Functional Neurosurgery 2018 BIENNIAL MEETING DENVER | June 2-5, 2018

University of Massachusetts Medical School UMASS

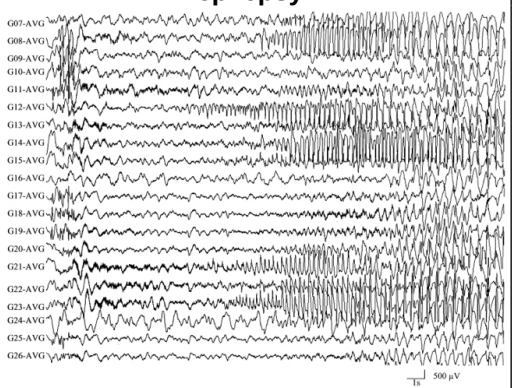
Introduction

About one third of epilepsy patients do not respond to medical treatment, but can still benefit from surgical intervention. Despite recent technological advances in epilepsy surgery, 30%-50% of patients with drug-resistant epilepsy never achieve seizure freedom. This is due, in part, to the lack of objective methods for identification of the epileptogenic brain areas. Several lines of evidence have shown that pathological high frequency oscillations (HFOs) at 100-500 Hz recorded via intracranial EEG are involved in epileptogenesis. However, to date there is no reliable approach to detect and classify pathological from normal HFOs for proper identification of epileptogenic activity.

Learning Objectives

-understand the role of high frequency oscillations in epileptogenesis.
-understand intracranial EEG-based biomarkers of epileptogenic activity.

iEEG recordings in a patient with focal epilepsy



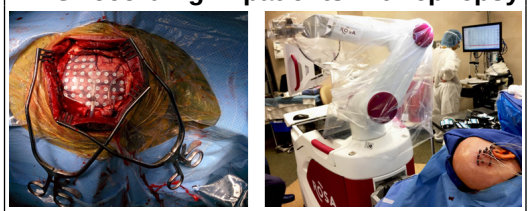
Traub et al. Epilepsia 2001; 42(2):153-70.

High frequency oscillatory activtiy in channels 13, 14, 21 and 22 prior to seizure onset

Methods

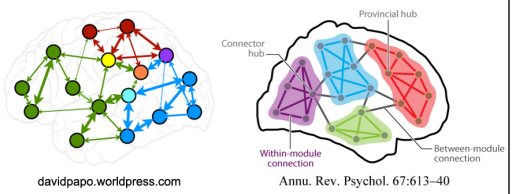
We used graph theoretical analysis of intracranial EEG recordings (subdural grids) in patients with drug-resistant epilepsy in order to identify pathological HFO network activity patterns. The high frequency oscillations were classified into ripple (80-250 Hz), fast ripple (250-500 Hz) and HFO (100-500 Hz) bands. Functional connectivity was assessed as mutual information of intracranial EEG signals recorded for each pair of electrode time-series.

iEEG recording in patients with epilepsy



iEEG recording via subdural eletrodes and SEEG.

Schematic diagram of brain networks introducing network terminology

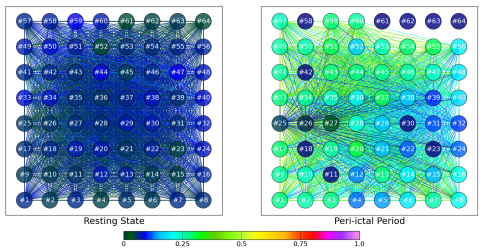


Brain networks consist of nodes (sites of iEEG recording) connected by links defined functionally based on correllation of oscillatory activity between each pair of nodes. Highly interconnected network communities of nodes known as modules are a hallmark of brain networks and play an important role in information processing.

Results

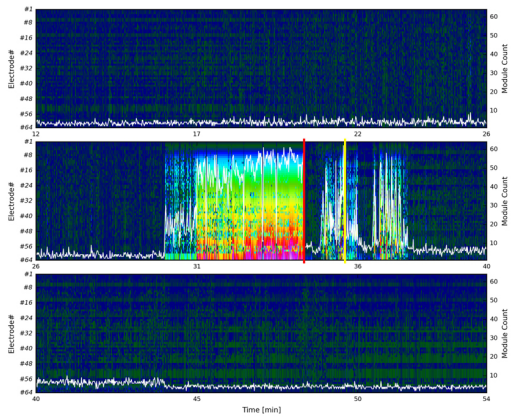
We found that during no-seizure(interictal) states, cortical networks at all high frequency bands were characterized by stable network structure (modular structure) measured by the average number of nodal communities. Irregular partitioning of this network architecture led to an increased average number of nodal communities during the pre-ictal period in all high-frequency bands (corrected p = 0.03). This "modular breakdown" was seen on average 3-4 minutes before the electrographic seizure onset.

Spatiotemporal dynamics of cortical high frequency network activity during interictal (resting state) and seizure periods.



High frequency network connectivity patterns show rapid changes prior to seizure onset but remain stable during the interictal period. Edge and node color represent nomalized mutual information coefficient between pairs of nodes and normalized cumulative strength of connections.

Temporal evolution of peri-ictal modular structure of high frequency seizure network in a patient with focal epilepsy.



Analysis of an extended segment of iEEG shows stable modular structure (white trace depicting number of modules) towards the end of an interictal period (top row). The number of modules increases in a dramatic and explosive fashion 3-4 minutes before the seizure onset (red vertical line). The modular network structure returns to interictal state after the end of the electrographic seizure activity (yellow vertical line).

Conclusions

Functional connectome-based measures of HFO dynamics in contrast to single-channel pathologic HFOs have a high potential in facilitating the development of novel biomarkers for epileptogenesis.

References

Fuertinger, S. et. al., (2016). "Modular breakdown of high frequency brain networks in human epilepsy."*Epilepsia*. Jul:57(7):1097-108. PMID: 27221325.