REPORT

Neurochemical changes in the pedunculopontine nucleus of hemiparkinsonian rats and effect of different treatments

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ABSTRACT

The present work focuses on the physiopathology of Parkinson's disease (PD), analyzing the alterations in neurotransmitter profile of the basal ganglia triggered by the degeneration of cells from the substantia nigra compacta (SNpc). For this purpose, the neurochemical, morphological and molecular changes of the pedunculopontine nucleus (PPN) of rats upon the induction of hemiparkinsonism were evaluated with surgical, immunochemical and molecular biology techniques together with cerebral microdialysis and behavioral tests, also examining the effect of systemic treatments with MK-801 or (-) nicotine or the results of subthalamic injury on these changes. The results evidenced an increase in the extracellular concentration (EC) of glutamate (Glu) ($p < 0.001$) and GABA ($p < 0.001$) as well as a higher density of muscarinic receptors, together with a statistically significant decrease in the density of BDZ gabaergic receptors ($p < 0.001$) and mu opioid receptors ($p < 0.01$) in the PPN of hemiparkinsonian rats. Our results also constitute the first published description of cell death in the PPN of hemiparkinsonian rats. All the treatments achieved a statistically significant decrease in the Glu ($p < 0.01$) and GABA ($p < 0.001$) EC in the PPN, with a neuroprotective effect on the dopaminergic cells of the ventral tegmental area and the SNpc itself. The administration of (-) nicotine improved the striatal expression of brain-derived neurotrophic factor ($p < 0.01$). We conclude that the PPN of hemiparkinsonian rats displays neurochemical changes which can be modified and/or reverted by the treatments described in this work. Our results had the added benefit of requiring the local manufacture of cerebral microdialysis cannulae, resulting in significant cost savings.

Keywords: pedunculopontine nucleus, dopamine, nicotine, MK-801

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