

论文

5-HT₂受体介导大鼠DRG神经元膜GABA-激活电流的增强作用

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摘要:

目的探讨5-HT对大鼠DRG神经元膜GABA-激活电流的调节作用及其机制。方法在新鲜分离的大鼠DRG神经元标本上,以全细胞膜片钳技术记录膜电流,用排管快速换液装置行胞外给药,以胞内透析技术分析信号转导途径。结果给予GABA可使多数受检细胞产生浓度依赖性内向电流(I_{GABA})。预加5-HT,可使 I_{GABA} 增加。此效应可被5-HT₂受体特异性激动剂 α -methyl-5-HT(1×10^{-6} mol·L⁻¹)所模拟,被5-HT₂受体选择性拮抗剂cyproheptadine所阻断。在部分细胞,5-HT本身可引起由5-HT₃受体介导的快速内向电流,但并未发现该电流与5-HT对 I_{GABA} 的增强作用有必然的联系。从GABA激活电流的量效曲线可见,预加5-HT后和对照曲线相比,阈浓度不变、EC₅₀值相近, I_{GABA} 最大值增加33.6%。胞内透析GDP- β -S或H-7可取消5-HT增强 I_{GABA} 的效应,而透析H-9无效。结论5-HT可增强GABA-激活电流,其机制为5-HT₂受体激活后通过PKC引起GABA_A受体胞内磷酸化所致。

关键词: 背根神经节 全细胞膜片钳记录 5-HT₂受体 GABA激活电流

5-HT₂ receptor mediated the potentiation of GABA-activated current in the membrane of the dorsal root ganglion neurons of rat

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Abstract:

Aim To explore the modulation of 5-HT on GABA-activated current (I_{GABA}) in the membrane of rat dorsal root ganglion (DRG) neurons and its mechanism. Methods Rat DRG neurons were isolated mechanically and enzymatically, on which whole-cell patch clamp recording and repatch technique for intracellular dialysis were performed. Results In the majority of neurons examined (92.0%, 69/75) GABA induced a concentration-dependent inward current. In neurons sensitive to GABA preapplication of 5-HT produced potentiation effect (82.6%, 57/69) on I_{GABA} . Preapplication of 5-HT at concentrations of 1×10^{-6} , 1×10^{-5} , 1×10^{-4} and 1×10^{-3} mol·L⁻¹ potentiated I_{GABA} by (35±8)% (n=8), (47±11)% (n=10), (65±17)% (n=9) and (75±18)% (n=11), respectively. This effect was mimicked by α -methyl-5-HT (1×10^{-6} mol·L⁻¹), a specific 5-HT₂ receptor agonist, and reversed by cyproheptadine, a selective 5-HT₂ receptor antagonist. The potentiation of I_{GABA} by 5-HT was irrespective to whether the I_{5-HT} presents or not in a subset of neurons. The concentration-response curves for GABA before and after pretreatment with 5-HT manifested the same threshold value and similar EC₅₀ (2.0×10^{-5} and 1.9×10^{-5} mol·L⁻¹, respectively), while the maximal value of I_{GABA} for the latter was 33.6% higher than that for the former. Intracellular dialysis with GDP- β -S or H-7 abolished the potentiation of I_{GABA} by 5-HT, while H-9 did not. Conclusion 5-HT can potentiate GABA-activated current via PKC-dependent phosphorylation of GABA_A receptor following the activation of 5-HT₂ receptor.

Keywords: whole-cell patch clamp recording 5-HT₂ receptor GABA-activated current dorsal root ganglion

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