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9-Methyl-β-carboline has restorative effects in an animal model of Parkinson's disease

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Abstract:
In a previous study, a primary culture of midbrain cells was exposed to 9-methyl-β-carboline for 48 h, which caused an increase in the number of tyrosine hydroxylase-positive cells. Quantitative RT-PCR revealed increased transcription of genes participating in the maturation of dopaminergic neurons. These *in vitro* findings prompted us to investigate the restorative actions of 9-methyl-β-carboline *in vivo*. The compound was delivered for 14 days into the left cerebral ventricle of rats pretreated with the neurotoxin 1-methyl-4-phenyl-pyridinium ion (MPP^+) for 28 days applying a dose which lowered dopamine by approximately 50%. Interestingly, 9-methyl-β-carboline reversed the dopamine-lowering effect of the neurotoxin in the left striatum. Stereological counts of tyrosine hydroxylase-immunoreactive cells in the substantia nigra revealed that the neurotoxin caused a decrease in the number of those cells. However, when treated subsequently with 9-methyl-β-carboline, the number reached normal values. In search of an explanation for the restorative activity, we analyzed the complexes that compose the respiratory chain in striatal mitochondria by 2-dimension gel electrophoresis followed by MALDI-TOF peptide mass fingerprinting. We found no changes in the overall composition of the complexes. However, the activity of complex I was increased by approximately 80% in mitochondria from rats treated with MPP^+ and 9-methyl-β-carboline compared to MPP^+ and saline and to sham-operated rats, as determined by measurements of nicotinamide adenine dinucleotide dehydrogenase activity. Microarray technology and single RT-PCR revealed the induction of neurotrophins: brain-derived neurotrophic factor, conserved dopamine neurotrophic factor, cerebellin 1 precursor protein, and ciliary neurotrophic factor. Selected western blots yielded consistent results. The findings demonstrate restorative effects of 9-methyl-β-carboline in an animal model of Parkinson's disease that improve the effectiveness of the respiratory chain and promote the transcription and expression of neurotrophin-related genes.

Key words:
neuronal regeneration, neurotrophins, respiratory chain, dopamine, Parkinson's disease, rat