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MECHANISMS OF SEIZURE-INDUCED 'TRANSCRIPTIONAL CHANNELOPATHY' OF HYPERPOLARIZATION-ACTIVATED CYCLIC NUCLEOTIDE-GATED CHANNELS

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Epilepsy may result from abnormal function of ion channels, such as those caused by genetic mutations. In addition, pathological alterations of the expression or localization of normal channels have been implicated in epilepsy generation and termed 'acquired channelopathies'. Altered expression levels of hyperpolarization-activated cyclic nucleotide-gated (HCN) channels—that conduct the hyperpolarization-activated current I_h —have been demonstrated in hippocampus of patients with severe temporal lobe epilepsy as well as in animal models of temporal lobe and absence epilepsies. Moreover, data from immature rat models suggest that seizure-induced changes in HCN expression levels early in life could play an important role in epileptogenesis. Here I discuss these data with specific reference to intracellular mechanisms that may regulate the seizure-induced HCN expression changes. Recent discoveries have implicated components of the signaling cascade regulating HCN transcription (e.g. CaMkinase II; Richichi et al., *Neurobiol Dis*, 2008) as well as factors that control the transport of HCN channels to specific subcellular compartments (e.g., the Rab8b-interacting protein TRIP8b; Shin et al., *Neurobiol Dis*, 2008). These new findings suggest that several mechanisms may interact to produce a complex picture of HCN channel dysregulation after seizures. Deciphering these interactions may reveal new targets for therapeutic