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论著

吗啡耐受及内脏痛敏的相关机理

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摘要 目的 吗啡耐受是一种潜在的痛觉过敏，慢性内脏炎痛刺激后也产生内脏痛敏。因此探讨慢性内脏炎痛刺激及吗啡耐受间共同的细胞机理及*N*-甲基-*D*-天冬氨酸（NMDA）受体相关的调节机理，为合理用药及药物开发提供实验依据。方法 利用急慢性内脏痛炎痛模型，直肠扩张痛阈测定及生物化学检测的方法进行机理研究。结果 结肠炎症和慢性吗啡耐受的大鼠均出现直肠扩张痛阈降低，即内脏痛敏现象，而慢性地佐环平（MK-801）和*L*-N^G-硝基精氨酸甲酯（*L*-NAME）处理吗啡组的平均痛阈未见明显改变。内脏炎痛和耐受组大鼠脊髓及海马部位一氧化氮合酶（NOS）上调，而MK-801和*L*-NAME预处理组含量无明显变化。慢性内脏炎痛及吗啡耐受组背角神经元［Ca^{2+}］$_i$显著增高，而MK-801预处理的炎痛及耐受组则无明显改变。结论 吗啡耐受和痛觉敏感化在机理上存在某些共同之处，均在NMDA受体的激活、一氧化氮生成及细胞内钙上发生可塑性变化。

关键词 吗啡耐受 痛觉过敏 痛阈 痛, 内脏 受体, N-甲基-D-天冬氨酸 钙, 细胞内 一氧化氮合酶

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Related neural mechanisms between visceral hyperalgesia and morphine tolerance

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Abstract

AIM Recently, morphine tolerance is thought as a kind of latent hyperalgesia. Visceral inflaming pain also is a major chronic pain syndrome. In the present study, the common cellular mechanism of chronic visceral inflaming pain and morphine tolerance and the regulation of *N*-methyl-*D*-aspartate(NMDA) receptor were investigated. **METHODS** Utilizing rat model of inflaming hyperalgesia produced by injecting bee venom to colon, colon-rectum distenision test and biochemical methods were used to study the mechanism. **RESULTS** Both dizocilpine (MK-801) and *L*-N^G-nitro arginine methyl ester (*L*-NAME) can prevent the visceral hyperalgesia and development of opioid tolerance. When visceral inflammation and developing of opioid tolerance, the nitric oxide synthase (NOS) concentration were increased in the spinal dorsal horn and hippocampus, these phenomena could be prevented by treatment with MK-801 and *L*-NAME. The significant increases in ［Ca^{2+}］$_i$ in the spinal dorsal horn were also observed in the superficial after chronic visceral inflammation and morphine tolerance. These phenomena could also be prevented by treatment with MK-801. Therefore, these observations suggest that hyperalgesia and morphine tolerance may be interrelated at the level of the superficial laminae of the dorsal horn by common neural substrates that interact at the level of NMDA receptor activation as well as nitric oxide production. CO NCLU SION[WTBZ]〓These results indicate that visceral hyperalgesia and morphine tolerance are associated with activation of NMDA receptors and the activation of NOS, followed by an increase in ［Ca 2+ ］ i within dorsal horn of the spinal cord. These results supported that there are some relative mechanism between morphine tolerance and visceral hyperalgesia. It may also provide scientific data for improved pain management with opiate analgesics.

Key words morphine tolerance hyperalgesia pain threshold pain visceral receptors N-methyl-D-aspartate calcium cytosolic nitric oxide synthase

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