PERIAQUEDUCTAL GREY METABOTROPIC GLUTAMATE RECEPTOR SUBTYPE 7 AND 8 SHOW OPPOSITE ACTIONS ON AMINO ACID RELEASE, NOCICEPTIVE BEHAVIOUR AND ROSTRAL VENTROMEDIAL MEDULLA ON AND OFF CELL ACTIVITY

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The involvement of periaqueductal grey (PAG) metabotropic glutamate subtype 7 ($mGlu_7$) and 8 ($mGlu_8$) receptors in modulating rostral ventromedial medulla (RVM) ongoing and tail flick related ON and OFF cell activities has been investigated. The role of PAG $mGlu_7$ receptor on thermoceptive threshold and on glutamate and GABA extracellular values has been also evaluated. Intra-ventrolateral PAG (S)-3,4-DCPG (2 and 4 nmol/rat) or AMN082 (1 and 2 nmol/rat), selective $mGlu_8$ and $mGlu_7$ receptor agonists respectively, caused dose dependent opposite effects on the ongoing RVM ON and OFF cell activities. Tail flick latency was increased or decreased by intra-ventrolateral PAG (S)-3,4-DCPG or AMN082 (2 nmol/rat) respectively. Intra-ventrolateral PAG (S)-3,4-DCPG reduced the pause and delayed the onset of the OFF cell pause. Conversely, AMN082 increased the pause and shortened the onset of OFF cell pause. (S)-3,4-DCPG or AMN082 did not change the tail flick-induced onset of ON-cell peak firing. The tail flick latency and its related electrophysiological effects induced by the highest dose of (S)-3,4-DCPG or AMN082 were prevented by MSOP (100 nmol/rat), a group III mGlu receptor antagonist. Intra-ventrolateral PAG perfusion with AMN082 (10 and 25 μM), decreased thermoceptive thresholds and glutamate extracellular levels. A decrease of GABA release was also observed. Taken together these results suggest that stimulation of PAG $mGlu_8$ or $mGlu_7$ receptors may relieve or worsen, respectively, pain perception. The opposite effects on pain behaviour correlate with the opposite actions played by $mGlu_7$ and $mGlu_8$ receptors on glutamate and GABA release and the ongoing and tail flick-related activities of the RVM ON and OFF cells. This study underlines the importance to focus further efforts to investigate mGlu8 receptor agonist analgesic potential and to develop a mGlu7 receptor antagonist, which may be a new promising pain relief agent.