IN VITRO EFFECT OF 3-HYDROXYISOBUTYRIC ACID ON ENERGY METABOLISM IN CEREBRAL CORTEX OF YOUNG RATS

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3-Hydroxyisobutyric aciduria (3HiBuria) is an inherited metabolic disease of the valine metabolism. Accumulation of 3-HiB and high urinary excretion is the biochemical hallmark of this disorder. Symptoms include repeated episodes of ketoacidosis and lactic acidemia, failure to thrive, brain dysgenesis, malformations and hypotonia. Considering that the pathophysiology of the brain alterations in this disorder are poorly known, the aim of the present work was to investigate the *in vitro* effect of 3-HiB (0.1, 0.5 and 1mM) on various parameters of energy metabolism, namely $^{14}CO_2$ production from glucose and acetate, and the activities of the respiratory chain complexes I-III, II, II-III, IV, succinate dehydrogenase and creatine kinase (CK) in cerebral cortex of 30-day–old rats. We observed that 1mM 3-HiB significantly reduced complex I-III and CK activities up to 20% and 30% respectively, without affecting the others evaluated parameters. Our results suggest that 3-HiB alters cellular energy homeostasis, which could explain, at least in part, the neurological alterations found in patients with 3HiBuria.
Financial support: FAPERGS, CNPq, PROPESq, PRONEX.