TITLE

IGF-II AS A NEUROPROTECTIVE AND NEUROPLASTIC FACTOR IN AN OXIDATIVE DAMAGE MODEL INDUCED BY GLUCOCORTICOIDS

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DOES THE STUDY INVOLVE RESEARCH IN ANIMAL OR HUMAN SUBJECTS? (TYPE "YES" OR "NO")

NO

HAVE THE EXPERIMENTAL PROCEDURES BEEN APPROVED BY A LOCAL ETHICS COMMITTEE? (TYPE "YES" OR "NO")

YES

BODY TEXT

IGF-II is a pleiotropic hormone widely distributed in the CNS, which triggers its functions by binding to IGF-IR, InsulinR and IGFII / M6P (IGF-IIR) receptors. Recently, it has been proposed that the effects of IGF-II, interacting with IGF-IIR, are relevant not only for metabolism, growth and development, but also for neurotransmitter release, memory consolidation and neuroprotection under neurodegenerative processes. The results of our research group prove that IGF-II exerts metabolic, antioxidant and neuroprotective effects in aging. On the other hand, it has shown to have neuroprotective actions in stress-related disorders mediated by glucocorticoids, and even in neurodegenerative pathologies such as Alzheimer's disease or neuropsychiatric disorders. In relation to glucocorticoids, it has been revealed that the exposure of neural cells to high levels or prolonged incubation periods, produce synaptic alteration, neurodegeneration and neuronal death. Mechanisms of glucocorticoid-damage are mediated by oxidative stress induced by an increase in ROS, mitochondrial damage, decrease in antioxidant defenses, lipid and protein membrane damage, etc. AIM: To study the antioxidant and neuroprotective effect of IGF-II in a model of oxidative damage induced by glucocorticoids in aging. METHODS: Primary adult rat neuronal cultures incubated with transient high levels of corticosterone (CORT) in the presence of low concentrations of IGF-II were used.

Oxidative damage was evaluated by measuring lipid hydroperoxides and cellular antioxidant status; neuronal function through mitochondrial cellular distribution, and quantification of synaptophysin and PSD95; synaptic functional evaluation with the endo / exocytosis of FM1-43 dye; and neurodegenarization with fluorojade staining experiments. RESULTS: Incubation of cells with CORT triggers oxidative damage, consuming antioxidant status. This oxidative stress produces damage and mitochondrial redistribution inducing synaptic changes, as shown the decrease in synaptophysin and PSD95 levels together with a decrease in the uptake and release of FM1-43, which may result in neurodegeneration. Incubation with IGF-II reverses these deleterious effects. CONCLUSIONS: Treatment of cells with IGF-II recovers the damage produced by CORT, restoring synaptic function and decreasing neurodegeneration. These outcomes can be attributed to an antioxidant effect mediated by the interaction of IGF-II with its specific IGF-IIR, which in turn mediates recovery of the redox balance via inhibition of ROS production, improvement of mitochondrial membrane potential / distribution and / or regulation of synaptic proteins.

KEY WORDS

IGF2; IGF2R; Mitochondria; Neuroprotection; OxidativeStress; Synapse.