Abstract

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Role of thiamine in Huntington's disease pathogenesis: In vitro studies.

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BACKGROUND: Oxidative stress accompanies neurodegeneration and also causes abnormalities in thiaminedependent processes. These processes have been reported to be diminished in the brains of patients with several neurodegenerative diseases.

OBJECTIVES: The aim of this work was to conduct a comparative analysis of the impact of supplemented thiamine on the viability of human B lymphocytes with CAG abnormal expanded huntingtin gene (mHTT) (GM13509) and control, B lymphocytes without mHTT (GM14467) through the following studies: determination of the supplemented thiamine concentrations, which are effective for cell growth stimulation after incubation in thiamine deficit conditions; determination of cell capability to intake the exogenous thiamine; evaluation of exogenous thiamine influence on the profile of the genes related to thiamine and energy metabolism; determination of ATP synthesis and activities of thiamine-dependent enzymes, KGDHC and BCKDHC in the intact cells and upon the exogenous thiamine.

MATERIAL AND METHODS: The following methods were used: EZ4U test for cell growth analysis; HPLC for determination of thiamine intake and ATP synthesis, qRT-PCR for evaluation of the gene profiles and spectrophotometric method for KGDHC and BCKDHC activities determination.

RESULTS: Maximal cell growth stimulation was observed at 2.5 mM in GM14467 up to 135% of the control culture and at 5.0 mM in GM13509 cells up to 165% of the control culture. Native levels of total ATP and KGDHC and BCKDHC activities in both cell types were comparable and did not changed upon thiamine deficit or supplementation. GM13509 cells showed more of an increase in growth stimulation upon thiamine supplementation than GM14467 cells and this effect was reflected in the increase of intracellular thiamine concentration.

CONCLUSIONS: The above results and reported changes in expression of GAPDH, IDH1 and SLC19A3 genes observed upon thiamine deficit conditions suggest that intracellular thiamine status and energy metabolism can have a role in HD pathogenesis.

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