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论著

预适应与后适应联合干预对脑缺血/再灌注损伤的保护作用

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摘要：

目的：探讨缺血预适应联合缺血后适应对大鼠脑缺血/再灌注(I/R)损伤的保护作用及可能的机制。方法：60只SD大鼠随机均分为假手术组，脑I/R组(模型组)，脑I/R+预适应(预适应组)，脑I/R+后适应组(后适应组)，脑I/R+预适应与后适应联合干预组(联合干预组)。采用线栓法制作大鼠脑I/R损伤模型，预适应在造模24 h和1 h前采用3个循环的大脑中动脉阻闭15 s/再通30 s的方法诱导，后适应于再灌注前采用3个循环的再灌注30 s/缺血15 s的方法诱导。造模后48 h，分别检测大鼠脑梗死体积，脑组织氧化应激指标及p-Akt与p-ERK1/2蛋白的表达。结果：预适应组与后适应组间脑梗死灶体积比较差异无统计学意义(P>0.05)，但均明显小于模型组，大于联合干预组(均P<0.01)。与假手术组比较，模型组出现脑组织氧化应激水平明显升高(SOD活性降低，MDA含量升高)，且脑组织p-Akt和p-ERK1/2表达上调(均P<0.01)。与模型组比较，预适应组脑组织氧化应激指标无明显差异(均P>0.05)，但p-Akt表达轻度上调、p-ERK1/2表达明显上调(P<0.05，P<0.01)，后适应组脑组织氧化应激水平明显降低(均P<0.01)，且p-Akt表达明显上调和p-ERK1/2表达轻度上调(P<0.01，P<0.05)。联合干预组脑组织氧化应激水平降低程度及p-Akt与p-ERK1/2表达上调程度均明显强于预适应组或后适应组(均P<0.01)。结论：预适应与后适应联合干预对脑缺I/R损伤的保护作用强于单独的预适应或后适应，可能与预适应与后适应的抗I/R损伤的机制不同且互补有关。

关键词： 脑缺血 再灌注损伤 缺血预处理 缺血后处理

Combined intervention of preconditioning and ostconditioning against cerebral ischemia/reperfusion injury

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Abstract:

Objective: To investigate the protective effect of combined ischemic preconditioning and postconditioning against cerebral ischemia/reperfusion (I/R) injury and the potential mechanism. Methods: Sixty SD rats were randomized into a sham operation group, a brain I/R group (model group), a brain I/R plus preconditioning group (preconditioning group), a brain I/R plus postconditioning group (postconditioning group), and a brain I/R plus preconditioning and postconditioning group (combined intervention group). The rat brain I/R injury model was createdby suture emboli method. Preconditioning was induced by 3 cycles of 15 s occlusion followed by 30 s recanalization of the middle cerebral artery twice respectively at 24 h and 1 h before model creation, and postconditioning was elicited by 3 cycles of 30 s reperfusion followed by 15 s ischemia
before long time reperfusion. The rats were sacrificed at 48 h after the reperfusion. The cerebral infarct volume and oxidative stress parameters as well as p-Akt and p-ERK1/2 protein expressions in the brain tissues were determined. Results: The cerebral infarct volumes showed no significant difference between the preconditioning
group and the postconditioning group (P>0.05), but both were smaller than that in the model group and larger than that in the combined intervention group (all P values<0.01). In the model group, the level of oxidative stress was markedly increased (SOD activity increased and MDA level decreased), and both p-Akt and p-ERK1/2 protein expressions in the brain tissues were upregulated compared with those in the sham group (all P<0.01). Compared with the model group, the oxidative stress parameters presented no evident difference in preconditioning group (P>0.05), but p-Akt expression was slightly upregulated and p-ERK1/2 was remarkably down-regulated (P<0.05 and P<0.01) In the postconditioning group, the level of oxidative stress was significantly decreased, and p-Akt expression was dramatically increased with a mild down-regulation of p-ERK1/2 expression (P<0.01 and P<0.05). In the combined intervention group, the oxidative stress decrease the p-Akt expression rise and p-ERK1/2 expression inhibition were significantly greater than those in either the preconditioning group or the postconditioning group (all P values<0.01). Conclusion: Combined treatment of preconditioning and postconditioning exerts stronger protective effect against cerebral I/R injury than either preconditioning or postconditioning alone.

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The mechanism is possibly due to the different but complementary protection of preconditioning and postconditioning against I/R injury.

Keywords: brain ischemia reperfusion injury ischemic preconditioning ischemic postconditioning

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