Regulation of hypothalamic neuropeptides gene expression in diet induced obesity resistant rats: possible targets for obesity prediction?

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Several factors play a role in obesity (i.e. behavior, environment, and genetics) and epigenetic regulation of gene expression has emerged as a potential contributor in the susceptibility and development of obesity. To investigate the individual sensitivity to weight gain/resistance, we here studied gene transcription regulation of several hypothalamic neuropeptides involved in the control of energy balance in rats developing obesity (diet-induced obesity, DIO) or not (diet resistant, DR), when fed with a high fat diet. Rats have been followed up to 21 weeks of high fat diet exposure. After 5 weeks high fat diet exposure, the obese phenotype was developed and we observed a selective down-regulation of the orexygenic neuropeptide Y (NPY) and peroxisome proliferator-activated receptor gamma (PPAR-γ) genes. No changes were observed in the expression of the agouti-related protein (AgRP), as well as for all the anorexigenic genes under study. After long-term high fat diet exposure (21 weeks), NPY and PPAR-γ, as well as most of the genes under study, resulted not be different between DIO and DR, whereas a lower expression of the anorexigenic pro-opio-melanocortin (POMC) gene was observed in DIO rats when compared to DR rats. Moreover we observed that changes in NPY and POMC mRNA were inversely correlated with gene promoters DNA methylation. Our findings suggest that selective alterations in hypothalamic peptide genes regulation could contribute to the development of overweight in rats and that environmental factor, as in this animal model, might be partially responsible of these changes via epigenetic mechanism.