

Role of Voltage-Gated Sodium Channel Nav1.2 in Dendrite Morphology and Synaptic Strength

Abstract

Voltage-gated sodium channels regulate electrical excitability of neurons and may be important during development in determining their morphological properties by a competition-based mechanism. We analyzed the functions of a voltage-gated sodium channel Nav1.2 in determining morphological properties of dendrites and regulating the strength of incoming synapses. We used dissociated cultures of rat hippocampal neurons. The amount of Nav1.2 was altered by its overexpression or knockdown with RNAi at 2 DIV, which corresponds to the point in development before the majority of synaptic contacts are established. All cells were fixed at 14 DIV and immunostained with dendritic and presynaptic markers. We found that early knockdown of Nav1.2 competitively weakens glutamatergic excitatory synapses projected onto the transfected neuron. By contrast, early overexpression of Nav1.2 does not affect synaptic morphology. We also measured the number of primary dendrites and performed Sholl analysis of dendrite branching. We found that early overexpression of Nav1.2 increases dendrite number and branching, while early knockdown correspondingly reduces both the number of primary dendrites, and the number of branches. Since the phenotype is not restored by global blockage of activity, most likely the dendritic arborization is affected by biochemical, as opposed to electrical, properties of sodium channel.