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论著

吡格列酮对淀粉样β蛋白片段1-42引起的大鼠学习记忆障碍及海马炎症反应的影响

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摘要 目的 观察吡格列酮（Pio）是否对学习记忆障碍有治疗改善作用。方法 大鼠随机分为正常对照组，淀粉样β蛋白片段1-42($A\beta_{1-42}$)损伤组，$A\beta_{1-42}$+Pio 20，40及80 mg·kg^{-1}组。于d 1和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 μL (2.0 mmol·L^{-1})制备大鼠痴呆动物模型，正常对照组注射等量生理盐水。同时，d 2开始进行Morris水迷宫实验，连续6 d；水迷宫实验结束后，Nissl染色观察海马CA1区锥体神经元改变和免疫组织化学法观察星形胶质细胞改变；Western蛋白印迹法检测白细胞介素（IL）-1β和诱导型一氧化氮合酶（iNOS）的表达水平。结果 脑室注射$A\beta_{1-42}$可引起大鼠学习记忆能力明显降低，表现为逃避潜伏期延长，原平台象限游泳时间占总时间的比例降低；形态学上表现为海马CA1区锥体神经元的损伤和星形胶质细胞的激活和浸润；同时海马IL-1β和iNOS蛋白表达也显著增加。Pio（40和80 mg·kg^{-1}）能明显改善大鼠学习记忆能力，减轻海马CA1区锥体神经元损伤和星形胶质细胞激活与浸润，抑制$A\beta_{1-42}$引起的IL-1β及iNOS蛋白表达增加。结论 Pio能改善$A\beta_{1-42}$损伤大鼠学习记忆障碍，抑制海马炎症反应可能是其机制之一。

关键词 吡格列酮 学习障碍 记忆障碍 海马 炎症

分类号 R964

Effects of pioglitazone on amyloid beta protein fragment 1-42-induced learning and memory disorders and inflammatory reaction in hippocampus in rats

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Abstract

AIM To observe whether pioglitazone (Pio) can improve amyloid beta-protein fragment 1-42 ($A\beta_{1-42}$) induced learning and memory disorders. **METHODS** The rats were randomly divided into normal group, $A\beta_{1-42}$ group and $A\beta_{1-42}$+Pio (20, 40 and 80 mg·kg^{-1}) groups. On d 1, the rats of control, model and Pio groups were given 0.2% DMSO and Pio ig, respectively. On d 2, single dose $A\beta_{1-42}$(5 μL, 2 mmol·L^{-1}) was given icv to model and Pio groups (after Pio given). Then, the rats of Pio groups were given Pio for 6 d. Morris water maze was used to measure the learning and memory performance on d 2 after icv $A\beta_{1-42}$. Nissl staining and immunohistochemical technique for glial fibrillary acidic protein were used to determine the morphology of pyramidal neurons and astrocyte′s activation and infiltration in hippocmpal CA1 regions. The levels of inducible nitric oxide synthase(iNOS) and interlukin(IL)-1β were determined by Western blot. **RESULTS** Intracerebroventricular injection of $A\beta_{1-42}$ in rats resulted in learning and memory impairments shown by longer escape latency and decreased percentage of time spent in the target quadrant. These behavioral dysfunctions were accompanied by astrocyte activation and infiltration, increased IL-1β protein expression and elevated iNOS level, the loss of pyramidal neurons in hippocampal CA1 regions. Pio (40 and 80 mg·kg^{-1}·d^{-1}) markedly improved the learning and memory impairment, attenuated pyramidal neurons damage, and reversed the $A\beta_{1-42}$-induced increases in IL-1β and iNOS activation. **CONCLUSION** Pio can improve the learning and memory impairment induced by $A\beta_{1-42}$, which maybe related to its inhibitory effect on inflammatory response in hippocampus.

Key words

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