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

Brambilla R1, Mazzucchelli M1, Ciamei A1, Fasano S1, Pakhotin P2, Krezel W2, Welzl H2, Wolfer DP3, Pags G5, Valverde O6, Marowsky A1, Porrazzo A1, Orban P1, Maldonado RC1, Ehrengruber MU7, Lipp HP3, Chapman P2

1 San Raffaele Research Institute and University, Milano, Italy
2 Cardiff School of Biosciences, Cardiff University, Cardiff, UK
3 Institute of Anatomy, University of Zürich, Zürich, Switzerland
4 Istituto di Psicobiologia e Psicofarmacologia CNR, Roma, Italy
5 Inst. of Signaling, Dev. Biology and Cancer Res. CNRS, Nice, France
6 Lab. de Neurofarmacologia, Universitat Pompeu Fabra, Barcelona, Spain
7 Brain Research Institute, University of Zürich, Zürich, Switzerland

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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