1,25-Dihydroxyvitamin D3 exerts neuroprotective effects in an ex vivo model of mild hyperhomocysteinemia

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INTRODUCTION: Elevated plasma homocysteine (Hcy) levels have been detected in patients with various neurodegenerative conditions. Studies of brain tissue have revealed that hyperhomocysteinemia may impair energy metabolism, resulting in neuronal damage. In addition, new evidence has indicated that vitamin D plays crucial roles in brain development, brain metabolism and neuroprotection. **OBJECTIVE:** The aim of this study was to investigate the neuroprotective effects of 1,25-dihydroxivitamin D3 (calcitriol) in cerebral cortex slices that were incubated with a mild concentration of Hcy. **METHODS:** Cerebral cortex slices from adult rats were first pretreated for 30 min with one of three different concentrations of calcitriol (50 nM, 100 nM and 250 nM), followed by Hcy for 1 h to promote cellular dysfunction. **RESULTS:** Hcy caused changes in bioenergetics parameters (e.g., respiratory chain enzymes) and mitochondrial functions by inducing changes in mitochondrial mass and swelling. Here, we used flow cytometry to analyze neurons that were double-labelled with Propidium Iodide (PI) and found that Hcy induced an increase in NeuN+/PI cells but did not affect GFAP+/Pi cells. Hcy also induced oxidative stress by increasing reactive oxygen species generation, lipid peroxidation and protein damage and reducing the activity of antioxidant enzymes (e.g., SOD, CAT and GPx). Calcitriol (50 nM) prevented these alterations by increasing the level of the vitamin D receptor. **CONCLUSION:** Our findings suggest that using calcitriol may be a therapeutic strategy for treating the cerebral complications caused by Hcy.

Key-words: 1,25-Dihydroxyvitamin D3; Vitamin D receptor; Mild hyperhomocysteinemia; Calcitriol.

Funding: FAPERGS, CNPq and CAPES.