CHRONIC GUANOSINE ADMINISTRATION CAUSES ANTIDEPRESSANT-LIKE ACTIVITY ASSOCIATED WITH AN INCREASED NEURONAL DIFFERENTIATION IN VENTRAL HIPPOCAMPUS

Ostermann P, Bettio LE, Neis VB, Brocardo PS, Patten AR, Gil-Mohapel J, Christie BR, Rodrigues ALS

Guanosine is a purine nucleoside that occurs naturally in the central nervous system (CNS). Following injury, guanosine is released from astrocytes in high concentrations. The proliferative effects of this nucleoside have been shown in both neural and glial populations and it seems to have a role in regenerative processes of the CNS. In addition, guanosine may also have neuritogenic effects in many cell types including hippocampal neurons. Given its known protective properties, the potential of guanosine as an antidepressant has been recently tested. Within this context, the present study sought to investigate the effects of chronic treatment with guanosine on the development of depressive-like behaviors in the tail suspension test (TST) and on adult hippocampal neurogenesis. Mice were administered guanosine for 21 days (5 mg/kg/day, p.o.) and subsequently submitted to the TST and open-field test. Following behavioral testing, animals were transcardially perfused and the brains were processed for immunohistochemical analysis of hippocampal cell proliferation and neuronal differentiation. Animals treated with guanosine showed a reduction in immobility time in the TST without alterations in locomotor activity, confirming the antidepressant-like effect of this compound. Quantitative microscopic analysis did not reveal significant alterations in the numbers of Ki-67- and proliferating cell nuclear antigen (PCNA)-positive cells in the hippocampal dentate gyrus of guanosine-treated mice. However, guanosine treatment resulted in a significant increase in the number of immature neurons, as assessed by immunohistochemistry for neurogenic differentiation protein (NeuroD). Interestingly, this effect is localized in the ventral hippocampus, a functionally distinct region of this structure known to regulate emotional and
motivational behaviors. Taken together, our results suggest that the antidepressant-like effects of chronic guanosine treatment may be associated, at least in part, with an increase in neuronal differentiation in the ventral hippocampus. Future research will elucidate whether guanosine treatment can have similar effects following injury.

**Keywords:** antidepressant; guanosine; hippocampus