癌变.畸变.突变 ISSN: 1004-616x CN:44-1063/R 2006; 18(5) :359-362

论著

铅对大鼠脑细胞凋亡的诱发作用及对fos、jun、P53基因和一氧化氮合酶表达影响的研究

安兰敏1;牛玉杰2;徐 兵2 ;刘 纳1

1.石家庄市卫生防疫站，河北 石家庄 050011；2河北医科大学，河北 石家庄 050011

收稿日期 2005-12-1 修回日期 2006-2-28 网络版发布日期:

摘要 目的：通过对醋酸铅诱导大鼠脑细胞凋亡及对fos、jun、p53基因和一氧化氮合酶表达的影响，进一步揭示铅的神经毒作用机理。方法：成年SD大鼠经腹腔注射醋酸铅染毒，分别用原位末端标记法观测细胞凋亡，用SP法测定脑组织中fos、jun、 p53及nNOS和iNOS的蛋白含量以检测其表达情况。 结果：各染铅组大鼠海马、皮层组织凋亡细胞数量明显增加，并和染铅剂量有良好的剂量效应关系；大鼠脑组织海马、皮层fos、jun、p53、iNOS表达阳性细胞数显著增加，表达强度有升高趋势；各剂量染铅组海马组织中nNOS表达明显升高，而皮层组织nNOS表达无明显变化；相关分析表明，铅诱导的神经细胞凋亡与fos、jun、p53及iNOS的表达呈正相关。结论：在铅诱导神经细胞凋亡的过程中，高表达的NOS使得NO生成过多进而引起DNA损伤，激活p53，同时使fos、jun表达增加也可激活p53，启动凋亡过程，诱导细胞发生凋亡。

关键词 铅；神经毒性；凋亡；fos基因； jun基因 p53基因； 一氧化氮合酶

Influence of Lead on the Apoptosis and the Expression of fos，jun，p53 and Nitric Oxide Synthase in Rat Brain

AN Lan-min1 ,NIU Yu-jie2 ,XU Bing2,LIU Na1

1. Health and Anti-epidemic Station of Shijiazhuang, Shiijazhuang, 050011,Hebei,china; 2.Hebei Medical University,Shiiazhuang, 050011 Hebei, China

Abstract BACKGROUND & AIM: To study the effect of lead acetate on the apoptosis and the expression of fos, jun, P53 and NOS and to provide some scientific basis for further delineation of the neurotoxic mechanisms of lead. MATERIAL AND METHODS: Mature and healthy Sprague-Dawley rats were randomly divided into four groups. Lead acetate was injected intraperitoneally. 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 fos, jun, P53 genes and nNOS, iNOS in hippocampus and cerebral cortex were measured by using immunohistochemical method. RESULTS: ① TUNEL showed that lead acetate induced apoptosis of cells from hippocampus, cerebral cortex in every treatment group ($P<0.05$), and there was a significant dose-response relationship.② The expression of fos, jun, P53 and iNOS increased in neural cells from hippocampus, cerebral cortex in every lead acetate treatment group compared with the control.③ The expression of nNOS significantly increased in hippocampus in every treatment group compared with the control.However the expression of nNOS in cerebral cortex showed no significant difference between the treatment groups and the control group.④ Correlation analysis demonstrated that apoptosis correlated positively with the expression of fos, jun, P53 and iNOS. CONCLUSION: The overexpression of P53, which was caused by damage of DNA elicited by the excessive amount of NO from the overexpression of NOS, induced apoptosis of neural cells. Lead acetate also induced the prolonged expression of fos and jun which may initiate the expression of P53 followed by apoptosis of neural cells.

Keywords lead neurotoxicity apoptosis fos gene jun gene nitric oxide synthase

DOI

通讯作者　安兰敏 lanmin-an@sina.com