ACUTE AND CHRONIC FLUOXETINE TREATMENTS ALTER NUCLEOTIDE HYDROLYSIS IN RAT BRAIN SYNAPTOSOMES

Zimmermann, F.F. [1], Pedrazza, E.L.[1], Pedrazza, L.[1], Senger, M.R.[2], Sarkis, J.J.F.[2], Bonan, C.D.[1]

[1]Laboratório de Neuroquímica e Psicofarmacologia, Faculdade de Biociências, PUCRS. [2]Depto. Bioquímica, ICBS, UFRGS.

Depressive disorders are chronic conditions that produce emotional and physical symptoms. Evidence indicates abnormalities of the neurotransmitters norepinephrine and serotonin in depression. Hippocampal serotonergic neurotransmission is modulated by adenosine. Adenosine, an important neuromodulator, can exert antidepressant effects by interaction with A_1 and A_{2A} receptors. Adenosine can be release by nucleoside transporter or produced by action of ecto-nucleotidases, which includes NTPDase and 5´-nucleotidase. Here we evaluated the effects of acute and chronic treatments of fluoxetine, a selective serotonin reuptake inhibitor, on ecto-nucleotidases from hippocampal and cerebral cortical synaptosomes of rats. After acute exposure (1 hour; 10mg/Kg, i.p.), fluoxetine did not alter ATP, ADP and AMP hydrolysis in cerebral cortex and hippocampus of rats. However, fluoxetine promoted a significant decrease of ATP hydrolysis (26%; 102.5±12.5 nmolPi/min/mg) and an increase of ADP (63%; 121.4±11.4 nmolPi/min/mg) and AMP hydrolysis (45%; 29.6±2.6 nmolPi/min/mg) in cortex after chronic treatment (14 days; 10mg/kg i.p.) when compared to control (138.4±5.4; 74.3± 7.9; 20.3±1.6 nmolPi/min/mg for ATP, ADP and AMP hydrolysis, respectively). Furthermore, this treatment did not alter the nucleotide hydrolysis in rat hippocampus. Altogether, this study has shown that both fluoxetine treatments may contribute differently for the regulation of extracellular nucleotide levels, modulating ecto-nucleotidase pathway.

Support: CNPq, CAPES, BPA/PUCRS.

Keywords: depression, adenosine, ecto-nucleotidases, fluoxetine.