

Participation of pre- and postsynaptic of 5-HT_{1A} receptors in mood regulation (modulation of depressive like behaviours)

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Serotonin (5-HT) is a monoamine neurotransmitter that plays an important role in physiological functions as sleep, feeding, sexual behaviour, temperature regulation, pain, and cognition as well as in pathological states including mood and anxiety disorders, psychosis and pain. The seven 5-HT receptor classes consist of 5-HT₁, 5-HT₂, 5-HT₃, 5-HT₄, 5-HT₅, 5-HT₆, 5-HT₇, which are further subdivided into 14 receptor subfamilies. All of these receptors - except for 5-HT₃ receptor which belongs to the family of ionic channels - belong to superfamily of seven-transmembrane-domain, G protein-coupled receptors (GPCRs). For serotonin GPCRs three main types of primary coupling to G proteins have been described. The 5-HT_{1A} receptors activates G_i/G_o proteins, the 5-HT_{2A} receptors activate G_q/G₁₁, and the 5-HT₄, 5-HT₆ and 5-HT₇ activate G_s. The 5-HT_{1A} receptor is found in presynaptic as well as in postsynaptic part of the serotonergic tract. Presynaptically, the receptor is the major somatodendritic autoreceptor on the soma and dendrites of serotonergic neurons where it acts as a "brake" to inhibit the activity of the entire 5-HT system and is thought to delay antidepressant response. The 5-HT_{1A} heteroreceptors are located on non-serotonergic neurons, primarily in the limbic areas, such as on the dendrites and soma of glutamatergic pyramidal neurons, and axon terminals of GABAergic and cholinergic neurons. It is supposed that autoreceptors impact the establishment of anxiety-like behavior and heteroreceptors affect behavior in the forced swim test, a depression-related test. Selective inactivation of presynaptic receptors results in antidepressant-like effects in rodents. Increased transcription of 5-HT_{1A} autoreceptor associates with depression and resistance to chronic SSRI treatment. Increases postsynaptic signaling (SSRI, TCA, Li, valproate, electroconvulsion). Chronic treatment with SSRI desensitizes presynaptic receptors. However, according to clinical data full 5-HT_{1A} blockade neither enhances nor cancels the antidepressant effect of fluoxetine in MDD patients. Suggesting the involvement of other 5-HT receptors (e.g., 5-HT₄ receptor).

In the present paper the influence of the 5-HT_{1A} receptor ligands on the biochemical pathways and the implication on depressive like behaviour will be discussed.

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