Diabetes *Mellitus* induced by strepzotocin change physiology of mitochondrial complex I mitochondria in central nervous system.

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Introduction: Diabetes *Mellitus* (DM) impacts million people and in 2015 caused 5 million deaths around the world. The hyperglycemia associated with DM causes severe complications that lead to premature death. These problems are related to oxidative stress caused by the high levels of reactive oxygen species (ROS). Studies have shown that in Type 1 diabetes (DM1) the generation of ROS occurs mainly thought mitochondria during oxidative phosphorylation. Moreover, brain produces more mitochondrial ROS and has the low antioxidant capacity. Thus, the brain is potentially very susceptible to the diabetes complications.
Objective: To evaluate mitochondrial contribution in the emission of ROS and the modulation of antioxidant system in the brain of rats with one month of hyperglycemia caused by DM1 induced by strepzotocin.
Methodology: Hydrogen peroxide generation was induced by stimulating mitochondrial complex I or II. Antioxidant enzymatic capacity was evaluated by measuring catalase, glutathione peroxidase/reductase and thioredoxin reductase activities. Mitochondrial respiratory capacity and mitochondrial complex I (CI) activity was measured by high resolution respirometry and NADH oxidation rotenone sensitive.
Results: We found that the CI mitochondrial activity by diabetic group, when stimulated with pyruvate, malate and glutamate, produces less ROS and consumes less oxygen than control group. There were no differences when mitochondrial complex II was stimulated with succinate. We also found that activity of thioredoxin reductase is higher in the diabetic group. Accordantly, the activity of mitochondrial complex I was decreased in diabetic group.
Conclusion: DM1 promotes a preferential inhibition of mitochondrial CI. Studies have shown that alterations in the CI activity are generally related neurodegenerative diseases. The results provide first functional evidence that links diabetes insulin-dependent to mitochondrial ROS depression and CI activity levels. These results can be involved in ROS umbalance in brain and cognitive degeneration.

Keywords: Diabetes *Mellitus* type 1, mitochondria, ROS production, mitochondrial complex I.

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