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Effects of nimodipine on acute cerebral ischemia and reperfusion injury of rats

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KEY WORDS nimodipine; cerebral ischemia; cerebral cortex; hippocampus; electroencephalography

AIM: To study the effect of nimodipine (Nim) on ischemic cerebral damage. **METHODS**: The four-vessel occlusion method was performed on rats. Monoamines were measured by fluorospectrophotometry. **RESULTS**: Intraperitoneal injection of Nim 0.75 and 1.5 mg·kg^{-1} quickened the recovery of EEG changes to 19 ± 3 and 17 ± 4 min ($P < 0.01$), respectively. Nim reduced the decreases of monoamines (NE, DA, 5-HT, and 5-HIAA) contents after 30-min cerebral ischemia and 1-h reperfusion. **CONCLUSION**: Nim protects the brain from ischemic damage.

Monoamine neurotransmitters may exacerbate the brain ischemic injury, nimodipine (Nim) has the protective effect which was attributed extensively to its calcium antagonist and vasodilatatory action[1], whereas the possible role of Nim on monoamine contents was often neglected. In the present study we observed the effect of Nim on rat EEG and brain monoamine contents under cerebral ischemia.

MATERIALS AND METHODS

Nim was synthesized by Xinhua Pharmaceutical Factory, Shandong, China. Sprague-Dawley rats (♂, n = 24, weighing 240 ± s 39 g) were used. MPF-4 fluoroscence spectrophotometer was made by Hitachi Corp, Japan.

Assessments were carried out in 4 groups: A) sham operation; B) ischemia and reperfusion; C) ischemia and reperfusion with Nim 0.75 mg·kg^{-1}; D) ischemia and reperfusion with Nim 1.5 mg·kg^{-1}.

The four-vessel occlusion and EEG recording were made[2,3]. Before ligating bilateral common carotid arteries and at the beginning of reperfusion, the rats of C and D groups were injected intraperitoneally (ip) with Nim 0.375 and 0.75 mg·kg^{-1}, respectively.

The rats were decapitated after reperfusion. The cerebral cortex and hippocampus were stored in liquid nitrogen. Monoamines were measured by fluorospectrophotometry.

All data were expressed as $\bar{x} \pm s$ and analyzed by t-test.

RESULTS

EEG The arrest of the blood supply to the brain caused a rapid disappearance of EEG activity. During recirculation the recovery time for the ischemia group was 39 ± 4 min (n = 6), but the amplitude was still severely inhibited at the end of recirculation. In treated rats, ip Nim 0.75 and 1.5 mg·kg^{-1} remarkably quickened the recovery of EEG changes to 19 ± 3 min and 17 ± 4 min (n = 6, $P < 0.01$ *vs* the ischemic rats), respectively.

Monoamines Compared with the sham operation group, cortex, hippocampus NE, DA, 5-HT, and 5-HIAA of ischemia group all decreased significantly. With ip Nim 0.75 and 1.5 mg·kg^{-1} the contents of NE, DA, 5-HT, and 5-HIAA in cortex and hippocampus all increased (Tab 1).

Tab 1. Effects of nimodipine on cortical and hippocampal monoamine contents (ng/g wet tissue) at cerebral ischemia and reperfusion. n = 6 rats, $\bar{x} \pm s$.
$^cP < 0.01$ *vs* sham operation.
$^dP > 0.05$, $^eP < 0.05$, $^fP < 0.01$ *vs* ischemia.

	NE	DA	5-HT	5-HIAA
Cortex				
Sham operation	301 ± 15	419 ± 28	403 ± 14	315 ± 29
Ischemia	168 ± 25^c	363 ± 25^c	325 ± 30^c	242 ± 19^c
Nim 0.75 mg·kg^{-1}	287 ± 18^f	416 ± 28^f	357 ± 33^d	302 ± 22^e
Nim 1.5 mg·kg^{-1}	290 ± 12^f	423 ± 18^f	367 ± 21^e	322 ± 18^e
Hippocampus				
Sham operation	252 ± 29	345 ± 17	492 ± 18	418 ± 41
Ischemia	127 ± 24^c	273 ± 40^c	301 ± 33^c	320 ± 22^c
Nim 0.75 mg·kg^{-1}	244 ± 25^f	321 ± 24^e	382 ± 33^f	377 ± 28^f
Nim 1.5 mg·kg^{-1}	257 ± 26^f	343 ± 14^f	401 ± 33^f	409 ± 35^f

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DISCUSSION

In the attempt to evaluate the cortical activity the EEG was recorded during the whole experiment. We observed the EEG was severely inhibited after 30 min and/or 1 h of the four-vessel occlusion. Treatment with Nim withdrew the inhibition. The observation suggested that Nim ameliorated the activity of the ischemic neurons.

The metabolic disorder of brain monoamine neurotransmitters occured during brain ischemia[4], so we selected the change of monoamine neurotransmitters as another indicator to observe the effect of Nim on cerebral ischemia. The decreased level of monoamine neurotransmitters was found in our experiment. Nim may antagonize the decrease of monoamine neurotransmitters. This gave the fact that Nim had the benificial effects on global transient ischemic injuries.

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尼莫地平对大鼠急性脑缺血再灌注损伤的作用

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关键词 尼莫地平; 脑缺血; 大脑皮质; 海马; 脑电描记术 再灌注损伤

A 目的: 研究尼莫地平(Nim)对脑缺血损伤的作用. 方法: 大鼠脑缺血模型采用四血管结扎法(4-VO), 单胺递质测定采用荧光分光光度法 结果: 腹腔注射尼莫地平 0.75 mg·kg^{-1}和 1.5 mg·kg^{-1}能显著改善缺血再灌注损伤的脑电活动, 脑电恢复时间可恢复到 19 ± 3 min 和 17 ± 4 min ($P < 0.01$), 尼莫地平还能明显减轻缺血 30 min 后再灌注 1 h 的单胺递质的降低. 结论: Nim 对缺血引起损伤的神经有保护作用

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