

Interactions between GS and GI protein-coupled receptors and their potential role in pathophysiology and treatment of brain disorders

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It was reported that G_{as} -coupled dopamine receptor D_1 and adenosine receptor A_{2A} form dimers with G_{ai} -coupled adenosine receptor A_1 and dopamine receptor D_2 , respectively. Similar dimer is formed by D_1 and D_2 receptors. Since these dimers are G_{aq} -coupled, the dimerization might have strong functional output. G_{as} and G_{ai} receptors play an important role in regulation of serotonin, norepinephrine and dopamine transmission. Since monoamines play an important role in pathophysiology of brain disorders, interactions between G_{as} and G_{ai} -coupled receptors might be a target for CNS drugs. Indeed, co-activation of D_1 and D_2 receptors stimulates neuronal activity in piriform cortex and suppresses hippocampal synaptic plasticity, social interactions and working memory in rats. It suggests that interactions between D_1 and D_2 receptors play a role in age, memory and cognitive disorders. Activation of A_{2A} receptors inhibits the firing activity of NE and DA neurons in locus coeruleus and ventral tegmental area, respectively. This inhibition reversed by subsequent blocking of A_{2A} receptors and restored by administration of agonists of D_2 or α_2 -adrenoceptors. Antagonists of A_{2A} receptors potentiate stimulatory effect of haloperidol on extracellular levels of NE and DA in prefrontal cortex and nucleus accumbens, respectively, and reduce haloperidol-induced catalepsy in rats. It suggests potential role of A_{2A}/D_2 and α_2 -adrenoceptor interactions in schizophrenia. In conclusion, recent observations suggest that molecular and functional interactions between G_{as} and G_{ai} -coupled receptors might be a common pattern playing an important role in pathophysiology and treatment of various CNS disorders.

Biography

Dr Dremencov completed his BSc in Biology (1996) and MMedSc (2000) in Neurobiology in Hebrew University of Jerusalem. Performed PhD studies in Bar-Ilan University (2005, Israel) and Postdoctoral fellowship in the University of Ottawa, Canada (2007). Senior scientist in Brains On-Line BV, BMC Netherlands, and University of Groningen, the Netherlands (since 2008). Member of the International College of Neuropsychopharmacology (ICNP) and laureate of ICNP Rafaelson Prize (2006) and Honorary Mention (2008). Member of European College of Neuro-psychopharmacology (ECNP) and winner of ECNP (2008) and Society of Biological Psychiatry (2007) Fellowship Awards. Author of two books, six book chapters, and thirty-three (33) peer-reviewed manuscripts and more than fifty (50) congress presentations.

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