

## 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血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 postconditioning 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 created by 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

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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. 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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