

Guanosine Enhances Glutamate Uptake and Utilization in Hippocampal Slices Under High Glutamate Levels

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INTRODUCTION: The glutamatergic excitotoxicity is involved in various pathological processes in the brain. In this context, astrocytes play an important role in glutamatergic system metabolizing and capturing glutamate (Glu). **OBJECTIVE:** The objective of this study was to investigate the mechanism of guanosine (GUO) exert neuroprotection in mice hippocampal slices incubated with different Glu concentrations. **METHODS:** The mice were sacrificed by decapitation and the hippocampi was removed, weighed and sliced in a chopper equipment (McIlwain) to 300um. These slices were preincubated at 4°C and then washed with media containing artificial cerebrospinal fluid (aCSF) containing glucose (5mM). After this process, the slices are incubated with different concentrations of Glu and GUO in different times in the metabolic bath with constant shaking at 37°C and aerated with a gas mixture (95%CO₂: 5%O₂), to observe the better neuroprotective effect of GUO. **RESULTS:** First, we analyzed the concentration of Glu that produce an increase in Glu utilization to CO₂ (L-[¹⁴C(U)]-Glu) without cell injury; we proceed a curve with different concentrations of Glu (0,30,100,300 and 1000uM) and different times (0 at 2h) and we observed that the concentration of 1000uM of Glu increase Glu oxidation in the time between 30-60 minutes of incubation without cell injury (measured by MTT and flow cytometry). In this condition (Glu concentration and time), we make a curve of GUO (0 at 300uM) and showed that 100uM of GUO increase (35%) Glu oxidation. Behind this result, we study the effect of 100uM of GUO on Glu uptake (L-[3,4-³H]-glutamate) in mice hippocampal slices incubated with 1000uM of Glu per 1h(30-60min) and in this situation GUO increase Glu uptake (around 45%). **CONCLUSION:** This is the first time that a study showed which GUO promotes an increase in Glu uptake and utilization together. However, more studies are necessary to determine if GUO act intracellularly or directly in membranes.

Key-words: Glutamate; Guanosine; Brain Energy Metabolism.

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