NEUROPROTECTIVE EFFECT OF GROWTH HORMONE (GH) IN HYPOXIC ORGANOTYPIC CULTURES OF CHICKEN CEREBELLUM

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Anti-apoptotic effects of growth hormone (GH) have been described in different cell types. In the central nervous system (CNS) GH has a role in neuroprotection, although the molecular mechanisms of these actions have not been fully elucidated. GH mRNA, GH and the GH receptor (GHR) are locally expressed in chicken cerebellum; this structure is particularly sensitive to damage by hypoxia-low glucose (HLG) conditions (95%N₂, 5%O₂, DMEM-Low Glucose, at 37°C), leading to neuronal apoptosis and/or necrosis. In the present study, we evaluated the anti-apoptotic effect of GH in organotypic cultures of chicken cerebellum under HLG. This model has the advantage of maintaining the cytoarchitecture of normal tissue. Immunohistochemical analysis showed the co-localization of GH with NeuN in granule neurons; with Calbindin in Purkinje cells and, to a less extent, with GFAP in glial cells although the cytoarchitecture of these slices was modified under hypoxia conditions, mainly in the Purkinje layer, because these cells showed disorganization. Locally expressed GH increased under HLG conditions as compared to the control group (596.6±70.8 vs. 311.3±43.8 ng GH/mg protein, respectively, as determined by ELISA). Caspase-3 activity increased importantly in HLG treated cultures when compared to the controls under normoxia (11.6±2.1 vs 3.8± 1.0 U/ml) but was significantly reduced after addition of 1 nM GH (to 6.0 ± 0.1 U/ml). Also, GH treatment (1 nM) provoked an increase of 29.1% in the expression of Bcl2 in cultures exposed to hypoxia when compared to hypoxia alone. These results suggest that GH may act as a survival/neuroprotective factor in this ischemia model through anti-apoptotic mechanisms.

(Supported by PAPIIT-DGAPA, UNAM 210209; CONACYT 118353 and 234456, *corresponding author).