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Low doses of dextromethorphan attenuate morphine-induced rewarding via the sigma-1 receptor at ventral tegmental area in rats.

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Abstract

Chronic use of morphine causes rewarding and behavioral sensitization, which may lead to the development of psychological craving. In our previous study, we found that a widely used antitussive dextromethorphan (known as a low affinity NMDA receptor antagonist), at doses of 10-20 mg/kg (i.p.), effectively decreased morphine rewarding in rats. In this study, we further investigated the effects and mechanisms of low doses of DM (μg/kg range) on morphine rewarding and behavioral sensitization. A conditioned place preference test was used to determine the rewarding and a locomotor activity test was used to determine the behavioral sensitization induced by the drug(s) in rats. When a low dose of DM (3 or 10 μg/kg, i.p.) was co-administered with morphine (5 mg/kg, s.c.), the rewarding effect, but not behavioral sensitization, induced by morphine was inhibited. The inhibiting effect of DM could be blocked by systemically administering a sigma-1 receptor antagonist, BD1047 (3 mg/kg, i.p.). When BD1047 (5 nmole/site) was locally given at the VTA, it also blocked the effects of a low dose of DM in inhibiting morphine rewarding. Our findings suggest that the activation of the sigma-1 receptor at the VTA may be involved in the mechanism of low doses of DM in inhibiting the morphine rewarding effect and the possibility of using extremely low doses of DM in treatment of opioid addiction in clinics.

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