



Presentation Abstract

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Presentation Title: Homeostatic synaptic scaling mediates distinct types of paroxysmal activity following brain trauma

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Topic: ++C.08.f. Networks

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Abstract: Epilepsy is commonly observed following brain trauma, however mechanisms that cause epileptic seizures are still not fully understood. Experimental and modeling studies suggested that homeostatic scaling of synaptic efficacy due to deafferentation resulting from head trauma could lead to epilepsy. Epileptic seizures involve large changes in ion concentrations, however, it remains unknown how homeostatic changes interact with ion concentration dynamics during interictal and ictal periods. In this study, we examined the effect of homeostatic synaptic scaling in a biophysically realistic cortical network model that included the dynamics of extra- and intracellular ion (Na⁺, K⁺ and Cl⁻) concentrations. In the model, trauma was induced by partial deafferentation of neurons and excitatory connections between neurons were then scaled by homeostatic processes to maintain a firing rate of about 5 Hz. We observed two distinct types of abnormal activity following deafferentation and synaptic scaling. Increases in synaptic strength led to intermittent periods of high frequency activity accompanied by a small increase in extracellular K⁺ concentration (from 3 to 4.5 mM) and followed by periods of low activity; this network state did not transition to full-scale seizures. However, application of a brief (1 sec) high frequency external stimulus transformed the network, inducing seizure-like events with extracellular K⁺ increasing up to 8-10 mM and repetitive transitions occurring between tonic and clonic states. This observation was in contrast to results obtained from the intact

(without deafferentation) network where the same external stimulation caused only a transient increase in firing rate followed by a return to the baseline after the stimulus was removed. Our study suggests the existence of bistability in the deafferented network, and that the threshold for the spike-wave type of epileptiform activity triggered by external input is reduced following deafferentation and homeostatic scaling. Overall, we show that a model considering interactions between ion dynamics and homeostatic processes can differentiate between interictal paroxysmal activity involving high frequency activity and full-fledged seizure as seen in experimental and clinical settings.

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