Modulation of autophagy in hypothalamus of diet-induced obese mice: impact on inflammation and apoptosis

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INTRODUCTION: Autophagy is an important process which regulates cellular homeostasis by degrading dysfunctional proteins, organelles and lipids. Recent data have shown that absence of autophagy in hypothalamic neurons in mice results in glucose intolerance and weight gain. Moreover, in POMC neurons autophagy is essential for the maintenance of axon growth. Therewith, our work aimed to investigate the impact on autophagy in diet-induced obese mice.

MATERIAL AND METHODS: For this, mice receive a high-fat diet (HFD) for 8 or 16 weeks. In another experiment, mice received HFD for 16 weeks and were treated with 25 µM of rapamycin intracerebroventricular for 5 days. We perform RT-PCR and western-blots to evaluate mRNA expression and protein content, respectively.

RESULTS AND DISCUSSION: The results show no difference on autophagy machinery with 8 weeks of HFD, but, there is a lower protein content of LC3-II in hypothalamus of mice which received HFD for 16 weeks. Also, Ulk1 gene expression was upregulated in obese animals. Next, we evaluated if upregulation of autophagy could exert an effect on metabolic parameters and protein content. We have found no significant results on glucose tolerance in animals with diet-induced obesity with rapamycin treatment. However, LC3 protein was increased and p62 was diminished, showing that there was an upregulation of autophagy in our treatment. Rapamycin in obese animals results in a lower content of BAX and pJNK. This results show that autophagy impairment may be important in development of obesity. CONCLUSIONS: We conclude that chronic exposure to high fat diet can lead to the loss of autophagy, an important mechanism of cellular homeostasis and its restoration could reverse, at least in part, inflammatory and apoptosis markers which are the main mechanisms involving dysregulation of energy balance on hypothalamic neurons.

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