

论著

## 镧对大鼠海马CA1区环磷酸腺苷应答元件结合蛋白磷酸化的影响

杨敬华, 巫生文, 刘秋芳, 张立丰, 齐鸣, 鲁帅, 蔡原

(中国医科大学公共卫生学院卫生毒理学教研室, 辽宁 沈阳 110001)

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**摘要** 目的 探讨镧的神经毒性作用机制。方法 40只Wistar孕大鼠通过自由饮水的方式随机分为正常对照组, LaCl<sub>3</sub> 0.25%, 0.5%和1.0%染毒组。染毒组仔鼠在断乳前通过母乳染毒, 断乳后通过自由饮水的方式染毒1个月。电感耦合等离子体质谱法检测海马CA1区镧含量; 磷酸二酯酶法检测海马CA1区钙调蛋白(CaM)活性; Western印迹法检测磷酸化钙调蛋白依赖性蛋白激酶IV(p-CaMKIV), 磷酸化环磷酸腺苷应答元件结合蛋白(p-CREB)和c-jun蛋白表达; RT-PCR法检测c-jun mRNA表达水平。结果 与正常对照组相比, LaCl<sub>3</sub> 0.25%, 0.5%和1.0%染毒组海马CA1区镧含量显著高于正常对照组, 分别为正常对照组的7.3, 12.0和20.0倍( $P<0.05$ ); 海马CA1区CaM活性显著降低, 分别为正常对照组的80.7%, 59.9%和30.6%( $P<0.05$ ); 海马CA1区p-CaMKIV表达降低, 分别为正常对照组的83.0%, 57.4%和27.7%( $P<0.05$ ), p-CREB表达显著降低, 分别降低了24.4%, 36.6%和73.2%( $P<0.05$ ), c-jun蛋白表达显著降低, 分别降低了36.1%, 45.9%和83.6%( $P<0.05$ ), c-jun mRNA表达显著降低, 分别降低了14.8%, 27.2%和76.5%( $P<0.05$ )。结论 镧可能与钙竞争结合于CaM, 造成海马CA1区CaM活性和CaMKIV, CREB磷酸化以及c-jun基因转录和蛋白表达水平下降, 从而损害大鼠的学习记忆能力。

**关键词** 镧 海马 环磷酸腺苷应答元件结合蛋白

分类号 R744.8, R994.3

## Effects of lanthanum on phosphorylation of cAMP response element binding protein in hippocampal CA1 area of rats

YANG Jing-hua, WU Sheng-wen, LIU Qiu-fang, ZHANG Li-feng, QI Ming, LU Shuai, CAI Yuan

(Department of Toxicology, College of Public Health, China Medical University, Shenyang 110001, China)

### Abstract

**OBJECTIVE** To explore the mechanism underlying neurotoxic effects of lanthanum (La). **METHODS** Forty Wistar rats in pregnancy were divided randomly into 4 groups: normal control, LaCl<sub>3</sub> 0.25%, 0.5% and 1.0% groups by drinking water freely. After birth, pups in LaCl<sub>3</sub> groups were administrated with La by lactation before weaning, and then given La by drinking water for 1 month. La content in the hippocampal CA1 area of pups was measured by inductively coupled plasma mass spectrometry, and calmodulin (CaM) activity in the hippocampal CA1 area of pups was determined by phosphodiesterase. The protein expression of phosphorylated-calmodulin dependent protein kinase IV (p-CaMKIV), phosphorylated-cAMP response element binding protein (p-CREB) and c-jun were measured by Western blotting, and c-jun mRNA was detected by RT-PCR. **RESULTS** Compared with normal control group, La content in the hippocampal CA1 area increased 7.3-, 12.0- and 20.0-fold in LaCl<sub>3</sub> 0.25%, 0.5% and 1.0%, respectively ( $P<0.05$ ); CaM activities in the hippocampal CA1 decreased to 80.7%, 59.9% and 30.6% ( $P<0.05$ ), the expression of p-CaMKIV in the hippocampal CA1 area was decreased to 83.0%, 57.4% and 27.7% ( $P<0.05$ ), the expression of p-CREB was decreased by 24.4%, 36.6% and 73.2% ( $P<0.05$ ), the expression of c-jun protein was decreased by 36.1%, 45.9% and 83.6% ( $P<0.05$ ) and the expression of c-jun mRNA was decreased by 14.8%, 27.2% and 76.5%, respectively. **CONCLUSION** The neurotoxic effect induced by La might be related to the fact that La could bind with CaM competitively and cause down regulation of CaM activity, CaMKIV and CREB phosphorylation, c-jun mRNA and protein expression in the hippocampal CA1 area and therefore injure learning and memory of rats.

**Key words** lanthanum hippocampus cAMP response element binding protein

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