

Ionic dynamics mediate tonic-clonic pattern generation in epilepsy

Many types of epileptic seizures involve repetitive periods of tonic (fast spiking) and clonic (bursting) activity. We found that the coexistence of tonic spiking and bursting states for a range of extracellular K^+ concentrations is critical for the maintenance of seizure-like activity. Increase of intracellular sodium concentration causing the disappearance of bistability between tonic spiking and bursting leads to a quick termination of seizures. We further report that reducing sodium spiking currents in pyramidal cell dendrites rids of bistability as well. In terms of dynamics of the model, the mechanism underlying the smooth transition is due to a safe bifurcation of a homoclinic orbit of a saddle-node equilibrium state terminating the quiescence period of bursting. We hypothesize that a similar topology of quiescence and tonic spiking manifold in a phase space of other high-order models guarantees an absence of sustainable seizure-like activity. Our results will likely have implications onto drug development and deepen our understanding of the origin of seizure.