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 (mGlu7) and 8 (mGlu8) receptors in modulating rostral ventromedial medulla (RVM) ongoing and tail flick related ON and OFF cell activities has been investigated. The role of PAG mGlu7 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 mGlu8 and mGlu7 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 mGlu8 or mGlu7 receptors may relieve or worsen, respectively, pain perception. The opposite effects on pain behaviour correlate with the opposite actions played by mGlu7 and mGlu8 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.