A computational model of glia-mediated seizure induction

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There is an increasing amount of evidence supporting a causal relation between chronic inflammation and seizures. Several proinflammatory cytokines have been studied in the context of seizure susceptibility and neuronal damage, including tumor necrosis factor $\alpha$ (TNF-$\alpha$). It is believed that, in certain conditions, TNF-$\alpha$ can increase neural excitability and facilitate infection-related seizures [1].

The effect is potentially related to a recent discovery that links TNF-$\alpha$ to homeostatic synaptic plasticity. Specifically, acute application or long-term glial production (during chronic activity blockade) of TNF-$\alpha$ increases AMPA receptor surface expression in hippocampal neurons [2], [3].

The regulation resembles synaptic scaling, a homeostatic mechanisms which globally adjusts synaptic strengths to maintain a certain synaptic drive to neurons. It is thought to ensure the stability of the cortex throughout development and during learning. Despite having a generally beneficial role, homeostatic mechanisms were proposed in models as a cause of neural hyperexcitability and epileptogenesis [4].

We have developed a computational model of glia-mediated synaptic scaling, in a network of spiking neurons interacting with the glial tissue. It is the first model to consider the mechanisms underlying synaptic scaling and the spatial effects that can arise from the diffusion of neuromodulators. Our model reproduces experimental findings linking chronic overexpression, systemic infection, or lesions to hyperexcitability and network bursts and is consistent with the idea that chronic inflammation can increase seizure predisposition.

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References