

Obese offspring mice have impaired inflammatory response after chronic treatment with LPS.

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Abstract

The insulin resistance is especially caused by inflammatory process in obesity. The activation of antiinflammatory cholinergic pathway is responsible to attenuate inflammation. The objective was investigate if the obese offspring have cholinergic antiinflammatory signalling damage and insulin resistance impaired. The inflammation LPS-induced was able to increase pIKK, IL-6, pSTAT3 levels and decrease gluconeogenesis in lean and obese offspring. The treatment seems to reduce $\alpha 7$ nAChR in offspring and increase to pAKT in obese offspring. Our data indicate which the maternal obesity impaired the cholinergic signalling and this can be affect glucose homeostasis through IL-6 signalling.

Key words:

Obesity, offspring, cholinergic.

Introduction

When the nicotinic of acetylcholine receptor agonist binds to the $\alpha 7$ subunit ($\alpha 7$ nAChR) the antiinflammatory cholinergic pathway is activated. The signal inhibits the expression of proinflammatory cytokines (IL-6, TNF- α), attenuating inflammation. According to the literature, the reduce inflammatory process caused by obesity improvement to insulin sensibility in lean individuals. However, the mechanism seems to be impaired in obese individuals. **Objectives:** evaluate if the obese offspring have cholinergic antiinflammatory signalling damage and insulin resistance impaired.

Results and Discussion

Methodology: After delivery the litter size (SC-Offspring; HFD-Offspring, 28 days-old) was stimulated. They received daily injections of LPS (1mg/kg) or saline solution (0,9%) via intraperitoneal for three days. The female offspring was used to Pyruvate Tolerance Test (PTT). The liver fragments of males was collected to Western blot and qPCR. The offspring (p28) was also perfused to immunofluorescence. **Results:** We observed increase in body weight gain in offspring of obese dams compared to control offspring (Image 1). The treatment with LPS reduced hepatic glucose production evaluated through PTT and decrease of G6Pase expression (Image 2). At the same time, the LPS treatment increased the inflammatory profile (pIKK and IL-6) and the pSTAT3 levels (Image 3). Although the mice treated with LPS present decrease in gluconeogenesis, obese offspring mice appear to have higher phosphorylation of AKT, including basal levels (Image 4). In the cholinergic pathway, we observed the distribution of the $\alpha 7$ nAChR in the liver and macrophages in immunofluorescence images (Image 5). The LPS seems to reduce the proteic content of $\alpha 7$ nAChR in the offspring (Image 4).

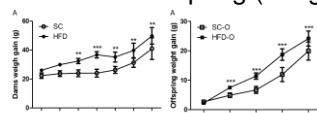


Image 1. Body weight of dams (A) and offspring (B). The values represent the mean \pm standard deviation. Means significantly different by unpaired t tests * $p < 0,05$; ** $p < 0,01$; *** $p < 0,001$.

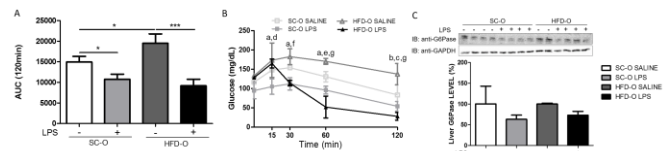


Image 2. Área under curve (A) and graphic representation of PTT. Immunoblotting representative of G6Pase (C). The values and bars represent the mean \pm standard deviation. For comparison of means was utilized ANOVA One-Way. * $p < 0,05$; ** $p < 0,01$. a= SC-O SALINE x SC-O LPS $p < 0,01$; b= SC-O SALINE x SC-O LPS $p < 0,05$; c= SC-O SALINE x HFD-O SALINE $p < 0,01$; d= SC-O LPS x HFD-O LPS $p < 0,001$; e= SC-O LPS x HFD-O LPS $p < 0,05$; f= HFD-O SALINE x HFD-O LPS $p < 0,01$; g= HFD-O SALINE x HFD-O LPS $p < 0,001$.

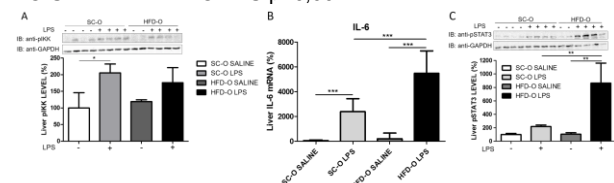


Image 3. Immunoblotting representative of pIKK (A) and pSTAT3 (C). Hepatic level mRNA IL-6 (B). For comparison of means was utilized ANOVA One-Way. * $p < 0,01$; ** $p < 0,01$; *** $p < 0,001$.

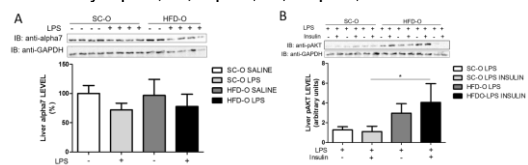


Image 4. Immunoblotting representative of alpha7 (A) and pAKT (B). The bars represent the mean \pm standard deviation. For comparison of means was utilized ANOVA One-Way. * $p < 0,01$.

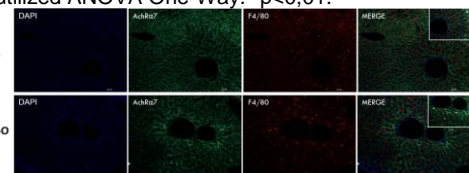


Image 5. Immunofluorescence images of liver offspring marked with F4/80 (red) and $\alpha 7$ nAChR (green).

Conclusions

Our data indicate that maternal obesity alter key components for the antiinflammatory cholinergic signalling. This damage may to prejudice the inflammation control in this mice through IL-6 signalling.

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