ANTIDEPRESSANT-LIKE EFFECTS OF GUANOSINE, KETAMINE AND FLUOXETINE IN THE CHRONIC UNPREDICTABLE STRESS: A COMPARATIVE STUDY

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Many pre-clinical studies use animal models based on stress exposition to investigate new putative antidepressants. Since the delay in the onset of action may be a serious issue in cases of increased risk of suicide, there is a demand for fast-acting antidepressants. In this context, guanosine, a purinergic nucleoside that presents modulatory effects on glutamatergic transmission as well as neurotrophic activity, may be a valuable target for investigation. Therefore, in the present study, a comparative analysis of the antidepressant-like effects of guanosine, ketamine and fluoxetine was conducted in an animal model of depression. The experiments were performed after approval of the protocol by the Ethics Committee of the Institution. The chronic unpredictable stress (CUS) protocol (14 days) was conducted in female Swiss mice and a single dose of guanosine (5 mg/kg, p.o.), ketamine (1 mg/kg, i.p.) or fluoxetine (10 mg/kg, p.o.) was administered 1 h or 24 h before mice were subjected to the tail suspension test (TST) and open-field test. In addition, mice hippocampi were used in order to evaluate pro and mature brain-derived neurotrophic factor (BDNF) immunoreactivity by Western Blot. CUS exposure caused a depressive-like behavior evidenced by the increased immobility time in the tail suspension test. All the administrations performed 1 h before the tests were able to abolish CUS-induced behavioral alterations in the TST. However, in the cohort of mice treated 24 h before the behavioral tests, ketamine or guanosine administrations, but not fluoxetine, abolished CUS-induced increase in the immobility time in the TST. None of the procedures caused changes in locomotor activity. Moreover, no alteration in pro-BDNF/total-BDNF ratio was observed. Taken together, our findings suggest that guanosine may exert an antidepressant-like effect that differs from the conventional drugs possibly by sharing similarities with the effects elicited by ketamine.

**Keywords:** antidepressant; guanosine; ketamine

**References:** 1. BETTIO LE, FREITAS AE, NEIS VB, SANTOS DB, RIBEIRO CM, ROSA PB, FARINA M, RODRIGUES AL. Guanosine prevents behavioral alterations in the forced swimming test and hippocampal oxidative damage induced by acute restraint stress. Pharmacol Biochem Behav, (127) 7-14, 2014.

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