Impairment of Mitochondrial Energy Homeostasis in Rat Heart by 3-Hidroxytetradecanoic Acid

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INTRODUCTION: Mitochondrial trifunctional protein (MTP) and isolated long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiencies are inborn errors of metabolism of fatty acid oxidation biochemically characterized by tissue accumulation of long chain 3-hydroxy fatty acids. Clinical presentation is characterized by a multiorgan involvement, being cardiac symptoms the most prominent clinical findings in these diseases. Reye-like syndrome with lactic acidemia is also found in these disorders possibly reflecting mitochondrial dysfunction. Therefore, considering that the pathophysiology of these disease is poorly known, we investigated the in vitro effects of 3-hydroxytetradecanoic acid (3HTA) on important parameters of energy homeostasis in mitochondrial preparations from heart of young rats.

MATERIAL AND METHODS: We evaluated the effect of 3HTA on respiratory parameters, estimated by oxymetry, NAD(P)H content, hydrogen peroxide production and membrane potential (ΔΨ) in rat heart mitochondrial preparations.

RESULTS AND DISCUSSION: 3HTA markedly increased state 4 respiration and diminished the respiratory control ratio. 3HTA also diminished mitochondrial membrane potential and matrix NAD(P)H levels, in addition to decreasing the production of hydrogen peroxide. These data supports an uncoupling effect for this fatty acid.

CONCLUSION: Our data indicate that 3HTA acts as uncoupler of oxidative phosphorylation in the heart, implying that this compound impairs brain mitochondrial energy homeostasis, a potential pathomechanism that could underlie at least in part the cardiac abnormalities found in LCHAD/MTP deficiencies.

Keywords: LCHAD deficiency, mitochondrial function, rat heart

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