Abstract View

MODEL FOR GENERATING FOCAL CORTICAL PAROXYSMAL ACTIVITY BY INCREASE OF EXTRACELLULAR POTASSIUM CONCENTRATION.

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In vivo recordings from intact cat neocortex and cortical slab preparations suggest a cortical origin for spike-wave (SW) and polyspike-wave (PSW) electrographic seizures. The oscillatory mechanisms underlying this paroxysmal activity were investigated in computational models of neocortical networks. Extracellular K^+ concentration $[K^+]$ was continuously computed based on neuronal K^+ currents and K^+ pumps as well as glial buffering. An increase of $[K^+]$ triggered a transition from normal, awake-like asynchronous firing to 2-4 Hz seizure-like activity. In this mode, the neurons fired periodic bursts and nearby neurons oscillated highly synchronously; in some neurons depolarization led to spike inactivation. A $[K^+]$ increase, which is sufficient to produce oscillations, could result from excessive firing (e.g., induced by external stimulation) or inability of K^+ regulatory system (e.g., after removal of glial buffering). A combination of a few currents including high-threshold Ca^{2+}, persistent Na^+, and hyperpolarization-activated depolarizing (I_h) currents was required to maintain 2-4 Hz activity. In a network model that included lateral K^+ diffusion between cells, increase of $[K^+]$ in a small region was generally sufficient to maintain paroxysmal oscillations in the whole network. Changes in $[K^+]$ could explain transitions between slow (2-4 Hz) bursting and fast runs, as observed in vivo. In the model, the oscillatory pattern (slow bursting or fast runs) depended on the absolute level of $[K^+]$ and also on the relative levels of $[K^+]$ around soma and dendrites. The model suggests that an increase of $[K^+]$ can transform random awake-like activity or slow-wave sleep oscillations into paroxysmal oscillations, reminiscent of electrographic SW/PSW seizures.
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