Do seizures propagate through communication hubs?

Mark A. Kramer, PhD‡; Eric D. Kolaczyk, PhD‡; Heidi E. Kirsch, MD, MS*

*UCSF Epilepsy Center, UCSF Department of Neurology; ‡ Department of Mathematics and Statistics, Boston University

OBJECTIVE

We explore the macroscopic characteristics of emergent ictal networks by considering intracranial electrocorticograph (ECoG) recordings from a human subject with intractable epilepsy. For eight seizures recorded from the subject, we compute the cross-correlation between all 2850 electrode pairs to define networks of interdependent electrodes during preictal and ictal time intervals. We analyze these networks by applying traditional measures from network analysis. We find at seizure onset a diffuse breakdown in global coupling, but also find local changes indicative of increased throughput of and between specific cortical and subcortical regions. We conclude that network analysis yields measures to summarize the complicated coupling topology emergent at a seizure onset. Using these measures, we attempt to identify spatially localized brain regions that may facilitate seizure maintenance and propagation, and serve as potential targets for focal therapies.

HUMAN SUBJECT DATA

The human subject we consider is a 39 year old right handed woman with medically refractory complex partial seizures. Scalp video-EEG telemetry captured eight seizures that all arose from the left frontotemporal region (this was her dominant hemisphere for language) with some semiological features atypical for mesial temporal onset. Because of the relatively diffuse scalp localization and the origin in the language dominant hemisphere, it was decided to implant subdural electrodes to better determine focal ictal onset and to map functional brain regions. The implanted electrodes consisted of an 8-by-8 electrode grid over the left frontotemporal region, a 6-contact electrode strip over the left suborbital frontal lobe, and two 6-contact left hippocampal depth electrodes. ECoG data were recorded continuously for five days and nine seizures were detected. Each seizure began near the distal end of the depth electrodes and, approximately 15 s later, was observed on the subdural electrode grid. ECoG epochs containing eight of the patient’s seizures were extracted from the clinical record and saved for further analysis in accordance with procedures approved by the UCSF and BU Committees on Human Research.

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METHODS

Ictal onsets were identified by a board-certified clinical neurophysiologist (HEK) to occur at the emergence of focal high-frequency, low-amplitude activity. We define preictal and ictal intervals by monitoring the low frequency, large amplitude power near these onsets. We show an example of the total low frequency power (upper trace) and voltage from a single electrode (lower trace) in the figure below (left).

Within each interval, we compute the cross-correlation between each electrode pair. We show the ECoG data recorded from an example electrode pair during the preictal and ictal intervals in the color figure above. We define two electrodes as coupled if the cross-correlation exceeds a threshold value of 0.75. We show the cross-correlation for this electrode pair in both intervals in the right figure above. The electrodes are coupled during the preictal interval. We indicate this by connecting the electrodes with an edge. We repeat this procedure for all 76 electrodes. For a single seizure, we find:

In this figure each red circle indicates an electrode from the grid, strip, and depth electrodes. We observe that the coupling topology is quiet complicated. How do we interpret the two graphs?

Qualitative Conclusions:

• Thinning of edges.
• Spatially localized effects.

RESULTS

The plots above show the degree (top row) and betweenness (bottom row) of each electrode averaged over the 8 seizures during the preictal (left column) and ictal (middle column) intervals. The size of the circle is proportional to the value calculated. We indicate the change in the measures at ictal onset in the right column. The color red (blue) indicates an increase (decrease) in the measure at ictal onset. The asterisks denote electrodes with statistically significant increases in betweenness at ictal onset.

INTERPRETATION

At seizure onset we observe: 1) a diffusive decrease in degree over the left temporal lobe, the left hippocampus, and the left suborbital frontal lobe, and 2) localized increases in betweenness. We interpret these results to suggest a broad disconnection of cortical regions that perhaps expose spatially localized communication hubs at seizure onset.

We identify the communication hubs as prospective surgical targets. Comparing these targets with the actual resected areas, we find little overlap. This subject continued to experience seizures two months following surgery.

We will test these preliminary results in future longitudinal studies comparing surgical outcome with network analysis measures, or invasive recordings and intervention in a simple physiological model of epilepsy.