Research Abstract:
Generic mechanisms of pathological and normal HFOs: An analytical approach

Stephen Gliske, Christian Fink, William Stacey*

Rationale
HFOs have been investigated as biomarkers of both normal physiology and epileptic tissue. Most prior research has focused on distinguishing the two based upon peak frequency into Ripples (<200 Hz) and Fast Ripples (>250 Hz). However, a potentially more accurate difference is that 'normal' HFOs are produced by post-synaptic potentials (PSPs) and 'pathological' HFOs by action potentials (APs). The goal of this work is to analyze the features of how AP-generated versus PSP-generated HFOs appear when recorded by an electrode and to determine generic mechanisms that produce them.

Methods
A computational model of hippocampal tissue, containing pyramidal cells, interneurons, and synaptic currents, simulated the output from both PSPs and APs as recorded by a nearby electrode. Various network parameters were simulated to produce HFOs by different generic mechanisms. A second model of explicitly-constructed event times was then used to generate recorded voltages independent of any specific network structure.

Results
Based upon their morphological characteristics, both PSPs and APs can readily generate HFOs with peak frequency < 200 Hz. Fast Ripples transiently emerge from the precise conditions that produce AP-Ripples. Surprisingly, HFOs can be generated even by completely uncoupled networks.

Discussion
These results suggest the HFOs are a generic property of highly active firing neurons, independent of any specific network structure or pathology, and that peak frequency cannot distinguish normal from abnormal Ripples. They also provide a generic, network-based explanation for the link between pathological Ripples and Fast Ripples.