P0729 / #4048

Topic: AS07 Aging and Neurodegenerative Disorders

ANTIOXIDANT AND NEUROPROTECTIVE ACTIONS OF IGF-II AGAINST GLUCOCORTICOID-INDUCED TOXICITY IN DOPAMINERGIC NEURONS.

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The neurodegenerative Parkinson's disease (PD) affects 1–3% of the population aged over 65. A wide range of pathways and mechanisms are involved in its pathogenesis, such as oxidative stress, mitochondrial dysfunction, inflammation and neuronal glucocorticoid-induced toxicity, which ultimately produce a progressive loss of nigral dopamine neurons. 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), an endocrine response marker to stress, and the dopaminergic neurotoxin 1-methyl-4-phenylpyridinium (MPP+). 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. 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 maintained the tyrosine hydroxylase expression and 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. This work revealed the potential neuroprotective role of the hormone IGF-II in a cell model of PD aggravated by mild to moderate hormonal stress. 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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DECISION MAKING IN PARKINSON'S DISEASE: A PRELIMINARY STUDY INVESTIGATING THE INFLUENCE OF DOPAMINE REPLACEMENT THERAPY ON DECISIONAL PROCESSES IN PATIENTS AFFECTED BY PARKINSON'S DISEASE

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Parkinson's disease (PD) is a neurodegenerative disease, mainly due to a loss of dopaminergic neurons in the substantia nigra, causing motor and non-motor symptoms. As the disease progresses, cortical regions and corticostriatal pathways are involved. Literature suggests that PD patients may display a propensity for making risky value-based decisions. This is due, at least in part, to the pathophysiological features of PD that involves neural structures supporting decisional processes (e.g., evaluating choice options assigning subjective values, processing reward-or-loss consequences), where dopamine and corticostriatal circuits are pivotal. It is hypothesized that dopaminergic medications may affect decision-making toward risky choices. The study aimed at investigating relationships between decision-making under ambiguous and risky conditions and dopaminergic therapy. Analyses involved 22 patients affected by idiopathic PD (10 males, age: 65.3 ± 6.78, education: 10.5 ± 3.95). Inclusion criteria were the absence of impulse control disorders and major cognitive impairments, and stable pharmacological treatment for at least two months. Participants underwent an assessment of decisional abilities under ambiguity and risk through the Iowa Gambling Task (IGT) and the Game of Dice (GDT), respectively. The medication regimens were recorded for each type of drug (i.e., levodopa, dopamine agonists, MAO-B inhibitor) and converted into Levodopa equivalent daily dosages (LEDDs). Data were analyzed through non-parametric statistics. Results showed negative correlations between LEDD of dopamine agonists and IGT (total gain: $\rho s = -.438$; second block netscore: $\rho s = -.489$) and between LEDD of levodopa and GDT (netscore: $\rho s = -.424$; number of safe choices: $\rho s = -.459$) ($p < .05$). No correlations emerged between decisional tasks and LEDD of MAO-B inhibitors or total LEDD. Findings supported a possible role played by levodopa and dopamine agonists in value-based decision-making, biasing decisional processes toward risky options. As well, findings can support the presence of different cognitive mechanisms underlying decision-making under ambiguity and risk.

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