Rapid Synthesis and Synaptic Insertion of GluR2 for mGluR-LTD in the Ventral Tegmental Area

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The activation of metabotropic glutamate receptors (mGluRs) leads to long-term depression (mGluR-LTD) at many synapses of the brain. The induction of mGluR-LTD is well characterized, whereas the mechanisms underlying its expression remain largely elusive. mGluR-LTD in the ventral tegmental area (VTA) efficiently reverses cocaine-induced strengthening of excitatory inputs onto dopamine neurons. We show that mGluR-LTD is expressed by an exchange of GluR2-lacking AMPA receptors for GluR2-containing receptors with a lower single-channel conductance. The synaptic insertion of GluR2 depends on de novo protein synthesis via rapid messenger RNA translation of GluR2. Regulated synthesis of GluR2 in the VTA is therefore required to reverse cocaine-induced synaptic plasticity.

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