ABSTRACT FOR THE GENERAL PUBLIC

Spatial analysis of the effects of L-DOPA on gene expression in the prefrontal cortex in a mouse model of Parkinson's disease

Anna Aleksandra Radlicka, Department of Molecular Neuropharmacology,
Maj Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

Parkinson's disease (PD) is the world's second most common neurodegenerative disease, and is associated with progressive loss of dopaminergic neurons in the midbrain. PD also affects other structures of the nervous system, which in turn leads to the development of motor and non-motor symptoms. The clinical diagnosis of PD is mainly based on motor impairment (muscle rigidity, resting tremor, bradykinesia), while the non-motor features are already present in the earlier phases of the disease and have a significant impact on the patients' quality of life. The non-motor symptoms include sleep and mood disruptions, smell loss, gastrointestinal conditions, hallucinations, dementia and cognitive dysfunction. Treatment of PD largely relies on drugs acting on the dopamine system, such as L-DOPA, a dopamine precursor, which is one of the most commonly used anti-parkinsonian medications. While L-DOPA alleviates the motor manifestations, studies demonstrate its mixed effects on the cognitive impairment, with some domains improved and others worsened.

About 30% patients with PD are diagnosed with dementia, and further 26% of non-demented individuals suffer from mild cognitive impairment. PD-linked cognitive dysfunction affects different functions, such as memory, attentional and executive processes. Many studies implicate a crucial role of the brain prefrontal cortex (PFC). They largely build upon neuroimaging techniques, while data on cellular or molecular processes underlying cognitive dysfunction in PD are relatively scarce. Scientific papers that describe gene expression changes in the PFC mostly analyze human tissue of treated PD patients and healthy controls, so separation of effects of the disease and the treatment is impossible. Moreover, the previously used methods did not allow a spatial analysis of gene expression in different anatomical and functional domains of the tissue.

The main goal of this project is a high-resolution analysis of spatial gene expression changes in the PFC in two groups of mice with progressive loss of dopaminergic neurons: mice treated with L-DOPA and mice treated with saline. We expect L-DOPA differentially affects distinct areas of the PFC in a mouse model of PD, what we shall observe as gene expression changes in specific anatomical areas such as cortex layers. Then, lists of differentially expressed genes will be used to explore cellular pathways and biological processes in which their products partake.

This project will explore a detailed impact of L-DOPA on the PFC on the molecular level in PD. The expected results may contribute to a better understanding of mechanisms related both to PD and the action of L-DOPA in respect to PD-linked cognitive impairment.