Abstract 3410

Insulin-like growth factor II neuroprotective effects against mitochondrial-oxidative and neuronal damage induced by CORT and MPP+ in dopaminergic neurons

Type: Abstract Submission

Topic: S_G. Disorders of the Nervous System / G.3 Parkinson's disease / G.3.a Molecular and cellular mechanisms

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Abstract Body

Aims: Parkinson's disease (PD) affects 1–3% of the population aged over 65. Stress seems to contribute to PD neuropathology, probably by dysregulation of the hypothalamic–pituitary–adrenal axis. Key factors are oxidative stress, mitochondrial dysfunction and neuronal glucocorticoid-induced toxicity. Insulin-like growth factor II (IGF-II) has shown antioxidant and neuroprotective effects in some neurodegenerative disorders. Therefore, our aim was to study IGF-II protective effects against oxidative damage on a cellular combined model of PD and mild to moderate stress, based on corticosterone (CORT) and the dopaminergic neurotoxin 1-methyl-4-phenylpyridinium (MPP+).

Methods: The dopaminergic neuronal cell line SN4741 (RRID:CVCL_S466) derived from mouse substantia nigra were exposed to 200 µM MPP+, 0.5 µM CORT or both, with or without 25 ng/mL IGF-II, for 2.5 or 6 h. Cell viability, oxidative stress parameters, mitochondrial and dopamine markers and intracellular signaling pathways were evaluated.

Results: The administration of MPP+ or CORT individually led to cell damage compared to control situations, whereas the combination of both drugs produced very considerable toxic synergistic effect. IGF-II counteracts the mitochondrial-oxidative damage, protecting dopaminergic neurons from death and neurodegeneration. IGF-II promotes PKC activation and nuclear factor (erythroid-derived 2)-like 2 antioxidant response in a glucocorticoid receptor-dependent pathway, preventing oxidative cell damage and maintaining mitochondrial function.

Conclusions: IGF-II capacity to protect nigral dopamine neurons against mitochondrial-oxidative damage induced by CORT and MPP+ was demonstrated. Thus, IGF-II is a potential therapeutic tool for prevention and treatment of PD patients suffering mild to moderate emotional stress.

Funding: UMA18-FEDERJA-004.

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