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Interaction between synaptic inhibition and glial-potassium dynamics leads to diverse seizure transition modes in biophysical models of human focal seizures. (English)

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Summary: How focal seizures initiate and evolve in human neocortex remains a fundamental problem in neuroscience. Here, we use biophysical neuronal network models of neocortical patches to study how the interaction between inhibition and extracellular potassium ($[K^+]_o$) dynamics may contribute to different types of focal seizures. Three main types of propagated focal seizures observed in recent intracortical microelectrode recordings in humans were modelled: seizures characterized by sustained ($\sim 30 - 60$ Hz) gamma local field potential (LFP) oscillations; seizures where the onset in the propagated site consisted of LFP spikes that later evolved into rhythmic ($\sim 2 - 3$ Hz) spike-wave complexes (SWCs); and seizures where a brief stage of low-amplitude fast-oscillation ($\sim 10 - 20$ Hz) LFPs preceded the SWC activity. Our findings are fourfold: (1) The interaction between elevated $[K^+]_o$ (due to abnormal potassium buffering by glial cells) and the strength of synaptic inhibition plays a predominant role in shaping these three types of seizures. (2) Strengthening of inhibition leads to the onset of sustained narrowband gamma seizures. (3) Transition into SWC seizures is obtained either by the weakening of inhibitory synapses, or by a transient strengthening followed by an inhibitory breakdown (e.g. GABA depletion). This reduction or breakdown of inhibition among fast-spiking (FS) inhibitory interneurons increases their spiking activity and leads them eventually into depolarization block. Ictal spike-wave discharges in the model are then sustained solely by pyramidal neurons. (4) FS cell dynamics are also critical for seizures where the evolution into SWC activity is preceded by low-amplitude fast oscillations. Different levels of elevated $[K^+]_o$ were important for transitions into and maintenance of sustained gamma oscillations and SWC discharges. Overall, our modelling study predicts that the interaction between inhibitory interneurons and $[K^+]_o$ glial buffering under abnormal conditions may explain different types of ictal transitions and dynamics during propagated seizures in human focal epilepsy.

MSC:

92C45 Kinetics in biochemical problems (pharmacokinetics, enzyme kinetics, etc.) Cited in 1 Document

92C50 Medical applications (general)

Keywords:

focal epilepsy; seizure dynamics; spike-wave discharges; gamma oscillations

Software:

XPPAUT

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