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The hypothalamic inflammation on a mice model of sepsis induced by cecal ligation puncture (CLP) procedure after the consumption of a short-term high-fat diet

Letícia F. Santucci*, Anelise C. P. Souza, Camilla Mendes, Camila Libardi, Alana Veras, Suleyma Costa, Pamela Lanza, Ísis Martins, Letícia Contieri e Tamires Santos, Márcio A. Torsoni.

Abstract

Studies has shown that the consumption of a high-fat diet induces hypothalamic and systemic inflammation. It is also known that nicotinic acetylcholine receptors (nAChRs) are involved in cholinergic anti-inflammatory response, in which the α7-subunit is the most expressive subtype doing this control in immune cells. This study investigated the effects of a short-term high-fat diet on modulating the anti-inflammatory pathway mediated by α7 receptor. 8-weeks-old Swiss mice consumed either short-term (3 days) high-fat diet (HFD-60% of fatty acids) or standard-chow. Both groups were submitted to either a CLP surgery, to induce polymicrobial sepsis, or an abdominal incision for exposure of the cecum, serving as the control group. We concluded that the consumption of a high-fat diet even for a short period is already capable of increasing hypothalamic anti-inflammatory markers and inhibiting the anti-inflammatory path-way.

Key words:

cholinergic anti-inflammatory reflex, cecal ligation puncture, high-fat diet.

Introduction

The consumption of a high-fat diet induces hypothalamic inflammation even prior to substantial weight gain (THALER et al., 2012). When exaggerated, the inflammatory effect can be more injurious than the pathogen itself. It is therefore important that there is a precise immunological homeostasis control, which occurs by the activation of macrophages that inhibit the production of proinflammatory cytokines (ANDERSSON & TRACEY, 2012). Dada published by our group suggest the loss of the cholinergic anti-inflammatory response in mice that has consumed just 3 days of high-fat diet (SOUZA, 2019). Thus it seems to exist a relation between reduction of cholinergic signaling and hypothalamic inflammation. We aimed to measure the hypothalamic inflammation activated by cecal ligation puncture (CLP) procedure in mice submitted to a 3 days high-fat diet.

Results and Discussion

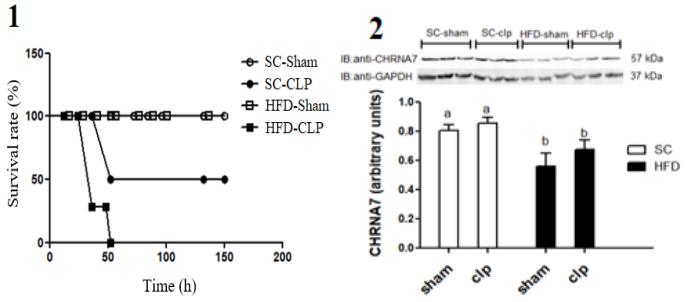

Figure 1. Survival Rate (percentage per hour) of 8 weeks-old Swiss mice fed by control (SC) or high-fat diet (HFD) for 3 days then submitted to CLP surgery or abdominal incision (Sham).

Figure 2. Hypothalamic chrnα7 expression compared to chrnα7 endogenous of mice that consumed control (SC) or high-fat (HFD) diet for 3 days then submitted to CLP procedure or abdominal incision (sham).

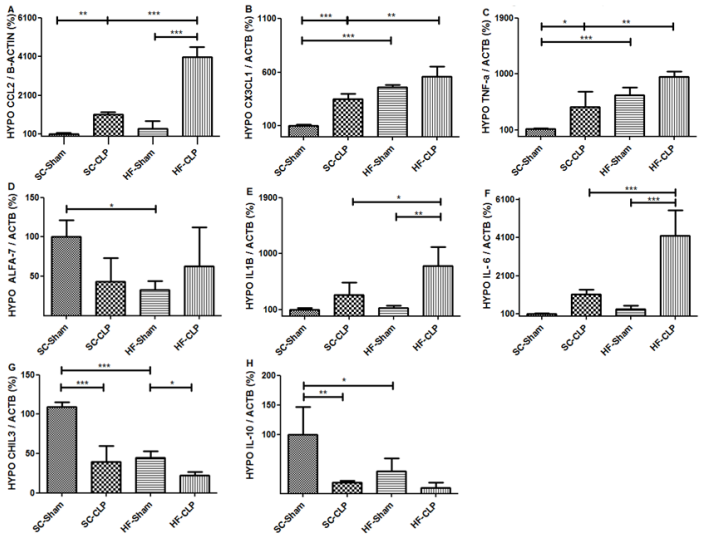

Figure 3. Hypothalamic mRNA expression levels of α7-subunit, chemokines (CX3CL1, CCL2 e Chil3) and cytokines (Il-6, TNF-α, IL-1ß e IL-10).

Conclusions

The lipid overload for a short period of time is capable of: increasing hypothalamic TNF- α levels; exacerbating inflammatory response after CLP-induced sepsis, showing an increase of inflammatory markers M1 (Ccl2, Cx3cl1, Tnf-α, Il-6 e Il-1β); reducing anti-inflammatory capacity with lower levels of Chil3 and Il-10 after CLP-induced sepsis; impairing the α7nAChR-mediated cholinergic anti-inflammatory response.

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