Influence of neurogenic improvement strategies on extinction and reinstatement of cocaine-induced conditioned place preference

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AIMS: Modulation of adult hippocampal neurogenesis (AHN) has been shown to influence the maintenance of drug-context associations. We aimed to study whether the enhancement of AHN by using a water maze spatial learning task (WM), solely or under conditions of neurogenesis stimulation (forced treadmill exercise), could facilitate extinction and prevent primed reinstatement of cocaine-context associations. METHODS: Adult male C57BL/6J mice (*N*=37) were trained in the Conditioned Place Preference (CPP) paradigm with ascending doses of cocaine (2, 4, 8, 16 mg/kg/d) and subsequently received bromodeoxyuridine (BrdU) injections to label newborn neurons. Then, experimental groups were submitted to 12 days of scheduled exercise and/or 8 days of spatial training in the WM. Sedentary and/or untrained groups stayed undisturbed in their home cages. When BrdU+ cells reached maturation (~6 weeks-old), all mice were tested for CPP memory retrieval. Finally, animals were submitted to forced CPP extinction and tested for CPP extinction and cocaine-primed reinstatement. RESULTS: Animals submitted either to the scheduled exercise protocol, training in the WM or both strategies combined, required fewer sessions to extinct cocaine-CPP associations than control animals. Furthermore, animals submitted to both environmental strategies showed a reduced reinstatement when compared to sedentary animals. These effects are partially related to the functional integration of the newborn neurons in the hippocampus. CONCLUSIONS: Both environmental strategies, alone and combined, can reduce the long-term persistence of cocaine-context associations, being AHN associated with these beneficial effects.

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