

Persistently modified h-channels after complex febrile seizures convert the seizure-induced enhancement of inhibition to hyperexcitability.

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Febrile seizures are the most common type of developmental seizures, affecting up to 5% of children.

Experimental complex febrile seizures involving the immature rat hippocampus led to a persistent lowering of seizure threshold despite an upregulation of inhibition. Here we provide a mechanistic resolution to this paradox by showing that, in the hippocampus of rats that had febrile seizures, the long-lasting enhancement of the widely expressed intrinsic membrane conductance I_h converts the potentiated synaptic inhibition to hyperexcitability in a frequency-dependent manner.

The altered gain of this molecular inhibition-excitation converter reveals a new mechanism for controlling the balance of excitation-inhibition in the limbic system. In addition, here we show for the first time that h-channels are modified in a human neurological disease paradigm.