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Melatonin protects against neurobehavioral and mitochondrial deficits in a chronic mouse model of Parkinson's disease

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Abstract

Neuronal oxidative stress and mitochondrial dysfunction have been implicated in Parkinson's disease. Melatonin is a natural antioxidant and free radical scavenger that has been shown to effectively reduce cellular oxidative stress and protect mitochondrial functions in vitro. However, whether melatonin is capable of slowing down the neurodegenerative process in animal models of Parkinson's disease remains controversial. In this research, we examined long-term melatonin treatment on striatal mitochondrial and dopaminergic functions and on animal locomotor performance in a chronic mouse model of Parkinson's disease originally established in our laboratory by gradually treating C57BL/6 mice with 10 doses of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (15 mg/kg, s.c.) and probenecid (250 mg/kg, i.p.) over five weeks. We report here that when the chronic Parkinsonian mice were pre-treated and continuously treated with melatonin (5 mg/kg/day, i.p.) for 18 weeks, the defects of mitochondrial respiration, ATP and antioxidant enzyme levels detected in the striatum of chronic Parkinson's mice were fully preempted. Meanwhile, the striatal dopaminergic and locomotor deficits seen in the chronic Parkinson's mice were partially and significantly forestalled. These results imply that long-term melatonin is not only mitochondrial protective but also moderately neuronal protective in the chronic Parkinson's mice. Melatonin may potentially be effective for slowing down the progression of idiopathic Parkinson's disease and for reducing oxidative stress and respiratory chain inhibition in other mitochondrial disorders.

Highlights

▸ The chronic Parkinson's mice show neurobehavioral and mitochondrial deficits. ▸ Chronic melatonin treatment fully protects against mitochondrial dysfunction. ▸ Chronic melatonin also moderately prevents neurobehavioral deficits. ▸ Melatonin slows down the progression of Parkinson's like disorder in mice.

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Keywords

Parkinson's disease; Chronic MPTP/probenecid model; Neurodegeneration; Neuroprotection; Mitochondrial dysfunction

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