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论文

二氮嗪对氯化锂-匹鲁卡品致痫大鼠海马神经元超微结构及自由基的影响

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摘要：

目的 观察线粒体ATP敏感性钾通道(mitoKATP)开放剂二氮嗪(DZ)对氯化锂-匹鲁卡品致痫大鼠海马神经元超微结构及自由基的影响，探讨mitoKATP开放剂对癫痫发作后神经元的保护机制。方法 随机将成年雄性Wistar大鼠80只，分为对照组、癫痫组（PILO组）、DZ组（DZ组）、DZ+5-羟基癸酸(5-HD)组（DZ+5-HD组），后两组用氯化锂-匹鲁卡品制作癫痫持续状态模型之前，DZ组用DZ 5mg/kg， DZ+5-HD组先用5-HD 8mg/kg，再用DZ 5mg/kg，皆腹腔内注射。观察各组大鼠行为学变化，分别在致痫后4、24、48h断头取脑，分离海马，电镜观察海马神经元的超微结构，检测海马中丙二醛（MDA）的含量及超氧化物歧化酶（SOD）、谷胱甘肽过氧化物酶（GSH-Px）的活力。结果 与对照组比较，PILO组与DZ+5-HD组可见神经元数目明显减少，细胞肿胀，细胞器减少，胞核内染色质凝聚，线粒体肿胀，嵴缺失，重者线粒体明显空泡化，以癫痫发作后48h最显著；DZ组大鼠癫痫发作的潜伏期延长，神经元损伤明显减轻，癫痫发作急性期的死亡率降低，DZ能明显降低大鼠癫痫发作后海马中MDA的含量，提高SOD、GSH-Px的活力，其作用能被5-HD阻断。结论 DZ可能通过降低大鼠癫痫发作后自由基的水平，提高抗氧化系统的反应性，减轻氧化应激损伤，从而减轻神经元的损伤，起到神经保护作用。

关键词： 癫痫；线粒体ATP敏感性钾通道；二氮嗪；超微结构；自由基；大鼠，Wistar

Effects of diazoxide on neuronal ultrastructure and free radicals in the hippocampus of epileptic rats induced by lithium-pilocarpine

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Abstract:

Objective To observe the effect of diazoxide(DZ), a mitochondrial ATP sensitive potassium channel (mitoKATP) opener, on neuronal ultrastructure and free radicals in the hippocampus of epileptic rats induced by lithium-pilocarpine, and explore the mechanism of the neuroprotective effect of DZ on epilepsy. Methods Adult male Wistar rats were randomly divided into four groups: the control group, the epilepsy group (PILO group), the diazoxide group (DZ group), and the DZ and 5-hydroxydecanoate (5-HD) group (DZ+5-HD group). The model of status epilepticus (SE) was induced by lithium-pilocarpine. Before preparation of the model, the DZ group was treated with 5mg/kg of DZ, intraperitoneally injected (ip); and the DZ+5-HD group was treated with 8mg/kg of 5-HD, ip, then 5mg/kg of DZ, ip. The change of behavior in rats was observed. 4, 24 and 48 hours after SE, the rats were sacrificed and the hippocampi were removed. The neuronal ultrastructure was observed by an electron microscope. The content of malondialdehyde (MDA), and activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) were measured with commercial assay kits. Results Compared with the control group, hippocampal neurons in the PILO group and the DZ+5-HD group were severely damaged after SE. The number of neurons was decreased, and the neurons were swellen. There were numerous clumps distributed throughout the nucleus. Mitochondrial swelling was accompanied by the disappearance of cristae and disruption of membrane integrity. In more severe cases, the mitochondria were vacuolar. The damage was most severe 48h after SE. In the DZ group, the epileptic paroxysm latent period was significantly prolonged, the damage of neurons was less severe, and the mortality rate of rats with SE was decreased. In the DZ group, the MDA content was significantly decreased while the activities of SOD and GSH-Px were significantly increased compared with those in the PILO group. The effect of DZ could be abolished by 5-HD. Conclusion The mitoKATP opener DZ can decrease the level of mitochondrial free radicals, thereby improve the response of the anti-oxidant system, and reduce oxidative stress after SE, so it can reduce neuronal injury and play an important role in neuroprotection after SE.

Keywords: Epilepsy; Mitochondrial ATP-sensitive potassium channel; Diazoxide; Ultrastructure; Free radicals; Rats, Wistar

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