HIGH-FAT DIET CONSUMPTION AND EARLY EFFECTS ON CHAPERONE MEDIATED AUTOPHAGY IN HYPOTHALAMUS OF MICE

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Chaperone mediated autophagy (CMA) consists in specific degradation system of proteins by lysosome. It is an important regulator of cell metabolism and its failure is related to the accumulation of dysfunctional proteins and loss of cellular homeostasis. The aim of this work was to determine the CMA status on hypothalamus of mice fed high-fat diet. Six weeks old Swiss mice were submitted to a normolipid diet (CT) or high-fat diet (HFD) for three days or one week. Body weight and food intake was measured daily. Western-blotting and coimmunoprecipitation was used to determine the content and association of proteins of CMA in hypothalamus of mice and qRT-PCR was used to measure gene expression of hypothalamic cytokines. After three days of HFD consumption there was an increase in body weight, food intake and white fat in HFD group compared to CT. Also, there was an increased expression of IL1β and increased content of JNK1 phosphorylation in HFD group. Regarding the content of CMA proteins, there was a decrease in the content of Lamp2a and Hsc-70 proteins in hypothalamus of HFD group and an increase association between Lamp2 and Hsc-70. After one week of HFD consumption mice showed increased body weight and white adipose tissue weight, with no alterations in food intake. There was a downregulation in IL1β gene expression and a lower association between Lamp2 and Hsc-70 proteins. These results suggests that CMA is rapidly modulated in response to high-fat diet consumption in hypothalamus of mice and this could be an important mechanism that could be related to the formation of protein aggregates and loss of hypothalamic homeostasis in obesity.

Key-words: Obesity, high fat diet, chaperone mediated autophagy (CMA).