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The CB1 receptor antagonist, AM281, improves recognition loss induced by naloxone in morphine withdrawal mice

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Background and Aims: Morphine withdrawal leads to the activation of endocannabinoid system and cognitive deficits. The aim of this study was to evaluate the effects of AM281, a cannabinoid antagonist/inverse agonist, on memory deficit following naloxone precipitated morphine withdrawal in mice. Male mice were made dependent by increasing doses of morphine (30–90 mg/kg) twice daily for 3 days. The object recognition task was used to evaluate memory dysfunction. The test comprised three sections: habituation for 15 min., first trial for 12 min. and test trial for 5 min. In this learning paradigm, the difference in exploration between a previously seen object and a new object is taken as an index of memory performance (recognition index). The recognition index was assessed on the third day of morphine treatment by the injection of 0.1 mg/kg naloxone 3 hr after the last doseof morphine. Chronic administration of AM281 at 2.5 mg/kg significantly improved the memory impairment, producing a recognition index of 36.0 ± 3.9 as compared with vehicle-treated data (recognition index = _3.1 ± 8.2%). A single dose of AM281 at 5 mg/kg improved the recognition index from _1.5 ± 3.9% in morphine withdrawal animals to 18.5 ± 11.6%. Concurrent administration of AM281 with morphine proved to be more effective in protecting the animals from losing their memory compared to acute action of AM281. None of these doses elicit withdrawal syndrome. These results indicate that cannabinoid antagonist may play a role in memory performance after morphine withdrawal.

Keywords: Morphine withdrawal; Memory deficit; Cannabinoid antagonit