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基础医学

帕潘立酮对地佐环平损伤脑皮层神经元的保护作用及其机制

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摘要：

目的 探讨帕潘立酮对地佐环平损伤大鼠脑皮层神经元的保护作用及机制。方法 取孕15d胎鼠脑皮层神经元体外培养，应用地佐环平损伤神经元，然后加入不同浓度的帕潘立酮。采用MTT技术检测脑皮层神经元的生长活性，采用酶标仪检测乳酸脱氢酶（LDH）的活性及激光共聚焦技术检测神经元细胞内Ca2+浓度观察神经元凋亡情况，通过神经元突起数目及长度检测神经元生长情况，应用实时定量PCR技术检测Akt1、GSK3β的表达变化。结果 与正常对照组相比，地佐环平损伤组神经元活性明显下降，LDH释放增加，细胞内游离钙离子浓度升高（P均＜0.01），神经元突起总长度下降,神经突起数目呈现不同程度的减少（P＜0.01），RT-PCR结果显示，Akt1及GSK3β表达下降（P＜0.01）；加入不同浓度的帕潘立酮能明显对抗地佐环平对神经元的损伤，MTT结果显示神经元活性升高（P＜0.01），LDH活性明显降低(P＜0.001)，细胞内游离Ca2+浓度显著下降（P＜0.01），神经突起数目和长度增加（P＜0.01），Akt1及GSK3β表达上升（P＜0.01）。结论 帕潘立酮对地佐环平损伤脑皮层神经元具有明显保护作用，可抑制细胞凋亡，并通过Akt1 GSK3β通路促进神经突起的生长。

关键词： 脑皮层神经元；帕潘立酮；地佐环平；保护作用

Protective effects and mechanisms of paliperidone on cortical neurons injured by dizocilpine

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Abstract:

Objective To investigate protective effects of paliperidone on cortical neurons injured by dizocilpine and associated mechanisms. Methods Cortical neurons were dissociated from embryonic rats at E15 and cultured in DMEM/F12 medium supplemented with 10% fetal bovine serum. After cortical neurons were injured by dizocilpine, paliperidone at different concentrations was added to detect their protection effects. MTT assay was adopted to detect cell viability. Lactate dehydrogenase (LDH) activity and intracellular Ca2+ concentration were measured with LDH cytotoxic assay kit and laser scanning microscope respectively. Total length and number of neurites were calculated with Image Pro-Plus software. mRNA expressions of Akt1 and GSK3β which associated with neurogenesis and neurodevelopment were detected by real time PCR. Results In contrast with control group, cortical neurons in dizocilpine group exhibited apparently reduced viability, increased concentration of intracellular calcium and LDH release (P＜0.01), declined number and total length of neurites (P＜0.01) and decreased expressions of Akt1 and GSK3βat mRNA level detected by RT-PCR assay (P＜0.01). Compared to dizocilpine group, viability of cultured cortical neurons was increased（P＜0.01） and LDH activity was declined due to the addition of paliperidone (P＜0.001). Intracellular Ca2+ concentration in paliperidone group was weaker than that in dizocilpine group (P＜0.01). The length and number of neurites in paliperidone group were greater than those in dizocilpine group (P＜0.01). Real-time PCR also showed that the expressions of Akt1 and GSK3β were higher in paliperidone group than those in dizocilpine group(P＜0.01). Conclusion Paliperidone can effectively protect cortical neurons from dizocilpine injury, inhibit neuron apoptosis and promote neurogenesis via Akt1-GSK3β signaling pathway.

Keywords: Cortical neuron; Paliperidone; Dizocilpine; Protection

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