

论著

## 吡格列酮对淀粉样 $\beta$ 蛋白片段1-42引起的大鼠海马有丝分裂原激活蛋白激酶p38信号传导通路变化的影响

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收稿日期 2008-1-16 修回日期 网络版发布日期 2008-9-25 接受日期 2008-3-28

**摘要** 目的 探讨吡格列酮(Pio)对淀粉样 $\beta$ 蛋白片段1-42( $A\beta_{1-42}$ )所致大鼠海马损伤的保护作用及其作用机制。方法 大鼠随机分为正常对照组,  $A\beta_{1-42}$ 损伤组,  $A\beta_{1-42}$ +Pio 20, 40 及80  $mg \cdot kg^{-1}$ 组。d 1与d 2, Pio处理组大鼠灌胃给予Pio, 正常对照组和 $A\beta_{1-42}$ 损伤组灌胃给予0.2%二甲亚砜。d 2给药处理后,  $A\beta_{1-42}$ 损伤组及Pio处理组大鼠左侧脑室内单次注射 $A\beta_{1-42}$  5  $\mu L$  ( $2.0 \text{ mmol} \cdot L^{-1}$ )制备大鼠痴呆模型, 正常对照组注射等量生理盐水。继续给药6 d, 处死大鼠, 取海马CA1区, Western蛋白印迹法观察磷酸化有丝分裂原激活蛋白激酶3/6(MKK3/6)、磷酸化有丝分裂原激活蛋白激酶P38(p38MAPK)、磷酸化活化转录因子2(ATF-2), 磷酸化有丝分裂原激活蛋白激酶活化的蛋白激酶2(MAPKAPK-2)和磷酸化热休克蛋白27(HSP27)的蛋白表达水平的改变。结果 脑室内注射 $A\beta_{1-42}$ 可引起海马CA1区磷酸化的MKK3/6、磷酸化的p38MAPK和磷酸化的ATF-2表达明显增加, 而磷酸化的MAPKAPK-2和磷酸化的HSP27表达明显降低。Pio可明显抑制 $A\beta_{1-42}$ 引起的磷酸化的MKK3/6、磷酸化的p38MAPK和磷酸化的ATF-2表达的增加; 逆转 $A\beta_{1-42}$ 引起的磷酸化的MAPKAPK-2和磷酸化的HSP27表达降低的变化。结论 Pio对 $A\beta_{1-42}$ 引起的海马神经损伤的保护作用可能与其抑制 $A\beta_{1-42}$ 引起的磷酸化p38MAPK信号传导通路的改变有关。

**关键词** [吡格列酮](#) [有丝分裂原激活蛋白激酶类](#) [信号传导](#)

分类号 [R966](#)

## Effects of pioglitazone on amyloid beta-protein fragment 1-42-induced mitogen-activated protein kinase p38 signal pathway in rat hippocampus

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### Abstract

**AIM** To observe the neuroprotective effects and protective mechanisms of pioglitazone(Pio) on amyloid beta-protein fragment 1-42 ( $A\beta_{1-42}$ )-induced neurotoxicity in rat hippocampus. **METHODS** The rats were randomly divided into normal group,  $A\beta_{1-42}$  group,  $A\beta_{1-42}$ +Pio group (20, 40 and 80  $mg \cdot kg^{-1}$ ). On d 1, the rats in normal, model and Pio groups were given 0.2% DMSO and Pio ig, respectively. On d 2, single dose  $A\beta_{1-42}$  ( $5 \mu L$ ,  $2 \text{ mmol} \cdot L^{-1}$ ) was given (icv) to rats in model and Pio groups (after Pio given). Then, the rats in Pio groups were given Pio for 6 d. Western blot was used to determine the expression of phospho-mitogen-activated protein kinase 3/6 (MKK3/6), phospho-mitogen-activated protein kinase p38 (p38MAPK), phospho-activating transcription factor-2 (ATF-2), phospho-mitogen-activated protein kinase activating protein kinase-2 (MAPKAPK-2) and heat-shock protein 27 (HSP27). **RESULTS** Intracerebroventricular injection of  $A\beta_{1-42}$  induced the increased expressions of phosphorylated MKK3/6, p38MAPK and ATF-2, but the decreased expressions of phosphorylated MAPKAPK-2 and HSP27, and these activated changes were inhibited by Pio. **CONCLUSION** It is possible that Pio prevents  $A\beta_{1-42}$ -induced neurotoxicity through suppressing the expression of p38MAPK signal pathway.

**Key words**

扩展功能

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