MedicalXpress

Common mechanism underlies many diseases of excitability

December 28 2009

Inherited mutations in voltage-gated sodium channels (Navs) are associated with many different human diseases, including genetic forms of epilepsy and chronic pain. Theodore Cummins and colleagues, at Indiana University School of Medicine, Indianapolis, have now determined the functional consequence of three such mutations.

As noted by Stephen Cannon and Bruce Bean, in an accompanying commentary, these results suggest that there might be a common mechanism for many channelopathies, diseases arising from mutations in ion channel genes such as those analyzed by Cummins and colleagues.

The authors studied the functional consequences of mutations in the human peripheral neuronal sodium channel Nav1.7, the human skeletal muscle sodium channel Nav1.4, and the human heart sodium channel Nav1.5, which are associated with an extreme pain disorder, a muscle condition characterized by slow relaxation of the muscles, and a heart condition and sudden infant death syndrome, respectively.

Expression of these mutated proteins in a rat-derived dorsal root ganglion neuronal system led to the conclusion that the mutations all altered opening of the sodium channels such that the channels quickly reopened after an electrical impulse had been fired by the nerve cell causing a resurgent sodium current that triggered a second electrical impulse to be fired rapidly after the first.

These observations are consistent with the diseases all being

characterized by excitability, over activity of cells that rely on electrical currents, such as nerve cells, skeletal muscle cells, and heart muscle cells.

More information: www.jci.org/articles/view/4080 … 5c50c65d9dc478d53b04

Provided by Journal of Clinical Investigation