Role of Na⁺/K⁺ ATPase in epileptogenesis

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Ionic changes are one of the prominent features of seizure. Ionic changes influence excitability through acting on various currents. In this study, we identify the role of ionic changes on Na⁺/K⁺ pump and its effect on excitability. We used combination of in vitro electrophysiology and computational modeling techniques to reveal the complex role of Na⁺/K⁺ exchange pump during the evolution of seizures. We found that increase of [Na⁺]i during epileptiform activity leads to higher activation of Na⁺/K⁺ ATPase; this increase mediates hyperpolarizing current by Na⁺/K⁺ pump that contributes to termination of seizure in an in vivo model of seizure. In contrast, in an in vitro model of continuous seizures, constant source of extracellular [K⁺] and activation of Na⁺/K⁺ ATPase promoted seizures by maintaining relatively low level of [Na⁺]i during seizures. When the Na⁺/K⁺ ATPase was reduced in the model, the continuous seizures transformed into repetitive type characterized by periods of silence. Seizure termination in this model was mediated by decrease in [Na⁺]i reversal potential, a consequence of significant elevation of [Na⁺]i during epileptiform under conditions of reduced Na⁺/K⁺ pump activity. Experimentally, in vitro slice preparation showed continuous seizure-like activity induced by elevation of [K⁺]o which was transformed to repetitive events by application of low dosage of strophanthidin (STDN) Na⁺/K⁺ ATPase antagonist. Overall, our study revealed different roles played by Na⁺/K⁺ ATPase in epileptogenesis and therefore, may suggest new target for antiepileptic drugs.