生物物理学报(2007) 23(1), 40-46

PDF文档

氯丙嗪抑制电压门控钠通道电流拮抗脑缺血损伤

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为探讨氯丙嗪对脑缺血的保护作用及其可能的离子通道机制，采用全细胞膜片钳技术，在急性分离的新生大鼠海马锥体细胞上研究氯丙嗪对电压门控钠通道电流（INa）的影响，利用线栓法建立大鼠脑缺血再灌注动物模型，研究氯丙嗪对脑缺血的保护作用。结果显示，大鼠缺血1 h后腹腔注射氯丙嗪（10 mg/kg），24 h后梗塞面积明显减小。30 μmol/L氯丙嗪可以减小钠电流幅值及使INa激活曲线左移。实验结果提示氯丙嗪可能通过抑制INa而拮抗大鼠脑缺血所引起的损伤。

Chlorpromazine against the damages of cerebral ischemia related to the inhibitory effects of voltage-gated sodium channel

The purpose of the study was to investigate the effects of chlorpromazine (CPZ) on cerebral ischemia in rats and their relative ion channel mechanism. Effects of CPZ were tested in vitro on voltage-dependent sodium channel (VGSC) using patch-clamp in freshly dissociated rat hippocampal neurons and in vivo using a rat model of experimental stroke caused by transient middle cerebral artery occlusion (MCAO). The results showed that CPZ at 10 mg/kg given 1 h after the initiation of MCAO was effective in reducing cerebral infarct volumes measured 24 h later. CPZ at 30 μmol/L reversibly reduced the amplitudes of Na+ current and activation process. In conclusion, CPZ is neuroprotective when given as a single administration after initiation of MCAO. These data indicate that CPZ may be a useful neuroprotectant in stroke therapy; its neuroprotective potential may come from the inhibitory effects of CPZ on Na+ channel.

关键词

钠电流(Na+ current); 膜片钳(Patch clamp); 神经元(Neurons); 缺血再灌注(Cerebral ischemia); 氯丙嗪(Chlorpromazine); 神经保护(Neuroprotective)