Optimal modulation of ion channels rescues neurons associated with epilepsy

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New research successfully reverses epilepsy-associated pathology by using a sophisticated single-cell modeling paradigm to examine abnormal cell behavior and identify the optimal modulation of channel activity. The study, published in the October 18th issue of *Biophysical Journal*, describes a procedure that may be useful for rescuing function in organs with excitable cells, such as the heart and pancreas.

Ion channels regulate the flow of ions into and out of the cell and are absolutely critical for a wide range of biological processes, including transmission of signals in the nervous system. Disrupting ion channel function can have disastrous consequences. For example, the severe neurological disorder epilepsy is characterized by spontaneous and recurrent seizures that are thought to be linked with ion channel dysfunction.

Dr. Erik Fransén from the Royal Institute of Technology in Stockholm was interested in examining neuronal excitability at the single-cell level and using sophisticated computational modeling to discover a way to restore normal neuronal function. "We studied ion channel alteration related to epilepsy," explains Dr. Fransén. "Previously, we showed that dysfunction of a specific potassium channel, KA, was linked to synchronicity, one of the key elements of epilepsy. In this current study, we focused on improving the functional behavior of the neuron and reversing pathological changes."

Dr. Fransén and colleagues studied the modulation of KA by substances

known to influence channel activation. Sophisticated ion channel simulations allowed the researchers to examine known modulatory substances and to determine the most beneficial concentration of the modulators for reduction of abnormal neuron activity. Importantly, the optimization method revealed specific combinations of modulators that reversed pathological changes in KA observed in a patient with epilepsy.

The authors suggest that the optimization procedure may have widespread application. "The method we developed to functionally correct a pathological neuron can be used for other brain diseases where alterations of ion channels are involved," concludes Dr. Fransén. "It may also be used in other organs with excitable cells, such as the heart or pancreas. For instance, atrial fibrillation is one of the most common sustained cardiac arrhythmias with an underlying pathology of cell hyperexcitability due to, among other things, alterations of ion channels."

More information: Reversing Nerve Cell Pathology by Optimizing Modulatory Action on Target Ion Channels, *Biophysical Journal*, Volume 101, October 2011 1871–187. doi: 10.1016/j.bpj.2011.08.055

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