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论著

铅对大鼠脑细胞凋亡的诱发作用及对P53基因表达影响的研究

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摘要 目的：为进一步揭示铅的神经毒作用机制，对醋酸铅诱导大鼠脑细胞凋亡及对P53基因表达的影响进行了研究。 方法： 取成年SD大鼠，每组6只，染毒剂量分别为25、50、100 mg/kg，连续染毒5 d，经升主动脉灌注4 %多聚甲醛内固定后分别取其海马、皮层部位脑组织，制备石蜡切片，用原位末端标记法观测细胞凋亡，免疫组化方法分别测定海马、皮层组织中P53的蛋白含量。 结果： 各剂量组大鼠海马、皮层组织凋亡细胞数量明显增加，显著高于对照组，并有良好的剂量反应关系；大鼠脑组织海马、皮层P53表达阳性细胞数显著增加，表达强度有升高趋势;铅诱导的神经细胞凋亡与P53的表达呈正相关。 结论：醋酸铅可以诱发大鼠皮层、海马细胞的凋亡，且与剂量呈正相关；醋酸铅可以促进大鼠海马、皮层细胞中P 53基因的表达，并有良好的剂量反应关系，提示P53可能作为调控因子参与铅对中枢神经系统损害的毒性过程；高表达的P 53启动凋亡过程，诱导细胞凋亡。

关键词 铅；大鼠；神经毒性；凋亡；P53基因

STUDIES ON THE APOPTOSIS AND THE EXPRESSION OF p53 BY LEAD IN RAT BRAIN

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Abstract Purpose：To provide some scientific basis for the revealment of neurotoxic mechanism of lead ,The present study was undertake to the effect of lead acetate on the apoptosis and the expression of P53. Methods: Mature and health Sprague- Dawley rats were divided into four groups randomly, six rats in every group. Lead acetate was given at the dosage of 25,50,100 mg/kg through ip for 5 days, respectively . The determination of apoptosis in hippocampus and cerebral cortex was made by terminal- deoxynucleotidyl transferase mediated d- UTP nick and labeling(TUNEL). The expression of P53 genes in hippocampus and cerebral cortex was observed by using immuno- histochemical method . Results: The results of TUNEL showed that lead acetate induced apoptosis f cells from hippocampus, cerebral cortex in every treatment group ($P < 0.05$), and there was a significant dose- response relationship.The expression of P53 increased in neural cells from hippocampus, cerebral cortex in every lead acetate treatment group compared with the control , and there was a significant dose- response relationship. Correlation analysis demonstrated that the apoptosis were positively correlated with the expression of P53. Conclusion: Lead may elicit apoptosis of rat neural cells from hippocampus, cerebral cortex , and the apoptosis was positive correlative with the lead dosage. Lead acetate may promote the expression of P53 genes， and there was a good dose- response relationship。 The results above suggested that P53 as a regular factor of apoptosis， may participate in the neurotoxical damaging to the central nervous system by lead. The overexpression of P53 induced the apoptosis of neural cells. Lead acetate may initiate the expression of P53 followed by he apoptosis of neural cells .

Keywords lead； rat； neurotoxicity； apoptosis； P53 gene

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