EFFECT OF ADMINISTRATION OF LINAGLIPTIN ON MITOCHONDRIAL RESPIRATORY CHAIN ACTIVITY IN THE BRAIN OF ADULT RATS.

Schraiber, R.B.; Guzatti, G.; Souza, L.R.; Prá, M.; Mello, A.H.; Rezin, G.T.

Laboratory of Clinical and Experimental Pathophysiology, Postgraduation Programme in Health Sciences, University of South Santa Catarina, Tubarão, Santa Catarina, Brazil.

Introduction: Obesity is a chronic disease whose incidence has been growing progressively. It is associated with the development of comorbidities, as well as present alterations in mitochondrial respiratory chain. Pharmaceutical strategies for the treatment of obesity include drugs that regulate food intake, thermogenesis, fat absorption, and fat metabolism. Moreover, drugs that act in the incretin system, such as linagliptin, are being investigated.

Objectives: This study evaluated the effect of acute and chronic administration of linagliptin, inhibitor drug of dipeptidyl peptidase-4, on mitochondrial respiratory chain activity in the brain of adult rats.

Materials and Methods: In acute administration, adult rats received a single administration of saline or linagliptin (1, 7.5 or 15mg/kg), orally. In chronic administration, adult rats received for seven days, once daily, oral administration of linagliptin (1, 7.5 or 15mg/kg) or saline. Twelve hours after the single (acute) or last (chronic) linagliptin or saline administration, the animals were euthanized by decapitation, the brain was removed and the hypothalamus, prefrontal cortex, cerebellum, hippocampus, corpus striatum and cortex were isolated to analyse the activity of complex I, II and IV of mitochondrial respiratory chain.

Discussion and Results: The animals that received acute administration of linagliptin have shown an increasing activity of complex I in the prefrontal cortex, cerebellum, hippocampus, striatum and posterior cortex. The activity of complex II was activated only in the prefrontal cortex, whereas the activity of complex IV was activated in the prefrontal cortex, cerebellum, hippocampus, corpus striatum and in the posterior cortex. In contrast, chronic administration of linagliptin inhibited the activity of complex I in the posterior cortex and inhibited that of the complex IV in the cerebellum, hippocampus and in the posterior cortex. The activity of the complex II didn’t change.

Conclusions: Our results have shown that acute administration of linagliptin increased the activity of complex I, II and IV of the mitochondrial respiratory chain, whereas chronic administration inhibited enzyme activity.

Acknowledgements: This study was supported by CNPq, FAPESC and UNISUL.

Key Words: obesity; linagliptin; energy metabolism