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MEK1/2 inhibitor U0126 blocks the expression of paternal behavior

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Mating-inexperienced male mice show aggressive behavior toward pup. However, they show parental behavior after the social experiences such as mating and seeing pups. Previously, we found that the GABAergic projection in the medial preoptic area (MPOA) is suppressed in the father mice in gestation experience (FGE) which experienced mating and staying with late pregnant female. This synaptic change was reversed by using G protein signaling inhibitor GDPβ. However, the mechanism of plastic changes in Me → MPOA pathway synapses induced by cohabitation with females remains unclear. In this study, we carried out the electrophysiological recordings from MPOA neurons of sexually inexperienced male mice and FGE. It was newly found that the amplitude of inhibitory post-synaptic potential of MPOA was significantly increased by U0126 in FGE mice. Furthermore, in order to validate the effects of U0126 on the behavioral pattern, U0126, was microinjected into MPOA of FGE mice, and a behavioral test in response to pup exposure was tested. As a result, in the group administered with U0126, the proportion of individuals exhibiting aggressive behavior toward pups increased significantly. These results suggest that signaling through MEK1/2 is involved in GABAergic synaptic plastic changes in MPOA that stop attacks and induce parenting behavior.