**IMPLICATIONS OF MATERNAL HIGH-FAT DIET ON CENTRAL LEPTIN SIGNALING IN NEWLY WEANED OFFSPRING OF MICE**

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**Abstract**

It is already known that maternal obesity can impact negatively the health of offspring. Therefore, this study aimed to assess proteins involved in hypothalamic leptin signaling in the offspring of obese dams fed with high-fat diet to analyze possible influences. Our results show that maternal high-fat diet can modulate the metabolism and that offspring from obese dams becomes more prone to develop obesity and leptin resistance.

*Key words: maternal obesity, hypothalamus, leptin signaling.*

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**Introduction**

Recently, early obesity has been linked to feeding behavior during pregnancy and lactation, which is not just able to cause changes in the intrauterine environment, such as the development of inflammation, but also lead to changes in milk composition and content of lipids, leading to metabolic programming in the offspring. This mechanism predisposes the offspring to developing obese phenotype and associated disorders. Thus, the aim of this study was to evaluate the proteins involved in the hypothalamic leptin and insulin signaling in the newly weaned offspring of dams fed with high-fat diet during pregnancy and lactation to investigate whether maternal obesity would be able to lead to resistance to these hormones at the central level.

**Results and Discussion**

Offspring of obese dams (HC-O) showed higher weight gain, food intake and adiposity compared to offspring of control dams (CC-O). In addition, key proteins involved in the central leptin signaling (JAK2 and STAT3) were evaluated and the results are shown in Figure 1. Comparing CC-O and HC-O groups, although JAK2 phosphorylation display a tendency to be lower in HC-O group (Figure 1A), we observed a significant decrease in STAT3 phosphorylation in HC-O group (Figure 1B) which can be strongly associated with impaired signal and hormonal resistance. Sun et al. (2012) and Masuyama and Hiramatsu (2014) found higher plasma concentrations of leptin and reduced sensitivity to this hormone in the offspring of obese dams, which is in agreement with the lower pathway activation observed in our study. In parallel, the HC-O group showed greater phosphorylation of inflammatory proteins JNK and IKK besides central insulin resistance which is associated with the response of the organism to exposure to saturated fatty acids from maternal diet and reinforces the presence of metabolic changes induced by epigenetic mechanisms (data not shown).

![Figure 1. Western blot analysis of p-JAK2 (A), p-STAT3 (B) in the hypothalamus of CC-O and HC-O offspring with 28 days normalized by total proteins. Data are means +/- SEM, n = 5 per group, * p <0.05, ** p <0.01](image)

**Conclusions**

According to the findings of this study and the literature we concluded that the metabolic programming is able to change important mechanisms in young offspring, leading to leptin and insulin resistance at the central level, contributing to the development of the obese phenotype and metabolic changes observed.

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**References**
