Knockout of ERK1 MAP kinase enhances synaptic plasticity in the striatum and facilitates striatal-mediated learning and memory

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Extracellular-signal regulated kinases (ERK1 and 2) are synaptic signaling components necessary for several forms of learning. In mice lacking ERK1, we observe a dramatic enhancement of striatum-dependent long-term memory, which correlates with a facilitation of long-term potentiation in the nucleus accumbens. At the cellular level, we find that ablation of ERK1 results in a stimulus-dependent increase of ERK2 signaling, likely due to its enhanced interaction with the upstream kinase MEK. Consistently, such activity change is responsible for the hypersensitivity of ERK1 mutant mice to the rewarding properties of morphine. Our results reveal an unexpected complexity of ERK-dependent signaling in the brain and a critical regulatory role for ERK1 in the long-term adaptive changes underlying striatum-dependent behavioral plasticity and drug addiction.

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