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Advanced approaches to the development of preclinical diagnosis of Parkinson's disease

The low efficiency of current symptomatic therapy of Parkinson's disease (PD) is explained by the late diagnosis and the onset of treatment of the disease. However, attempts to develop a preclinical diagnosis of PD, mainly by searching for biomarkers such as changes in biological fluids and non-motor functions, did not lead to the development of a technology recommended for clinical use. A drawback of this methodology is searching biomarkers in patients at the clinical stage, although there is no guarantee that they are characteristic for preclinical stage. Indeed, all biomarkers identified so far are nonspecific. We upgraded this methodology, considering as preclinical biomarkers only those changes in body fluids, which are found both in untreated patients and in animal models of clinical (symptomatic) and preclinical (presymptomatic) stages of PD. We believe that detection of the same biomarker in patients and symptomatic animals indicates an adequate reproduction of pathogenesis along this metabolic pathway, and its detection in presymptomatic animals suggests its specificity for preclinical stage. We showed that only a small part of the changes found in blood and tears in PD patients are characteristic of symptomatic and presymptomatic MPTP-treated mice, and they can serve as preclinical diagnostic biomarkers. In addition, we developed a fundamentally new approach to the early diagnosis of PD, a provocative test, by treating presymptomatic mice with α-methyl-p-tyrosine, a reversible inhibitor of dopamine synthesis. Systemic administration of this inhibitor in a preselected dose leads to a reversible decrease in dopamine level in the striatum up to the threshold (30%), resulting in short-term motor disorders. In control, although the dopamine level decreases under α-methyl-p-tyrosine administration, it does not reach the threshold level and does not cause motor disorders. Thus, we have proposed a new methodology for the development of preclinical diagnosis of PD.

Biography

Michael Ugrumov, MD, PhD, Head of Laboratory of Neural and Neuroendocrine Regulations at the Institute of Developmental Biology of Russian Academy of Sciences (RAS), Professor of Department of Psychology at the National Research University "Higher School of Economics" (Moscow), Vice-President of the Russian Society for Physiology, President of the Russian Society for Neurochemistry. Ugrumov is a member of the Russian Academy of Sciences, European Academy of Science and Arts, Serbian Academy of Sciences and Arts, French National Academy of Pharmacy and was nominated as a visiting Professor at Tokushima University Medical School (Japan), SUNY Upstate Medical University (Syracuse, USA), University P. Et M. Curie (Paris, France), University Medical School of Ulm (Germany). Ugrumov was awarded the prize of the American society of Experimental Biologists, the Order of merit for France, the Orbeli Prize and Sechenov Prize of the Russian Academy of Sciences.

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