The antihyperalgesic effect of cytidine-5'-diphosphate-choline in neuropathic and inflammatory pain models.

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Abstract

This study was designed to test the effects of intracerebroventricularly (i.c.v.) administered CDP-choline (cytidine-5'-diphosphate-choline; citicoline) and its metabolites in rat models of inflammatory and neuropathic pain. The i.c.v. administration of CDP-choline (0.5, 1.0 and 2.0 µmol) produced a dose and time-dependent reversal of mechanical hyperalgesia in both carrageenan-induced inflammatory and chronic constriction injury-induced neuropathic pain models in rats. The antihyperalgesic effect of CDP-choline was similar to that observed with an equimolar dose of choline (1 µmol). The CDP-choline-induced antihyperalgesic effect was prevented by central administration of the neuronal high-affinity choline uptake inhibitor hemicholinium-3 (1 µg), the nonselective nicotinic receptor antagonist mecamylamine (50 µg), the α7-selective nicotinic ACh receptor antagonist, α-bungarotoxin (2 µg) and the γ-aminobutyric acid B receptor antagonist CGP-35348 (20 µg). In contrast, i.c.v. pretreatment with the nonselective opioid receptor antagonist naloxone (10 µg) only prevented the CDP-choline-induced antihyperalgesic effect in the neuropathic pain model while the nonselective muscarinic receptor antagonist atropine (10 µg) did not alter the antihyperalgesic effect in the two models. These results indicate that CDP-choline-elicited antihyperalgesic effect in different models of pain occurs through mechanisms that seem to involve an interaction with supraspinal α7-selective nicotinic ACh receptors, and γ-aminobutyric acid B receptors, whereas central opioid receptors have a role only in the neuropathic pain model.

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