INTRACEREBROVENTRICULAR ADMINISTRATION OF OCTANOIC ACID ELICITS MITOCHONDRIAL DYSFUNCTION IN RAT BRAIN

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Introduction: Medium chain acyl-CoA dehydrogenase deficiency (MCADD) is one of the most common fatty acid oxidation defect. This disease is characterized by high levels of octanoic acid (OA) in tissues and blood of patients. The main symptoms include lethargy, vomiting, hypoglycemia, cortical palsy and can progress to coma or death and they are presented in the form of acute metabolic crisis. Objectives: The objective of this work was to evaluate the activity of mitochondrial enzymes in brain structures of rats subjected to intracerebroventricular administration of OA. Materials and methods: Sixty-day-old male Wistar rats were divided into two groups: OA group that received one intracerebroventricular administration of OA (1.66 μmol/2 μL), and control group, that received 2 μL of artificial cerebrospinal fluid. One hour after the administration the animals were euthanized and cerebral cortex, hippocampus, striatum, and cerebellum were removed. These structures were used to assess the activities of the respiratory chain complexes I-IV, as well as creatine kinase (CK), citrate synthase (CS), succinate dehydrogenase (SDH), and malate dehydrogenase (MDH) activities. Results and conclusions: It was observed a decrease of complex I activity in striatum and hippocampus of rats receiving OA. Furthermore, complexes II and II-III activities were inhibited in all brain structures by OA administration, while complex IV activity were inhibited in cerebral cortex, striatum, and cerebellum. Moreover, SDH activity was diminished in cerebral cortex, striatum, and cerebellum of OA group animals. On the other hand, MDH activity was increased only in cerebral cortex, while CS activity was activated in hippocampus of these animals. In addition, CK activity was increased in cerebral cortex, while it was inhibited in hippocampus and cerebellum. These results suggest that OA administration elicits mitochondrial dysfunction in brain of rats, which could be implicated in the pathophysiology of brain damage found in MCADD patients.

Key Worlds: MCADD; Mitochondrial dysfunction; Octanoic acid.

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