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 A2A receptor antagonist DMPX (3 mg/kg, i.p). Similarly 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.