

Repeated Doses of MK-801 Disrupts Reconsolidation and Prevents Reinstatement of a Morphine Withdrawal-Induced Conditioned Place Aversion

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Environmental cues that have been associated with drugs have a long lasting ability to evoke cravings in recovering addicts. In order to reduce the probability of relapse, extinction therapy has been used to disassociate the conditioned drug cues from the drug effects. While this is a useful technique it has not had tremendous clinical success because the effects of extinction are context-specific and prone to spontaneous recovery. D-cycloserine (DCS), a drug that enhances glutamate transmission and consolidation of new memories, including extinction, may reduce the probability of relapse. Other studies have shown that brief re-exposure to drug cues can return the memory induced by those cues to a labile form that reconsolidates. This reconsolidation can be disrupted by various amnesic drugs, such as propranolol or MK-801. This could be a superior treatment option to extinction, because blocking reconsolidation may erase, not just suppress, the original memory. In my first experiment, I found that DCS failed to facilitate extinction or block stress-induced reinstatement of a morphine withdrawal-induced conditioned place aversion (CPA) in rats. Subsequent attempts to block reconsolidation of the CPA using a single dose of propranolol and MK-801 were also unsuccessful. However, repeated doses of 0.2 mg/kg of the NMDA receptor antagonist MK-801 were able to partially block reconsolidation and prevent stress-induced reinstatement. Thus, repeated, brief reactivation of a well consolidated drug memory followed immediately by an amnesic agent, such as MK-801, would seem to hold promise as a means of potentially eliminating such memories.