Abstract


The antinociceptive effects of centrally administered CDP-choline on acute pain models in rats: the involvement of cholinergic system.

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OBJECTIVE: This study investigates the antinociceptive effect of intracerebroventricular (i.c.v.) injection of cytidine-5'-diphosphate choline (CDP-choline; citicoline) and the involvement of cholinergic mechanisms in rats.

METHODS: Three different pain models were utilized: thermal paw withdrawal test, mechanical paw pressure test and acetic acid writhing test.

RESULTS: The i.c.v. administration of CDP-choline (0.5, 1.0 and 2.0 micromol) produced dose and time-dependent antinociception. Equimolar dose of choline (1 micromol; i.c.v.) produced antinociceptive response similar to the one observed in CDP-choline given animals. On the other hand, cytidine (1 micromol; i.c.v.) failed to produce response in the thermal paw withdrawal test and the mechanical paw pressure test but in the writhing test in which it produced significant antinociceptive effect. CDP-choline-induced antinociception was prevented by the neuronal high affinity choline uptake inhibitor HC-3 (1 microg; i.c.v.), the nonselective nicotinic receptor antagonist mecamylamine (50 microg; i.c.v.) and by the alpha(7)-selective nicotinic receptor antagonist, MLA (25 microg; i.c.v.). However, it was not changed by the nonselective muscarinic receptor antagonist atropine (10 microg; i.c.v.) in the thermal paw withdrawal test and mechanical paw pressure test. In the writhing test, all antagonist pretreatments produced blockade similar to that obtained from CDP-choline injected animals. CDP-choline did not impair the motor performance of rats as evaluated by a rota-rod test.

CONCLUSION: Therefore, it can be postulated that CDP-choline exerts an antinociceptive effect mediated by a central cholinergic mechanism. Activation of specific alpha(7)-nicotinic cholinergic receptors through the activation of presynaptic cholinergic mechanisms appears to be involved in the antinociceptive effect of this drug.

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