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论著

肢体缺血预处理通过激活有丝分裂原激活蛋白激酶p38减轻脑缺血导致的大鼠海马CA1区神经元凋亡和脑水肿

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摘要 目的 旨在探讨肢体缺血预处理（LIP）能否减轻脑缺血过程中海马CA1区神经元凋亡和脑水肿。方法 72只永久凝闭椎动脉的Wistar大鼠随机分为6组：假手术，LIP(双侧股动脉夹闭10 min，间歇10 min，3次循环)，脑缺血，LIP+脑缺血，DMSO和SB 203580+LIP+脑缺血组。各组大鼠中6只在脑缺血后3 d处死，TUNEL染色计数凋亡细胞；6只在脑缺血后24 h处死，测定脑组织含水量。结果 TUNEL染色显示，假手术和LIP组海马CA1区偶有TUNEL阳性细胞；脑缺血组海马CA1区可见大量棕黄色着色的TUNEL阳性细胞，与假手术组及LIP组相比，细胞数量明显增加；LIP+脑缺血组，TUNEL阳性神经元数与脑缺血组相比明显减少，提示LIP明显抑制缺血引起的海马CA1区锥体细胞凋亡；有丝分裂原激活蛋白激酶p38拮抗剂SB 203580+LIP+脑缺血组，海马CA1区阳性染色锥体细胞明显增加，与DMSO+LIP+脑缺血组相比有显著性差别，表明SB 203580可拮抗LIP抑制凋亡的作用。与假手术和LIP组比较，脑缺血组脑组织含水量明显增加，表明LIP降低了脑缺血引起的脑组织含水量增加；LIP前应用SB 203580可抑制LIP的脑保护作用，使脑组织含水量较LIP+脑缺血组显著增加。结论 LIP能够减轻脑缺血过程中海马CA1区神经元凋亡和脑水肿，可能与活化有丝分裂原激活蛋白激酶p38有关。

关键词 有丝分裂原激活蛋白激酶类 缺血预处理, 肢体 SB 203580 细胞凋亡 脑水肿 脑缺血

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Limb ischemic preconditioning attenuates neuronal apoptosis in CA1 hippocampus and brain edema evoked by brain ischemia via activating mitogen-activated protein kinase p38 in rats

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Abstract

AIM To observe whether limb ischemic preconditioning (LIP) could attenuate pyramidal neuronal apoptosis of the CA1 hippocampus and brain edema evoked by brain ischemia in rats. **METHODS** Seventy-two rats whose bilateral vertebral arteries occluded permanently were randomly assigned into 6 groups: sham, LIP(bilateral femoral arteries were clamped for 10 min, 3 times, in a 10 min interval), brain ischemic insult, LIP+brain ischemic insult, DMSO+LIP+brain ischemic insult and SB 203580+LIP+brain ischemic insult groups. Assays for neuronal apoptosis were performed using TUNEL staining. The percentage of wet over dry tissue weight of the brain was measured by weighing method. **RESULTS** There were almost no TUNEL-positive cells in the CA1 hippocampus in either sham or LIP group. Clear TUNEL-positive pyramidal neurons of the CA1 hippocampus and increase in brain water content were detected in rats subjected to brain ischemic insult. But the number of TUNEL-positive cells and the increase in brain water content were significantly decreased in LIP+brain ischemic insult group compared with that in brain ischemic insult group, indicated that LIP prevented the occurrence of apoptosis of pyramidal neurons of the CA1 hippocampus and brain edema induced by brain ischemic insult. Pretreatment with SB 203580, an inhibitor of mitogen activated protein kinase p38(p38 MAPK), significantly increased the number of TUNEL-positive cells and brain water in SB 203580+LIP+brain ischemic insult group compared with that in DMSO+LIP+brain ischemic insult group, indicated that SB 203580 blocked the protection of LIP against neuronal apoptosis in the CA1 hippocampus and brain edema. **CONCLUSION** LIP could attenuate pyramidal neurons apoptosis of the CA1 hippocampus and brain edema evoked by brain ischemia, which maybe related to the activation of p38 MAPK.

Key words mitogen activated protein kinases ischemic preconditioning limb SB 203580 apoptosis brain edema brain ischemia

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