Pharmacological preconditioning of the brain: a possible interplay between opioid and calcitonin gene related peptide transduction systems

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Abstract: The present study has been undertaken to investigate the possible link between calcitonin gene related peptide (CGRP) and opioid receptor transduction systems in the neuroprotective mechanism of pharmacological preconditioning. Occlusion of the bilateral carotid artery for 17 min, followed by reperfusion for 24 h, was employed to produce ischemia and reperfusion (I/R) induced cerebral injury in mice. Cerebral infarct size was measured by using triphenyltetrazolium chloride staining. Memory was assessed using the Morris water maze (MWM) test. Degree of motor incoordination was evaluated using the inclined beam walk test, rota-rod test, and lateral push test. Morphine (8 mg/kg, ip), an opioid agonist, and capsaicin (0.1 mg/kg, iv), a CGRP releasing agent, were administered 24 h before surgery to separate groups of animals to induce pharmacological preconditioning. Bilateral carotid artery occlusion, followed by reperfusion, produced a significant increase in the cerebral infarct size and impaired memory as well as motor coordination. Morphine-induced (8 mg/kg, ip) neuroprotective effects were completely decreased by sumatriptan (8 mg/kg, iv), a CGRP release inhibitor, administered 1 h before and 6 h and 12 h after morphine administration. Capsaicin-induced neuroprotection was decreased by naloxone (5 mg/kg, ip, an opioid antagonist) administered 1 h before and 6 h and 12 h after capsaicin administration. These findings indicate that the transduction systems mediating morphine- and capsaicin-induced pharmacological preconditioning in brain are possibly interlinked with one another.

Key words: preconditioning, morphine, capsaicin, CGRP, opioid, neuroprotection