TITLE: Modeling seizures and treatments

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Background: .Changes in neuronal synchrony is thought to play an important role in onset and progression of a seizure. To understand how and why synchrony changes to produce seizures, it is necessary to characterize how neurons responds to inputs, such as synaptic inputs from other constituent neurons in its network, or to external perturbations such as deep brain stimulation (DBS). We use phase response curves to measure how these perturbations affect the next firing times of neurons when neurons are firing periodically. Changes in the neurons' sensitivity to inputs caused by epileptogenic ion channel mutations, antiepileptic drugs, or intrinsic changes in the neurons (such as firing rate), can change the synchronizability of a network of neurons. Stimulating neurons using DBS electric field sat certain frequencies can elicit chaotic activity in periodically firing neurons and alter synchronization of networks. By desynchronizing or synchronizing populations, we are able to affect the duration of different phases of tonic-clonic seizures.

Methods: Experiments are done in computer simulations and in vitro. Computer simulations of neurons are used to simulate the effects of synaptic inputs and DBS electric fields under control, epileptogenic mutation and drug conditions. These modeling experiments are then confirmed with electrophysiology experiments using whole cell patch-clamp and a dynamic clamp to measure the neuron's PRCs under different conditions and inputs. Finally networks are simulated using models generated using data acquired experimentally from neurons. In these simulations we determine how networks behave differently under epileptiform and treatment conditions.