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Serotonin receptors interactions in the regulation of behavior and central nervous system functioning

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Motivation and Aim: Brain serotonin (5-HT) is a principal player in the mechanisms of brain and behavioral plasticity. This neurotransmitter plays an important role in the regulation of multiple physiological functions and types of behavior. Polyfunctionality of the brain 5-HT is due to a large variety of the receptors mediating 5-HT action on neurons. Currently, 14 different subtypes of 5-HT receptors are known in 5-HT receptor superfamily. With exception of the 5-HT_3 receptor, that is ligand-gated ion channel, all other 5-HT receptors belong to the G-protein coupled receptor family [1]. Considerable structure-specific differences in the density as well as in physiological effects of 5-HT receptors was shown [1, 2]. The recent data indicate that all receptor types have multiple signaling cascades and some of the receptors could couple with more than one G-protein. Additionally, some of receptors could form hererodimers with other brain receptors and proteins that significantly affect central nervous system functioning. Such interplay between different kinds of 5-HT receptors multiplies functional effects of 5-HT system [3–6].
Methods and Algorithms: Our studies showed that heterodimeric complexes could be formed both by different receptors of the same brain system and by receptors of different brain systems even if receptors belong to different superfamilies. Thus, the ability to form heterodimers was shown for 5-HT1A and 5-HT7 receptors from the serotonin G-protein-coupled receptors family as well as for serotonin G-protein-coupled receptor 5-HT2A and brain-derived neurotrophic factor TrkB receptor, belonging to the family of receptors with enzymatic activity. It was demonstrated that formation of heterodimeric complexes significantly affects the function of at least one of composing receptors that sometimes has an impressive behavioral effects. Additionally, it was revealed that serotonin G-protein-coupled 5-HT4 receptor is able to form heterodimers with molecule of cell adhesion L1. This interaction significantly affects neuronal architecture.
Conclusion: Growing body of evidence indicate that receptors heterodimerization is an additional factor in the regulation of the functional activity of the brain neurotransmitter and neurotrophic systems and, hence, behavior. The obtained data draw attention to receptor complexes as new targets for pharmacological correction of behavioral pathologies.
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