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Neuroplasticity in the nigrostriatal system of MPTP-treated mice at presymptomatic and early symptomatic stages of Parkinsonism

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Parkinson's disease (PD) is characterized by a long development at preclinical (asymptomatic) stage and the first appearance of motor dysfunctions at a loss of most dopaminergic (DA-ergic) neurons, nigral cell bodies and striatal axons, and a depletion of 60-70% DA in the striatum. The goal of this study was to search mechanisms of neuroplasticity serving to prevent motor dysfunctions at presymptomatic stage and the triggers of a transition to symptomatic stage evaluating DA synthesis (tyrosine hydroxylase (TH) mRNA, protein, activity), release (microdialysis in vivo, slices), uptake (slices), degradation (MAO mRNA, activity) at original models. At presymptomatic stage motor dysfunctions were prevented due to plasticity of survived DA-ergic neurons that was manifested by enhanced TH activity, increased spontaneous and stimulated release of DA, and decreased MAO B activity. Noteworthy, striatal DA was synthesized not only in DA-ergic axons but also in non-dopaminergic neurons containing individual enzymes, TH or aromatic L-amino acid decarboxylase, in cooperation. At symptomatic stage, despite maintaining of DA synthesis in DA-ergic neurons at the control level and an increase of DA synthesis in monoenzymatic neurons, intercellular level of DA dropped up followed by an appearance of motor disorders. Major triggers of motor dysfunctions appeared to be a decrease of spontaneous and stimulated release of striatal DA and an increase of MAO A activity. PD models of preclinical and early clinical stages, specified in this study are suitable for development of preventive pharmacotherapy serving to improve compensatory processes and inhibit triggers of motor dysfunctions.

Biography

Michael Ugrumov, academician of Russian Academy of Sciences has completed his MD at Institute of Evolutionary Physiology & Biochemistry (Leningrad), PhD at Institute of Developmental Biology, Professorship at University Medical School (Moscow). Head of Laboratory of Neural and Neuroendocrine Regulations at Institute of Developmental Biology RAS, Vice-President of Russian Physiological Society. Member of European Academy of Science and Arts, Serbian Academy of Science and Arts, French National Academy of Pharmacy. He has published more than 200 papers in peer reviewed journals and served as an editorial board member of 8 International and Russian journals.

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