DEPLETION OF OREXIN AFFECTS THE DISCRIMINATIVE STIMULUS AND REWARDING EFFECTS OF MDMA IN MICE

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Orexinergic neurons widely project to the brain and regulates the arousal and reward circuits by activation of the monoaminergic neurons. Psychostimulants induce several behavioral effects, such as the discriminative stimulus and rewarding effects in animals mediated by regulation of monoaminergic neurons. Psychostimulants have been used to treat human narcolepsy, which is closely related to deficiency of orexin. However, little information regarding the abuse potential of psychostimulants in case of orexin deficiency is available. Therefore, present study was designed to investigate the effects of orexin deficiency on the relative abuse liability of MDMA in mice. We found that MDMA substituted for the discriminative stimulus effects of methylphenidate in orexin KO, but not wild type (WT), mice trained to discriminate between methylphenidate and saline. However, orexin deficiency did not affect the release of dopamine as well as 5-HT induced by MDMA. In the present study, we found that the rewarding effects of MDMA was established in orexin KO mice, but not in WT mice, as measured by conditioned place preference paradigm. These findings indicate that MDMA could be recognized as methylphenidate-like psychostimulant in orexin KO mice, unlike in the case of WT mice, which induce fragility to MDMA abuse.