

Evaluation of the subunit $\alpha 7$ expression of nicotinic acetylcholine receptor and activation of proteins (JAK2/STAT3 and CREB) of cholinergic anti-inflammatory pathway in the offspring mice spleen with obesity induced by maternal high fat consumption

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Abstract

Gestational obesity is one of the most common obstetric risks and its prevalence has been increasing substantially. It is known that in obesity there is a loss of the cholinergic signalling responsible for the anti-inflammatory reflex which leads to an immune system imbalance. We hypothesize that the offspring (28 days old) of the maternal high fat diet consumption during the gestational and the lactation periods shows an impaired cholinergic anti-inflammatory reflex. From this point on, an increase of inflammatory cytokines in the HFD-O spleen, such as TNF and IL1 β , was observed, and this increase seems to be responsive to the smallest phosphorylation of STAT3 and the increase of the expression of NFkB.

Key words:

obesity, inflammatory, cholinergic.

Introduction

Obesity is a public health problem and it is known that the mother gestational obesity affects the offspring health adversely, in the short and long term. The innate immune system activation has its intensity controlled by the cholinergic anti-inflammatory reflex, where the connection of acetylcholine in the $\alpha 7$ subunit of the $\alpha 7$ nAChR cholinergic receptor induces the activation of STAT3 and reduces the activation of NFkB and the production of the anti-inflammatory cytokines. This way, the cholinergic anti-inflammatory reflex controls the immune function of the cells attenuating the recruiting of the macrophages and inhibiting the production of inflammatory cytokines. However, it has been described in the obesity a greater activation of the pro-inflammatory pathways. **Aim:** To evaluate the effects of maternal high fat diet (HFD) consumption on cholinergic anti-inflammatory pathway in spleen of mice offspring.

Results and Discussion

Methodology: After delivery the litter size (SC offspring, SC-O; HFD offspring, HFD-O 28 days-old) was stimulated, by i.c.v. injection, with saline or nicotine, after the spleen was collected to be evaluate. **Results:** The amount of protein and RNAm of $\alpha 7$ nAChR between SC-O and HFD-O was not different. The central stimulus with nicotine did not alter the expression of $\alpha 7$ nAChR either. Furthermore, the expression of $\alpha 7$ nAChR receptors in the spleen of the HFD-O and SC-O mice was investigated through immunofluorescence in optics microscopy, although the effect of maternal obesity was not observed. The HFD offspring showed a greater expression of STAT3 in the spleen (**Figure 1A**). However, it is necessary that phosphorylation of STAT3 takes place so that the cholinergic pathway plays an anti-inflammatory role. Interestingly, despite the STAT3 increase, there was a smaller phosphorylation of it (**Figure1B and C**). Besides, the reduction of p-STAT3 may have ended up in a bigger protein expression of NFkB in the HFD-O (**Figure D**). Due to the greater expression of NFkB in this group, an increasing tendency in the genic expression of inflammatory cytokines, such as TNF and IL1 β , can be

observed, which seems to have been reversed with the nicotine ICV injection (**Figure 2A and B**).

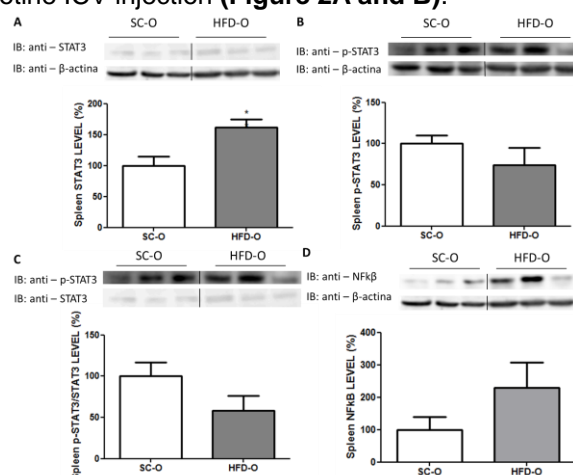


Figure 1. Representative Immunoblotting of the expression **A)** STAT3, **B)** p-STAT3, **C)** p-STAT3 normalized by STAT3 and **D)** NFkB in the spleen of 28 days old mice of SC-O and HFD-O group. (n=3/group). *p< 0,05, ** p< 0,01 e *** p< 0,001.

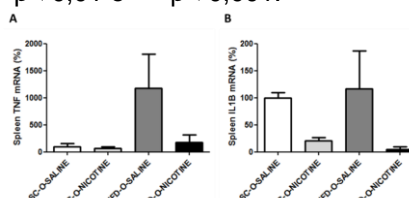


Figure 2. The genic expression per Real time in the spleen of the 28 days old offspring **A)** of TNF and **B)** IL1 β (n= 3 - 4/group).

Conclusions

The maternal high-fat diet consumption shows a reduction of p-STAT3 and an increase of NFkB that could be related to cholinergic anti-inflammatory signalling impaired culminating in the exacerbated production of inflammatory cytokines.

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