Cerebellar ataxia, learning deficit, and Purkinje cell dysfunction caused by loss of BK-type Ca2+-activated K+ channels

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Malfunctions of potassium (K) channels are increasingly implicated as causes of neurological disorders. However, the functional roles of the BK channels - a unique calcium- and voltage-activated potassium channel type - has remained elusive. Here we report that mice lacking BK channels (BK-/-), surprisingly, show complete loss of cerebellar learning in the form of the conditioned eye blink reflex. Furthermore, these mice show abnormal locomotion and pronounced deficiency in motor coordination, which are likely consequences of cerebellar learning deficiency. At the cellular level, the BK-/- mice showed a dramatic reduction in spontaneous activity of the BK-/- cerebellar Purkinje neurons, which generate the sole output of the entire cerebellar cortex and, in addition, enhanced short term depression at the sole output synapses of the cerebellar cortex, in the deep cerebellar nuclei. The impairing cellular effects caused by the lack of postsynaptic BK channels, were found to be due to depolarization-induced inactivation of the action potential mechanism.

These results identify previously unknown roles of potassium channels in mammalian learning, cerebellar function and motor control. In addition, they provide a novel animal model of cerebellar ataxia.

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