Modulation of JAK2/STAT3, CREB proteins and cholinergic anti-inflammatory pathway in offspring obese dams: implications for the control antiinflammatory response in the liver.


Abstract
Maternal obesity can cause deleterious effects to offspring in perinatal period and adult life. Activation of proinflammatory pathways and metabolic disturbs are frequently observed in offspring of obese dams. Cholinergic anti-inflammatory pathway participate of control of inflammatory response through a7 subunit nicotinic acetylcoline receptor (a7AChR), JAK2 and STAT3 proteins. Reduced activity of this pathway lead to high level of inflammatory cytokines. The objective was evaluate the effect of maternal consumption of high-fat diet fed during pregnancy and lactation in liver expression of a7AChR, STAT3 proteins and cytokines. We observed high level of a7AChR mRNA but reduced a7AChR protein. Besides nicotine ICV injection incresed liver IL-10 expression in SC-O mice but in HFD-O mice nicotine did not alter the IL-10 expression.

Key words:
Obesity, inflammation, cholinergic.

Introduction
The maternal obesity during pregnancy and lactation may cause deleterious effects to offspring. The acetylcoline binding to a7 subunit nicotinic acetylcoline receptor (a7AChR) is able to initiate the cholinergic antiinflammatory reflex. The signal activates JAK2/STAT3 proteins and inhibits an pro-inflammatory cytokines transcription factor (NFKB). This allows decrease macrophages recruitment by immune system, attenuating inflammation. However, this mechanism seems to be damage in obeses individuals.

Aim: To evaluate the effects of maternal high fat diet (HFD) consumption on liver cholinergic anti-inflammatory pathway of mice offspring.

Results and Discussion
Methodology: Offspring mice (28 days-old) (SC offspring, SC-O; HFD offspring, HFD-O 28 days-old) has received saline or nicotine (0,3µg/animal-ICV) and fragments of liver were collected to perform western blot and qPCR analysis.

Results: HFD-O mice presents higher a7AChR expression than SC-O mice. Nicotine injection increased a7AChR expression in SC-O mice but in HFD-O mice did not occur additional effect (Fig. 1A). In contrast a7AChR protein level was reduced in HFD-O compared to SC-O mice. Nicotine injection did not affect proteins level in both groups (Fig. 1B). Nicotine increased IL-10 mRNA in SC-O group but did not alter in HFD-O mice (Fig. 1C). The pSTAT3 protein level seems to have folded up in SC-O but not in HFD-O mice (Fig. 1D). Additionally, we did not find increase in hepatic gene expression of TNF and converse enzyme mRNA of TNF (ADAM17). At the same time, we did not observe differences in total NFKB or pNFKB. The increase of antiinflammatory cytokine (IL-10) associate to increase of pSTAT3 can reflect the activation of cholinergic antiinflammatory pathway. Both effects were observed only in offspring from control dams. This shows that offspring from HFD dams seems to have cholinergic antiinflammatory pathway impaired.

Conclusions
The maternal high-fat diet consumption during pregnancy and lactation showed be able alter gene expression and proteic content to a7AChR in offspring liver. The nicotinic agonist did not be able activate the cholinergic antiinflammatory pathway in the offspring liver of obese dams.

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