Biological roles of transcriptional networks activated in the brain by psychotropic drugs

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The adaptivity of human behavior is conditioned by the plasticity of the brain. It is assumed that the etiopathogenesis of psychiatric disorders is related to the development of maladaptive neuroplastic alterations. Psychotropic drugs have a unique ability to initiate processes that reverse pathological changes and stimulate therapeutic effects. Therefore, it is critically important to understand the biological basis of the effects of psychoactive compounds at the molecular level. The ongoing tasks are to identify factors and processes involved in the control of drug-induced brain plasticity.

Our previous research revealed the three main gene expression patterns regulated in response to treatment with psychotropic drugs (including antidepressants, antipsychotics and psychostimulants). Based on the published results we predicted that expression of the gene networks is connected to different types of neural cells and distinct functional profiles. However, further investigation of the biological significance of the harmonized expression of relatively large groups of genes has been limited.

The project plan includes the use of publicly available human genetic resources and a database of phenotypic information (both, deposited in the UK Biobank) to determine the biological significance of the observed changes in gene expression. As part of the planned work, we will search for the associations of polymorphisms that occurred in drug-regulated genes with the physiological, biochemical, and clinical parameters. The use of population data and whole-genome sequencing technology will provide novel interpretations for the results of transcriptomic studies. The next stage of research will include the use of a variety of bioinformatics tools and methods to determine the mechanisms of transcriptional regulations and to assign the observed alterations into specific populations of brain cells. The end goal of this project is to identify molecular switches that trigger a cascade of neuroplasticity-related processes.

Understanding the mechanisms of regulation of neuroplasticity would be used at the early stages of screening and development of prototype psychotropic drugs.