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项迎春,廖美华,田允,黄继云,陶蓉蓉.反复重度低血糖对糖尿病大鼠海马PKA/PKC/CaMKⅡ磷酸化信号通路的影响[J].中国现代应用药学,2013,30(6):586-590

反复重度低血糖对糖尿病大鼠海马PKA/PKC/CaMKⅡ磷酸化信号通路的影响

Recurrent Severe Hypoglycemia Induced Disturbance of Hippocampal PKA/PKC/CaM Phosphorylation Signaling in Diabetic Rats

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中文关键词： 2型糖尿病 低血糖 蛋白激酶A 蛋白激酶C 钙调素依赖蛋白激酶Ⅱ 认知功能

英文关键词:type 2 diabetes hypoglycemia PKA PKC CaMKⅡ cognitive function

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中文摘要:

目的 观察2型糖尿病大鼠在诱发反复重度低血糖时海马组织中蛋白激酶A(PKA)、蛋白激酶C(PKC)、钙调素依赖蛋白激酶Ⅱ(CaMKⅡ)磷酸化信号通路相关蛋白水平变化，探讨其在认知功能损害中的作用。方法 将大鼠随机分为4组：对照组、糖尿病组、反复重度低血糖组和糖尿病反复重度低血糖组。用链脲佐菌素(STZ)建立2型糖尿病大鼠模型；对照组、糖尿病组给予生理盐水，反复重度低血糖组和糖尿病反复重度低血糖组给予普通胰岛素连续注射4 d使呈反复重度低血糖状态(<2.0 mmol·L^{-1})。Western blot 法检测各组大鼠海马组织PKA/PKC/CaMKⅡ磷酸化信号通路相关蛋白翻译后磷酸化的表达水平。结果 与正常组相比，糖尿病反复重度低血糖组大鼠海马区磷酸化PKA蛋白表达水平增高(P<0.05)，其上游ERK磷酸化水平也增高(P<0.05)；而PKC、CaMKⅡ信号通路的相关蛋白表达，差异无统计学意义(P>0.05)；与糖尿病组、反复重度低血糖组相比，糖尿病反复重度低血糖组大鼠海马区PKA、PKC、CaMKⅡ相关蛋白表达差异无统计学意义(P>0.05)。结论 糖尿病诱发反复重度低血糖的情况下，PKA磷酸化水平发生明显改变，提示可能与重度低血糖致脑损伤和认知功能障碍相关联。PKA磷酸化表达变化可能可以作为敏感生化指标。

英文摘要:

OBJECTIVE To observe the change of protein expression on PKA/PKC/CaMK Ⅱ

phosphorylation signal pathway in the hippocampal tissue of type 2 diabetic rats induced by recurrent severe hypoglycemia and explore the effect of cognitive impairment on the brain. METHODS Forty adult SD rats were randomly divided into 4 groups: control group, diabetes group, recurrent severe hypoglycemia group and diabetes recurrent severe hypoglycemia group. By using STZ method to establish mode of type 2 diabetes. The rats in control group and diabetes group were injected with normal saline. The rats in recurrent severe hypoglycemia group and diabetes recurre severe hypoglycemia group were treated with ordinary insulin continuously for 4 day to present the state of recurrent severe hypoglycemia (<2.0 mmol·L^{-1}). Western blo method was used to detect the protein phosphorylation expression of PKA/PKC/CaMKⅡ related phosphorylation protein. RESULTS In the rat hippocampus, the protein phosphorylation level of PKA was significant higher in diabetes recurrent severe hypoglycemia group than that in control group($P<0.05$). Similarly, the upstream ERK phosphorylation level was also significant higher. PKC, CaMK Ⅱ related protein phosphorylation level showed no significant different between control group and diabetes recurrent severe hypoglycemia group($P>0.05$). Compare with diabetes group a recurrent severe hypoglycemia group, PKA, PKC, CaMK Ⅱ related protein phosphorylat level in diabetes recurrent severe hypoglycemia group showed no significant differe ($P>0.05$). CONCLUSION PKA phosphorylation level was dramatically increased in the