

2-CHLORO-2'-C-METHYL-N⁶-CYCLOPENTYLADENOSINE, A HIGHLY SELECTIVE ADENOSINE A₁ RECEPTOR AGONIST, HAS ANTINOCICEPTIVE ACTIVITY IN THE RAT

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The effect of 2-chloro-2'-C-methyl-N⁶-cyclopentyladenosine (2'-Me-CCPA), a potent and highly selective adenosine A₁ receptor agonist, on nociceptive responses in acute and chronic pain has been investigated in this study. Systemic administrations of 2'-Me-CCPA (2.5-5 mg/kg, i.p.) reduced the nociceptive response to thermal stimuli in the plantar test. The analgesic effect of 2'-Me-CCPA was antagonized by DPCPX (3 mg/kg i.p), a selective A₁ receptor antagonist, but not the A_{2A} receptor antagonist DMPX (3 mg/kg, i.p). Similar microinjection of 2'-Me-CCPA (0.5-1-2 nmol/rat) into the periaqueductal grey (PAG) generated a dose-dependent anti-nociceptive response in the plantar test in a way inhibited only by DPCPX (0.5 nmol/rat). In order to measure 2'-Me-CCPA therapeutic potential, the analgesic activity was tested in an persistent inflammatory pain condition, the formalin test. Systemic 2'-Me-CCPA (2.5 and 5 mg/kg, i.p) inhibited in a dose dependent manner the second phase of formalin-induced pain behaviour. Also in this case the analgesic effect of 2'-Me-CCPA was blocked by DPCPX (3 mg/kg, i.p.). Intra-PAG 2'-Me-CCPA (0.5-1-2 nmol/rat) reduced both the early and the late phase of formalin-induced pain behaviour, and this effect was antagonized by DPCPX (0.5 nmol/rat). In conclusion, systemic and intra-PAG adenosine A₁ stimulation reduced pain behaviour in the plantar and in the formalin tests. The stimulation of PAG adenosine A₁ receptors proved more effective in the formalin test, since it completely abolished both the early and delayed phases.