



Interaction between histamine and morphine at the level of the hippocampus in the formalin-induced orofacial pain in rats

Esmaeal Tamaddonfard¹, Amir Erfanparast¹, Amir Abbas Farshid²,
Emad Khalilzadeh¹

¹Division of Physiology, Department of Basic Sciences, ²Division of Pathology, Department of Pathobiology, Faculty of Veterinary Medicine, Urmia University, Urmia 57153-1177, Iran

Correspondence: Esmaeal Tamaddonfard, e-mail: e_tamaddonfard@yahoo.com and e_tamaddonfard@urmia.ac.ir

Abstract:

The present study explored the interaction between histaminergic and opioidergic systems at the level of the hippocampus in modulation of orofacial pain by intra-hippocampal microinjections of histamine, pyrilamine (an antagonist of histamine H₁ receptors), ranitidine (an antagonist of histamine H₂ receptors), morphine (an opioid receptor agonist) and naloxone (an opioid receptor antagonist) in separate and combined treatments. Orofacial pain was induced by subcutaneous (*sc*) injection of formalin (50 μl, 1%) in the upper lip region and the time spent face rubbing was recorded in 3 min blocks for 45 min. Formalin (*sc*) produced a marked biphasic (first phase: 0–3 min, second phase: 15–33 min) pain response. Histamine and morphine suppressed both phases of pain. Histamine increased morphine-induced antinociception. Pylramine and ranitidine had no effects when used alone, whereas pretreatments with pyrilamine and ranitidine prevented histamine- and morphine-induced antinociceptive effects. Naloxone alone non-significantly increased pain intensity and inhibited the antinociceptive effects of morphine and histamine. The results of the present study indicate that at the level of the hippocampus, histamine through its H₁ and H₂ receptors, mediates orofacial region pain. Moreover, morphine *via* a naloxone-reversible mechanism produces analgesia. In addition, both histamine H₁ and H₂ receptors, as well as opioid receptors may be involved in the interaction between histamine and morphine in producing analgesia.

Key words:

histamine, histamine H₁ and H₂ receptors, morphine, naloxone, hippocampus, orofacial formalin test, rats
