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论著

铅暴露导致小鼠学习记忆功能障碍及海马蛋白激酶B表达降低

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摘要 目的 探讨蛋白激酶B(PKB)在慢性铅暴露所致小鼠学习记忆功能障碍中的作用。方法 5~6周龄小鼠交配后,铅暴露组仔鼠通过胎盘、乳汁和饮水饲醋酸铅2.4,4.8和9.6 mmol·L^{-1},连续42 d。第42天水迷宫实验测平台潜伏期;检测血及脑铅浓度;Sanna方法检测仔鼠海马CA1区长时程增强(LTP)和群峰电位幅值(PS);Western印迹法检测脑海马总PKB(t-PKB)及磷酸化PKB(p-PKB)的表达。结果 与正常对照组相比,铅暴露组小鼠寻找平台时间明显延长(P<0.05)。正常对照组血铅为(0.05±0.02)mg·L^{-1},铅暴露组分别为0.29±0.06,0.91±0.15和(1.46±0.37)mg·L^{-1};正常对照组脑铅为(0.12±0.056)μg·g^{-1},铅暴露组分别为2.07±0.55,10.18±1.51和(14.20±2.63)μg·g^{-1}。学习记忆降低程度与血铅、脑铅浓度成正相关(r=0.678, r=0.645, P<0.01)。高频刺激后,正常对照组的PS幅值明显升高,为刺激前的1.76倍,而铅暴露组PS幅值下降到刺激前的85%。与正常对照组比较, 暴露铅4.8及9.6 mmol·L^{-1}组, PS幅值明显下降(P<0.01)。铅暴露组的LTP诱发成功率亦有所下降。小鼠海马CA1区LTP损伤程度与血铅、脑铅浓度呈正相关(r=0.659, r=0.638, P<0.01)。铅暴露组小鼠脑海马p-PKB表达均明显降低,并具有浓度效应关系。p-PKB表达与血脑铅浓度呈负相关(r=-0.840, r=-0.813, P<0.01),与学习记忆能力损伤程度呈负相关(r=-0.668,P<0.01)。铅对小鼠海马神经元细胞t-PKB的表达无影响。结论 慢性铅暴露可导致学习记忆功能下降, 可能与海马p-PKB表达下降有关。

关键词 蛋白激酶B 铅 海马 学习记忆 长时程增强 群峰电位幅值

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Impairment of learning and memory and decreasing of protein kinase B expression in mice hippocampus induced by lead

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Abstract

OBJECTIVE To explore the effect of protein kinase B (PKB) expression on learning and memory in hippocampus neuron of mice exposed to chronic lead. **METHODS** Young mice were exposed to acetic lead 0, 2.4, 4.8 and 9.6 mmol·L^{-1} by placenta,milk and drinking water for 42 d consecutively, after mice of 5-6 weeks were mated. Morris water maze was determined in postnatal 42 d to observe the capability of spatial learning and memory, blood and brain lead was determined in mice. The population spike (PS) amplitude in CA1 region mice in four groups were alternatively determined by Sanna method. The expression of total PKB (t-PKB) and phosphorylated PKB (p-PKB) determined by Western blotting. **RESULTS** The mean time of finding the platform in lead exposure group was higher than that of the control group (P<0.05). Compared with blood lead in control group (0.05±0.02)mg·L^{-1}; blood lead in lead exposure groups was 0.29±0.06, 0.91±0.15 and (1.46±0.37)mg·L^{-1}, respectively. Compared with the brain lead in control group was (0.12±0.056)μg·g^{-1} tissue, brain lead in lead exposure groups was 2.07±0.55, 10.18±1.51 and (14.20±2.63)μg·g^{-1}, respectively. Chronic acetic lead exposure could damage the capability of spatial learning and memory in mice obviously; the damage

level was positive correlated with the concentration of blood and brain lead(r=0.678 and 0.645, P<0.01). After the application of the high frequency stimulation (HFS), the PS amplitude in control group increased in relation to baseline amplitude to 176%, while in chronic lead exposure group decreased to 85%. PS amplitude of lead 4.8 and 9.6 mmol • L^{-1} groups was significantly lower then that in the corresponding control group(P<0.01). The incidence of long-term potentiation(LTP) induction of lead exposure group decreased significantly. The damage level of LTP in lead exposure group was positive correlate with the concentration of blood and brain lead(r=0.659, r=0.638, P<0.01). The expression of p-PKB in hippocampus of lead exposure group was decreased significantly dose-dependently. The