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Poster Presentation Review

Are Depression and Anxiety Affected by Adenosine A_{2A} Receptors?

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Abstract

Adenosine acts as neuromodulator in the brain, which its involvement in a wide range of brain processes and diseases has been studied, such as epilepsy, sleep, anxiety, panic disorder, Alzheimer's disease, Parkinson's disease and schizophrenia. Adenosine receptors have been detected: A_1R, A_2AR ($A_{2A}R$), $A_{2B}R$, and A_3R. A_1R and A_2R inhibit cAMP production, while $A_{2A}R$ and $A_{2B}R$ stimulate cAMP production. These receptors are distributed in various areas of the central nervous system. $A_{2A}R$ is highly expressed in the olfactory bulb, caudate putamen, nucleus accumbens, and tuberculum olfactorium. The function of several receptors such as dopamine D2 receptor (D2R) is influenced by activation of adenosine A_2A receptor. Three distinct dopamine projection pathways are formed from the substantia nigra–ventral tegmental area complex. Mesocortical pathway and mesolimbic pathway are known as first and second pathways. Axons project to the striatum, described nigrostriatal pathway known as third pathway. This pathway completes the neural circuits of the basal ganglia responsible for motor control, although recent document also points to a very important role in the motor changes associated with severe depression. Adenosine A_2A receptor and D_2R are co-localized in the dorsal and ventral striatum and are mutual inhibitors. On one hand, $A_{2A}R$–D2R heteromers are formed and, when the $A_{2A}R$ is activated, conformational changes are transferred to the D2R. This ultimate to a reduction in D2R recognition and signaling; on the other hand, D2R activation inhibits cAMP mediated-effects of $A_{2A}R$ by inhibiting adenylyl-cyclase. Finally, recant study showed that $A_{2A}R$ overexpression is associated with depression, which may describe the depressive signs seen in aging, chronic stress, and Alzheimer's disease. We hypothesized that changes in expression of $A_{2A}R$ in nigrostriatal system may contribute in creation of depression with motor disorders.

Key words: Depression, Anxiety, Mesocortical Pathway, Mesolimbic Pathway, A_{2A} Receptors.

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