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The behavioral signs of aversion in an interaction between nitric oxide into CA1 and naloxone

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Introduction: Naloxone is a proper antagonist that adequately shows signs of dependence on drugs of abuse. Only a single injection of this mu-opioid receptor antagonist, the naloxone, is used to appear the withdrawal signs confirming the dependence on drugs of abuse. The effect of nitric oxide (NO) on expression of behavioral signs in a place aversion response to naloxone was investigated.

Materials and Methods: The animals, Wistar rats (250-350 g), were injected naloxone (0.1-0.4 mg/kg, i.p.) using a five-day schedule of an unbiased place conditioning task. The animals were cannulated in accordance with the rat hippocampal CA1 coordinates provided by Poxinos's atlas of the rat brain. After 1 week recovery the behavioral measurements began. The place aversion was initially induced by naloxone therapy. The NO producer, Larginine (0.003-3 µg/rat, intra-CA1) was injected into the CA1 once prior to naloxone response testing. An inhibitor of NO production, the L-NAME (0.03-3 µg/rat, intra-CA1), was pre-microinjected to the injection of the NO precursor. All data were analyzed by ANOVA after data reviewing provided by Ethovision system.

Results: The results show that naloxone induced a significant conditioned place aversion. The intra-CA1 L-arginine, significantly improved the conditioned place aversion induced of naloxone. But, this response was reversed by L-NAME pre-injection to L-arginine. The naloxone treated groups showed in addition, a significant increase in compartment entering as well as wet dog shaking (WDS). However, the L-arginine plus naloxone treated animals, showed a depressed WDS while showing increased compartment entering. The L-NAME pre-treated group, those receiving L-NAME prior to the cumulative naloxone-L-arginine response, showed increase in the rearing-behavior.

Discussion: This finding may indicate that the NO into CA1 area interacts with naloxone in inducing the behavioral signs of aversion.

Key Words: Naloxone, Nitric oxide, CA1, Place aversion, Behavioral signs

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