Neuroprotective Effect of Guanosine Against Glutamate or Ab $_{25-35}$-induced toxicity

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Neurodegenerative disorders such as stroke or Alzheimer Disease involve glutamatergic excitotoxicity and amyloid β (Aβ) deposition in the brain, respectively. Previous studies in our laboratory showed that guanosine (GUO) is neuroprotective to hippocampal slices submitted to oxygen and glucose deprivation. Additionaly, GUO enhances glutamate (Glu) uptake in cortical slices and cultured astrocytes. So, the objective of this study was to evaluate the potential neuroprotective effect of GUO against glutamate-induced cell death in hippocampal slices or $A\beta_{25-35}$-induced toxicity in differentiated human neuronal SHSY5Y cells. Hippocampal slices were preincubated for 30 minutes with GUO (30-300μM) followed by co-treatment with 1mM Glu (1h) and then maintained for additional 6h in culture medium. Twenty-four hours after seeding, SHSY5Y cells were sequentially differentiated with 10μM retinoic acid (5 days) and 1ng/ml BDNF (3 days). To evaluate neuroprotection of GUO against Aβ-induced toxicity, differentiated SHSY5Y cells were preincubated for 24h with GUO (30-1000μM) and exposed for additional 24h with aggregated $A\beta_{25-35}$ (10μM). Cell viability was determined by (3,4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay. Glu or aggregated $A\beta_{25-35}$ reduced cell viability by 30% and 23% in hippocampal slices or SHSY5Y neuronal cells, respectively. GUO (100μM) fully prevented (91,7%) glutamate-induced hippocampal slices toxicity and GUO (300 μM) partially (89%) prevented Aβ-induced SHSY5Y neuronal cell death. These results demonstrate that GUO is neuroprotective against two different toxic stimuli (glutamate and $A\beta_{25-35}$) which are involved in neurodegenerative processes in the central nervous system.

Key words: Guanosine, Glutamate, $A\beta_{25-35}$, neurodegeneration

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