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Abstract View

REPEATED DOSES OF MELATONIN PROTECTS AGAINST FOCAL CEREBRAL ISCHEMIA IN THE RAT.

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We studied the time window of neuroprotection against focal ischemia by a single dose or repeated doses of melatonin (MT) at 5 mg/kg. Adult male Sprague-Dawley rats (280 to 360 g) were anesthetized with sodium pentobarbital (60 mg/kg, I.P.) to undergo reversible right-sided endovascular middle cerebral artery occlusion (MCAO) for 3 hours. Arterial blood pressure, heart rate and cerebral blood flow were monitored, and rectal temperature was kept between 36.5 and 37.5 °C throughout anesthesia. The control rats received 1 I.P. dose of the vehicle at the onset of ischemia, whereas experimental groups of rats received either 1 I.P. dose of MT at 0 or 60 minutes after onset of ischemia or 3 doses of MT at 1, 24, and 48 hours after onset of ischemia. The rats were decapitated on day 3 of MCAO, and their brains were stained with 2% triphenyltetrazolium chloride for determination of infarction. Results were compared using 2-tailed student's t test. When compared to the relative infarct volume of 27.0±4.6% (mean±SEM; 7 rats) in the control group, a single (5 mg/kg) I.P. dose of MT did not significantly reduce the relative infarct volume (20.1±4.1% in the 0-minute group [8 rats]; 19.8±3.2% in the 60-minute group [9 rats]). Nevertheless, the relative infarct volume was significantly reduced to 13.9±3.4% (8 rats, $P < 0.05$) in the group which received 3 doses of MT. There was no significant difference in hemodynamic parameters among the groups. Thus, repeated doses rather than a single dose of exogenous MT protects against focal cerebral ischemia, when given 60 minutes after onset of ischemia.

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