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Inhibition by MK-801 of Morphine-Induced Conditioned Place Preference and Postsynaptic Dopamine Receptor Supersensitivity in Mice

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Intraperitoneal injection of morphine (5 mg/kg) in mice every other day for 8 days produced conditioned place preference (CPP). CPP effects were evaluated by assessing the difference in time spent in the drug-paired compartment and the saline-paired compartment of the place conditioning apparatus. The injection of a non-competitive NMDA antagonist, MK-801 (0.05 and 0.1 mg/kg, i.p.), prior to and during morphine treatment in mice inhibited morphine-induced CPP. The development of postsynaptic dopamine (DA) receptor supersensitivity in mice displaying a morphine-induced CPP was evidenced by the enhanced response in ambulatory activity to the DA agonist, apomorphine (2 mg/kg). MK-801 inhibited that development of postsynaptic DA receptor supersensitivity. MK-801 also inhibited apomorphine-induced climbing behavior, suggesting that MK-801 inhibits dopaminergic activation mediated via the NMDA receptor.

These results suggest that the development of morphine-induced CPP may be associated with the development of postsynaptic DA receptor supersensitivity. The development of morphine-induced CPP and DA receptor supersensitivity may be closely related to NMDA receptor-mediated dopaminergic activity, since morphine-induced changes in sensitivity to apomorphine, as well as apomorphine-induced climbing behavior in morphine treated mice, were both blocked by MK-801.