Melatonin attenuates hippocampal neuron apoptosis and oxidative stress during chronic intermittent hypoxia via up-regulating B-cell lymphoma-2 and down-regulating B-cell lymphoma-2-associated X protein

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ABSTRACT

Objective: To investigate the neuroprotective effect of melatonin against chronic intermittent hypoxia (CIH), the major pathophysiologic features of obstructive sleep apnea syndrome.

Methods: This study was conducted between January 2011 and September 2012 in Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China. Thirty 8-week Wistar rats were randomly divided into 3 groups (10 each): a control group, a vehicle-treated CIH group; and a melatonin-treated (10 mg/kg) CIH group. Rats were exposed to either intermittent hypoxia (IH) (oxygen concentration changing periodically from 21.78±0.65 to 6.57±0.57%), or air-air cycling at a rate of 30 cycles/hour, 8 hour/day for 4 weeks.

Results: The CIH exposure led to a significant decrease in superoxide dismutase (SOD) activity and anti-apoptotic protein B-cell lymphoma-2 (BCL-2) expression in the hippocampus of CIH group rats compared with that of the control group and melatonin-treated CIH group. In contrast, hippocampal neuronal apoptosis increased significantly in parallel to an augment in 3,4-methylenedioxymphetamine (MDA) content and pro-apoptotic protein Bcl-2-associated X protein (BAX) expression in CIH group than the other 2 groups. Melatonin administration abrogated the increase in MDA activity, as well as BAX expression, and restored SOD activity and BCL-2 expression to nearly their normal levels.

Conclusion: These results indicate melatonin can inhibit hippocampal neuron apoptosis following CIH by scavenging reactive oxygen species, up-regulating anti-apoptotic protein BCL-2 and down-regulating pro-apoptotic protein BAX, and thus, alleviate CIH-induced oxidative stress injury and produce neuroprotection effects.


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