



Histamine reverses cognitive deficits in deprived rats tested in avoidance memory consolidation through a H2 receptor-dependent mechanism

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Resumo

Maternal deprivation is known to result in long-lasting neurochemical, behavioral and brain structural effects. We investigated whether the cognitive aspects of these deficits might be related to the disruption of the histaminergic system in the brain in memory consolidation of aversive tasks. Pregnant Wistar rats were individually housed and maintained on a 12:12 h light / dark cycle with food and water freely available. The mothers were separated from their pups for 3 h per day from postnatal day 1 (PND-1) to PND-10. To do that, the dams were moved to a different cage and the pups maintained in the original home cage, which was transferred to a different room kept at 32 ° C. After they reached 120-150 days of age, maternal-deprived and non-deprived male rats were submitted to pharmacological and behavioral studies. We show that when infused into the CA1 region of the dorsal hippocampus immediately after training in an inhibitory avoidance task, histamine induce a dose-dependent mnemonic effect in deprived rats without altering locomotor activity, exploratory behavior, anxiety state of the avoidance responses. Histamine (10mM/1µl per side) reverse cognitive deficit in deprived rats in avoidance consolidation test carried out 24 hrs after training session. The same histaminergic effect was mimicked by the histamine N-methyltransferase inhibitor SKF-91844 (10mM/1µl per side) as well as by the H2 receptor agonist Dimaprit (10mM/1µl per side) and it was blocked completely by the H2 receptor antagonist ranitidine (50mM/1µl per side). The promnesic action of histamine was unaffected by the H1 receptor antagonist pyrilamine (50mM/1µl per side), the H3 receptor antagonist thioperamide (50mM/1µl per side), and the NMDA receptor polyamine-binding site antagonist ifenprodil (50mM/1µl per side). When infused by themselves, the antagonists did not affect inhibitory avoidance memory consolidation. Several evidences suggest that brain histamine is

involved in memory consolidation in the hippocampus. Our data indicate that deprived rats shows cognitive deficits in inhibitory avoidance when the subjects were tested 24 h after training session. But when given into CA1, histamine reversed the cognitive deficit through a mechanism that involves activation of H2 receptors. That findings suggest that maternal deprivation affects memory processing at adulthood and these memory impairment can be mediated by modification of the histaminergic system in the rat brain.