Inhibitory effects of pre-ictal brain rhythms on seizure propagation

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Introduction

Hypothesis
- Sub-50 Hz iEEG rhythms act as a regulatory mechanism that reduces neuronal firing. Strong regulatory rhythms will inhibit the spread of ictal activity.

Motivation
In sensory and motor cortex, the power of sub-50 Hz iEEG rhythms (e.g., theta in motor cortex) is anti-correlated with high gamma band (70-200 Hz) power, which is a robust correlate of local action potentials. This appears to be a general property of most of neocortex (Honey et al., in prep). We think that these high gamma rhythms may act as a regulatory mechanism that decreases the excitability of neurons. If true, then strong regulatory rhythms should inhibit the spread of ictal activity into an area and prevent marked increases in mean population firing rate.

Types of Propagation

Pre-ictal Baselined Spectrograms

Conventional Propagation
- The latency of first spectral power change in each channel following left hippocampal seizure onset in Patient 1. Purple bars=SD, Red horizontal lines=Mean.
- Latency of first increase in high gamma power in each channel following left hippocampal seizure onset in Patient 1. Purple bars=SD, Red horizontal lines=Mean.

Conventional Propagation Latency
- The latency of each channel was correlated with the mean regulatory frequency power in the 30 sec prior to ictal onset.
- Median latency across all channels for each patient was calculated across seizures, and channel propagation times were calculated for all patients.

High Gamma Propagation Latency
- The latency of high gamma propagation to each channel was correlated with the mean regulatory frequency power in the 30 sec prior to ictal onset.
- Propagation latencies and regulatory frequency power were calculated across seizures and channel propagation times were calculated for all patients.

Propagating iEEG rhythms are filtered with a simple wavelet to obtain a temporally varying power spectrum.

Conventional Propagation
- Although these data fit expectations, across patients the effect is not robust MN [SD] r=0.04 (0.16)
- Although these data fit expectations, across patients the effect is not robust MN [SD] r=0.38 (0.17)

Conventional propagation analysis described above.

Predicting Propagation Times

Conventional Propagation
- Logistic Regression, 5/6 Patients
- Utility of predictions for left out patient are evaluated with area under the curve (AUC), maximum accuracy, chance accuracy, and proportion of correct predictions (where we predict high gamma ictal activity if probability exceeds 50%). AUC is reliably greater than 0.5 (one-tailed permutation test, p<0.02, 0.5<0.58)

Identifying Regulatory Frequencies

Example 12-14 Hz & High Gamma Power Pre-ictal Time Series
- The 1-50 Hz frequency that shows the minimal correlation with high gamma power is the putative regulatory frequency for that channel.
- Frequency with correlation closest to -1

Pre-ictal power timecourses were computed for all frequencies in the 1-50 Hz range (2 Hz bins) and were correlated with preictal high gamma power.

Pre-ictal High Gamma Power Correlations Predict Ictal High Gamma Activity
- Channels that do not show high gamma ictal activity tend to have low high gamma regulatory frequency power correlations in the preictal period.

Predicting Ictal Involvement

Conclusions
1. The relative power of putative regulatory frequencies does not robustly predict the relative speed of ictal propagation. This may be due to factors we have not controlled for (e.g., the strength of the ictal activity in areas immediately upstream from each region) and the difficulty with measuring rhythm power immediately preceding high gamma ictal propagation.
2. The preictal sub-50 Hz correlation with high gamma power reliably predicts if a channel will exhibit high gamma ictal activity. This observational effect might stem from the inhibitory effect of ictal regulatory rhythms. However it might also be due to IIDs or an accident of anatomy. Future work will investigate these possibilities.

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