Differential roles for ERK1 and ERK2 MAP kinases in neuronal signaling and behavioral plasticity

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Extracellular-signal regulated kinases (ERK1 and 2) are believed to be synaptic signaling components necessary for several forms of learning. In mice lacking ERK1 we observed a dramatic enhancement of ERK2-dependent neuronal signaling, as measured in the hippocampus, striatum and neocortex. Surprisingly, electrophysiological and behavioral analysis revealed that altered modulation of ERK2 signaling in the ERK1 mutants affected neuronal plasticity in a region-specific manner. In fact, in ventral striatum (nucleus accumbens), tetanic stimulation of cortical inputs elicited enhanced synaptic potentiation in ERK1 mutants, but no such facilitation was observed in either the CA1 region of the hippocampus or the basolateral nucleus of the amygdala. These changes in striatal plasticity were associated with a striking enhancement of learning, as revealed by two different operant conditioning tasks. Our results suggest a previously unsuspected function of ERK1 and they demonstrate that the relationships between biochemical signaling events, physiology and behavior vary markedly among distinct brain areas.

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