

## 论文

### 二氮嗪预处理对A $\beta$ 1-42作用神经元KATP各亚基表达的影响

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#### 摘要:

**目的** 探讨ATP敏感的钾离子(KATP)通道开放药物二氮嗪防治A1-42细胞毒性作用的分子机制。**方法** 采用细胞原代培养的方法, 培养大鼠皮层神经元并进行鉴定。将原代培养的细胞随机分为对照组、单纯A $\beta$ 1-42干预组、二氮嗪预处理1h后A $\beta$ 1-42干预组、单纯二氮嗪预处理组和单纯A $\beta$ 42-1干预组(A $\beta$ 1-42反序列对照), 各组又分为24、72h两个亚组。采用免疫荧光双染及免疫印迹法, 观察干预后不同培养时间(24、72h)细胞KATP通道各亚基Kir6.1、Kir6.2、SUR1、SUR2蛋白表达水平的变化。**结果** 与对照组比较, 单纯A1-42处理24h组Kir6.1、SUR2显著升高(P<0.05), 二氮嗪预处理后A $\beta$ 1-42作用细胞24h组各亚基表达均无明显变化; 二氮嗪预处理后A $\beta$ 1-42作用细胞72h组与单纯A1-42处理72h组KATP通道各亚基表达均明显升高(P<0.05), 而二氮嗪预处理后A $\beta$ 1-42作用细胞72h组与单纯A1-42处理72h组相比Kir6.1、Kir6.2、SUR2表达显著下调(P<0.05)。**结论** 二氮嗪预处理可完全逆转A1-42作用神经元24h所引起的Kir6.2及SUR1的表达上调, 只能部分逆转A1-42作用神经元72h所引起的Kir6.1、Kir6.2、SUR2的表达增加, 可能会维持神经细胞正常生理功能, 起到防治A1-42细胞毒性作用。

**关键词:** 淀粉样 $\beta$ 蛋白; 细胞毒素类; 钾通道, 电压门控; 二氮嗪

### Effects of diazoxide on expressions of KATP subunits in neurons treated with A $\beta$ 1-42

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#### Abstract:

**Objective** To investigate the possible molecular mechanism of mitochondrial ATP-sensitive potassium (KATP) channel opener diazoxide in preventing cytotoxicity of A $\beta$ 1-42. **Methods** Primary neurons were cultured and evaluated by immunocytochemistry. Cells were randomly divided into 5 groups: the control group, the A $\beta$ 1-42 group, the diazoxide+A $\beta$ 1-42 group, the diazoxide group and the A $\beta$ 42-1 group. After treatment for 24h or 72h, subunits of KATP(Kir6.1, Kir6.2, SUR1 and SUR2) were detected by double immunofluorescence and immunoblotting. **Results** ① Being treated with A $\beta$ 1-42(2 $\mu$ mol/L) for 24h, expressions of Kir6.1 and SUR2 were significantly up-regulated, and the changes could be completely reversed by pretreatment with diazoxide(1mmol/L)for 1h(P<0.05). ② There were significant increases in all KATP subunit expression levels after exposure to A $\beta$ 1-42 for 72h, and up-regulation of Kir6.1, Kir6.2 and SUR2 except SUR1 could be partly reversed by pretreatment with diazoxide (1mmol/L) for 1h(P<0.05). **Conclusion** Diazoxide could reverse enhanced expressions of KATP subunits in neurons caused by exposure to A $\beta$ 1-42, which may explain, in part, the effect of diazoxide on resistance to the toxicity of A $\beta$ 1-42.

**Keywords:** Amyloid beta protein; Cytotoxins; Potassium channels, voltage gated; Diazoxide

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