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Effect of GDNF on depressive-like behavior, spatial learning and key genes of the brain dopamine system in genetically predisposed to behavioral disorders mouse strains

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The effect of Glial Cell Line-Derived Neurotrophic Factor (GDNF) on behavior and brain dopamine system in predisposed to depressive-like behavior ASC (Antidepressant Sensitive Cataleptics) mice in comparison with the parental "nondepressive" CBA mice was studied. In seven days after administration (800 ng, i.c.v.) GDNF decreased escape latency time and the path traveled to reach hidden platform in Morris water maze in ASC mice. GDNF enhanced depressive-like traits in both "nondepressive" CBA and "depressive" ASC mice. In CBA mice, GDNF decreased functional response to agonists of D1 (Chloro-APB hydrobromide) and D2 (Sumanirole maleate) receptors in tail suspension test, reduced D2 receptor gene expression in the substantianigra and increased Monoamine Oxidase A (MAO A) gene expression in the striatum. GDNF increased D1 and D2 receptor genes expression in the nucleus accumbens of ASC mice, but failed to alter expression of catechol-O-methyltransferase, dopamine transporter, MAO B and tyrosine hydroxylase genes in both investigated mouse strains. Thus, GDNF produced long-term genotype-dependent effect on behavior and the brain dopamine system. GDNF pretreatment 1) reduced D1 and D2 receptors functional responses and D2 receptor gene expression in s. nigra of CBA mice; 2) increased D1 and D2 receptor genes expression in n. accumbens of ASC mice and 3) improved spatial learning in ASC mice. GDNF enhanced depressive-like behavior both in CBA and ASC mice. The data suggest that genetically defined variance in the cross-talk between GDNF and brain dopamine system contributes to the variability of GDNF-induced responses and might be responsible for controversial GDNF effects.

Biography

Naumenko became head of the department of Behavioral Neurogenomics at the Institute of Cytology and Genetics in 2014 followed by defense of doctoral (Dr.Sc.) thesis in physiology in 2012. He has completed his PhD in physiology at the Institute of Cytology and Genetics in 2006 after he graduated from Novosibirsk State University as molecular biologist in 2005. He joined the department of Behavioral Neurogenomics while he was a student in 2002 and began to study the role of different types of serotonin receptors in the regulation of genetically determined defensive behavior in animal models. Now he studies the molecular mechanisms of serotonin receptor interaction and their role in the mechanisms of aggressive behavior and depression. Naumenko is also studying the cross-talk between neurotrophic factors and brain neurotransmitters in the regulation of different kinds of behavior.

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