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论著

JNK阻断剂CEP-11004对铝诱导的大鼠皮层神经元凋亡的保护作用

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摘要 目的 为探讨铝诱导神经元凋亡的信号传递机制及铝的神经毒性机制，并为防治神经退行性疾病提供线索，研究应激活化蛋白激酶（又称c-jun N末端激酶，SAPK/JNK）的阻断剂CEP-11004（KT 8138）对氯化铝（$AlCl_3$）诱导大鼠皮层神经元凋亡的保护作用。方法 SD乳大鼠大脑皮层神经元培养，FDA荧光染色法检测神经元存活率，Hoechst33258核荧光染色，琼脂糖凝胶电泳检测细胞凋亡，SAPK/JNK分析试剂盒作激酶分析。结果 一定剂量的$AlCl_3$（10～1000 μmol·L^{-1}）可降低皮层神经元存活率，诱导大鼠皮层神经元凋亡，SAPK/JNK的磷酸化水平明显升高（对照组的4.2倍，P<0.01），SAPK/JNK被激活。但是，当CEP-11004（1～10 μmol·L^{-1}）预孵6 h后再加入1000 μmol·L^{-1} $AlCl_3$染毒6 h，SAPK/JNK的磷酸化水平呈剂量依赖性地降低（分别是对照组的2.3，1.2和0.9倍，P<0.05），CEP-11004通过抑制细胞凋亡而促进皮层神经元的存活，对大鼠皮层神经元产生保护作用。结论 CEP-11004可能通过抑制SAPK/JNK的活性，对$AlCl_3$诱导的皮层神经元凋亡产生保护作用。

关键词 蛋白激酶抑制剂 CEP-11004 铝 凋亡 信号传递

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Protective effect of JNK inhibitor CEP-11004 on the $AlCl_3$-induced apoptosis in cortical neurons of rat pups

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Abstract

AIM To clarify the signal transduction mechanism of apoptosis induced by $AlCl_3$ and the mechanism of neurotoxicity of aluminum. **METHODS** Cortical neurons were separated and cultured from newborn (less than 24 h) Sprague-Dawley(SD) rats. The method of FDA fluorescein staining was used to detect the viability of cortical neurons. Hoechst33258 nucleus staining and agarose gel electrophoresis were used to observe the characters of apoptosis. And SAPK/JNK assay kit was used to measure SAPK/JNK activity.]**RESULTS** $AlCl_3$ (10－1000 μmol·L^{-1}) decreased the viability and induced apoptosis of cortical neurons. The phosphorylation of SAPK/JNK increased significantly (4.2 times a s compared to control, P<0.01), and the activity of SAPK/JNK was elevated when cortical neurons were cultured with 1000 μmol·L^{-1} $AlCl_3$ for 6 h. But when the cortical neurons were pretreated with CEP- 11004 (1－10 μmol·L^{-1}) for 6 h prior to treatment with 1000 μmol·L^{-1} $AlCl_3$ for 6 h, the phosphorylation of SAPK/JNK decreased significantly in a dose-dependent manner (2.3, 1.2 and 0.9 times as compared to control respectively, P<0.05). It indicated the JNK inhibitor CEP-11004 promoted the survival of cortical neurons by blocking apoptosis and protected the neurons. **CONCLUS ION** CEP-11004 inhibited the activation of SAPK/JNK to protect cortical neurons from apoptosis induced by aluminum chloride.

Key words protein kinase inhibitor CEP 11004 aluminum apoptosis signal transduction

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