Possible involvement of supraspinal opioid and GABA receptors in CDP-choline-induced antinociception in acute pain models in rats.

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OBJECTIVE: Cytidine-5'-diphosphate choline (CDP-choline; citicoline) is an essential endogenous compound normally produced by the organism and is a source of cytidine and choline. Our recent studies on acute pain models demonstrate that intracerebroventricularly administered CDP-choline produces antinociception via supraspinal alpha-7 nicotinic acetylcholine receptors-mediated mechanism in rats. However, it remains to be elucidated which other supraspinal mechanisms are involved in the antinociceptive effect of CDP-choline.

METHODS: In this study, we investigated the role of the supraspinal opioidergic, GABAergic, alpha-adrenergic and serotonergic receptors in CDP-choline-induced antinociception. The antinociceptive effect of CDP-choline was evoked by the intracerebroventricular (i.c.v.) administration. Two different pain models were utilized: thermal paw withdrawal test and mechanical paw pressure test.

RESULTS: The i.c.v. administration of CDP-choline (0.5, 1.0 and 2.0 micromol) produced dose-dependent antinociception. Non-specific opioid receptor antagonist naloxone (10 microg; i.c.v.) and GABA(B) receptor antagonist CGP-35348 (20 microg; i.c.v.) pretreatments inhibited the antinociceptive effects of CDP-choline (1.0 micromol; i.c.v.). In contrast, the alpha-1 adrenergic receptor antagonist prazosin (20 microg; i.c.v.), alpha-2 adrenergic receptor antagonist yohimbine (30 microg; i.c.v.) and non-specific serotonin receptor antagonist methysergide (20 microg; i.c.v.) pretreatments had no effect on CDP-choline-induced antinociception in the thermal paw withdrawal test and in the mechanical paw pressure test.

CONCLUSION: Therefore, it can be postulated that i.c.v. administered CDP-choline exerts antinociceptive effect mediated by supraspinal opioid and GABA(B) receptors in acute pain models. Furthermore, supraspinal alpha-adrenergic and serotonergic receptors do not appear to be involved in the antinociceptive effect of CDP-choline.

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