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Presentation Abstract

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Presentation Title:	A computational model of neuronal and glial homeostatic synaptic plasticity in posttraumatic epileptogenesis
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Abstract:	Homeostatic synaptic plasticity (HSP) is involved in the emergence of epileptic activity that follows head trauma. The homeostatic scaling of synaptic strengths is believed to be regulated by the spiking activity of postsynaptic neurons. Recent evidence indicates that trauma-induced HSP might be at least in part regulated by active signaling from glial cells, and from astrocytes in particular. Neuronal and glial HSP mechanisms are likely to operate on different spatial scales. A goal of this study was to examine and compare neuronal and glial mechanisms for HSP in posttraumatic epileptogenesis. We developed a large-scale computational model comprised of 6,400 (80x80) pyramidal neurons and interneurons (PY/IN ratio 4:1) organized in a 2D square lattice with locally random synaptic connectivity. Deafferentation was modeled as a reduction in the rate of external input to a preset fraction of neurons that allowed controlling both the severity and the spatial organization of trauma. Following deafferentation, homeostatic plasticity adjusted synaptic strengths to bring the network-averaged

firing rate to the target value of 5 Hz. Both neuronal (through synaptic scaling based on postsynaptic activity) and glial (through synaptic scaling based on presynaptic activity) HSP mechanisms were incorporated in the model. Paroxysmal activity appeared in the network when the fraction of lesioned neurons exceeded some critical value. Bursts were generated at the boundary between intact and deafferented tissue and propagated into the latter. In the absence of the neuronal HSP mechanism, the dependence of the rate of paroxysmal activity on the trauma volume could be modulated by varying the spatial scale of glial HSP mechanism. In the presence of neuronal HSP mechanism, the rate of paroxysmal activity was high and nearly independent of the trauma volume. When the experimentally observed morphological changes of astrocytes in the traumatized tissue were included in the model, there was a reduced rate of paroxysmal discharges even in the presence of neuronal HSP. This study shows that neuronal and glial mechanisms of homeostatic plasticity might have complementary roles in posttraumatic epileptogenesis. The model suggests that morphological remodeling of astrocytes (experimentally observed immediately after trauma event) might be a protective mechanism aimed to reduce the incidence of paroxysmal discharges caused by HSP.

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SYNAPTIC PLASTICITY

EPILEPTIFORM

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