Antiallodynic effects of intrathecal orexins in a rat model of postoperative pain

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摘要

Abstract

Orexin A and B (hypocretin 1 and 2) are the endogenous ligands of orexin receptors, a G-protein-coupled orphan receptor family containing orexin 1 (OX1) and orexin 2 (OX2) types. Orexin A induces analgesia in acute and inflammatory pain models. We further elucidated the possible antiallodynic effect of intrathecal orexins in a rat model of postoperative pain. Mechanical allodynia was induced by incising the rat hind paw and evaluated with the withdrawal threshold to von Frey filament stimulation. Intrathecal orexin A (0.03-1 nmol) and orexin B (0.1 – 3 nmol) dose dependently attenuated the incision-induced allodynia. Orexin A (ED50 = 0.06 nmol) is more potent than orexin B. The effects of orexin A and B were abolished by their respective antibodies, but not by naloxone, and were attenuated by suramin and strychnine, the P2X purinergic and glycine receptor antagonists, respectively. SB-334867, an OX1 receptor antagonist, at 30 nmol completely blocked the effect of orexin A but, even at 100 nmol, only partially antagonized the effect of orexin B. Orexin A antibody, SB-334867, suramin, strychnine, or naloxone enhanced the incision-induced allodynic response. It is concluded that intrathecal orexins reduce incision-induced allodynia through OX1 receptors. Glycine and P2X purinergic receptors, but not opioid receptors, might be involved in the antiallodynic effects of orexins. Endogenous orexin might be released after incision injury to activate the spinal OX1 receptors as an endogenous analgesic protector.