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Enhanced Electrical Responsiveness in the Cerebral Cortex With Oral Melatonin Administration After a Small Hemorrhage Near the Internal Capsule in Rats

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Introduction

Intracerebral hemorrhage (ICH) can cause direct brain injury at the insult site and indirect damage in remote brain areas. Although a protective effect of melatonin (ML) has been reported for ICH, its detailed mechanisms and effects on remote brain injury remain unclear.

Method

To clarify the mechanism of indirect neuroprotection after ICH, we first investigated whether ML improved motor function after ICH and then examined the underlying mechanisms. The ICH model rat was made by collagenase injection into the left globus pallidus, adjacent to the internal capsule. ML was orally administrated (15 mg/kg) for 7 days after ICH.

Result

ML treatment resulted in significant recovery of motor function after ICH. Retrograde labeling of the corticospinal tract by Fluoro-Gold revealed a significant increase in numbers of positive neurons in the cerebral cortex. Immunohistological analysis showed that ML treatment induced no difference in OX41-positive activated microglia/macrophage at day 1 (D1) but a significant reduction in 8-hydroxydeoxyguanosin-positive cells at D7. Neutral red assay revealed that ML significantly prevented H2O2-induced cell death in cultured oligodendrocytes and astrocytes but not in neurons. Electrophysiological response in the cerebral cortex area where the number of Fluoro-Gold-positive cells was increased was significantly improved in ML-treated rats.

Conclusion

These data suggest that ML improves motor abilities after ICH by protecting oligodendrocytes and astrocytes in the vicinity of the lesion in the corticospinal tract from oxidative stress and causes enhanced electrical responsiveness in the cerebral cortex remote to the ICH pathology.