

**2-CHLORO-2'-C-METHYL-N<sup>6</sup>-CYCLOPENTYLADENOSINE, A HIGHLY SELECTIVE ADENOSINE A<sub>1</sub> RECEPTOR AGONIST, MODULATES THE ONGOING AND TAIL FLICK –RELATED ACTIVITY OF RVM ON AND OFF CELLS**

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The periaqueductal grey (PAG) and the nuclei of the rostral ventromedial medulla (RVM) constitute part of the endogenous antinociceptive pathway, where two classes of neurons, ON and OFF cells, have specific roles in pain modulation. The effect of a potent and highly selective adenosine A<sub>1</sub> receptor agonist, the 2-chloro-2'-C-methyl-N<sup>6</sup>-cyclopentyladenosine (2'-Me-CCPA), on the ongoing and tail flick-related activity of RVM ON and OFF cells has been investigated in this study. Microinjection of 2'-Me-CCPA (2 nmol/rat) into the ventrolateral PAG caused a decrease in the firing activity of the pro-nociceptive ON cells and a very rapid increase in the firing activity of the anti-nociceptive OFF cells. The effects of the 2'-Me-CCPA (2 nmol/rat) were blocked by 5 min pre-treatment with DPCPX (0.5 nmol/rat), a selective A<sub>1</sub> receptor antagonist, but not by DMPX (0.5 nmol/rat), a selective A<sub>2A</sub> receptor antagonist. Both antagonists were inactive *per se* at the doses used. Tail flick latency was increased by intra-PAG microinjections of 2'-Me-CCPA (0.5-1-2 nmol/rat) in a dose dependant manner. Intra-PAG pre-treatment with DPCPX (0.5 nmol/rat), but not with DMPX (0,5 nmol/rat), reversed the increase in tail flick latency induced by 2'-Me-CCPA 2 nmol rat. Intra-PAG 2'-Me-CCPA modified the tail flick-related neuronal activities in both ON and OFF cells. In particular, 2'-Me-CCPA reduced the OFF cell pause and delayed the ON cell onset of burst. The 2'-Me-CCPA also reduced the tail flick-induced ON cell peak firing, and delayed the onset of the OFF cell pause. This study suggests that PAG adenosine A<sub>1</sub> receptors control the ongoing and tail flick-related activity of the RVM ON and OFF cells in a way that is consistent with PAG-mediated analgesia. PAG adenosine A<sub>1</sub> receptors may represent a pharmacological target for inducing pain relief.