

论文

甲基苯丙胺对瞬时外向钾电流影响

王军¹, 蒋雷², 环飞¹, 程洁¹, 高蓉¹, 肖杭¹

1. 南京医科大学公共卫生学院 教育部重点实验室, 江苏 南京 210029;
2. 江苏省人民医院急诊中心

摘要:

目的 观察甲基苯丙胺(Meth)对瞬时外向钾电流的影响及原因。**方法** 将怀孕18 d SD大鼠胎鼠海马神经元分为对照组和Meth处理组,利用全细胞膜片钳方法记录外向瞬时钾电流变化;采用原位末端转移酶标记技术(TUNEL)观察Meth引起的细胞损伤作用;利用逆转录聚合酶链反应(RT-PCR)方法观察瞬时外向电流成分中Kv1.4、4.1、4.2和4.3表达,并通过western-blot方法观察Kv4.2蛋白表达。**结果** 与对照组比较,Meth能引起瞬时外向钾电流增大 $[(120.1 \pm 19.6) \text{ pA/pF}] (P < 0.01)$,与对照组 (1.00 ± 0.18) 比较,Meth处理组凋亡率为对照组的 (7.11 ± 0.95) 倍 $(P < 0.01)$,钾通道抑制剂4-氨基吡啶(4-AP)明显抑制神经元凋亡 $(P < 0.01)$;Kv4.2可能是外向电流成分中主要贡献者,Meth能上调Kv4.2通道蛋白表达;与Kv4.2上调密切相关的Kchip2/3、Kchip4、CaMK2蛋白表达增高。**结论** Meth引起的瞬时钾电流增大可能通过Kv4.2上调来实现,但其机制仍需进一步探讨。

关键词: 甲基苯丙胺(Meth) 瞬时外向钾电流 Kv4.2 细胞凋亡

Effects of methamphetamine on transient outward K⁺ currents

WANG Jun, JIANG Lei, HUAN Fei, et al

Department of Toxicology, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu Province 210029, China

Abstract:

Objective To investigate the effects of methamphetamine(Meth) on the transient outward K⁺ currents and its mechanisms.**Methods** Hippocampal neurons were harvested from 18-day-old embryonic rats and divided into control and Meth treated group.The currents were recorded with the whole cell patch clamp and the cell damage was detected by the TdT-mediated dUTP nick end labeling(TUNEL) assay.The mRNA expressions of Kv1.4,Kv4.1,Kv4.2,and Kv4.3 were evaluated by reverse transcription-PCR(RT-PCR).Furthermore,the expression of Kv4.2 was detected with western-blot after the treatment of Meth.**Results** Meth significantly increased the transient outward K⁺ currents $(120.1 \pm 19.6 \text{ pA/pF}, P < 0.01)$ compared with the control group $(87.4 \pm 12.5 \text{ pA/pF})$ and caused neuronal damage(control group: 1.00 ± 0.18 vs Meth treated group: $7.11 \pm 0.95, P < 0.01$).However,4-aminopyridine(4-AP),the antagonist of the transient currents,substantially retarded the cell damage induced by Meth $(4.96 \pm 1.32, P < 0.01)$.Moreover,Kv4.2 might be the main contributor in transient currents.With western-blot assay,we observed that Meth up-regulated the Kv4.2 expression and the expressions of Kchip2/3,Kchip4,and CaMK2,which were closely associated with the expression of Kv4.2,were also up-regulated.**Conclusion** The up-regulation of Kv4.2 might be involved in Meth induced transient outward K⁺ current increments,however,the mechanisms still need to be clarified.

Keywords: methamphetamine transient outward K⁺ current Kv4.2 cell apoptosis

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通讯作者: 肖杭,E-mail: hxiao@njmu.edu.cn

作者简介:

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