



FACULDADE DE MEDICINA DE RIBEIRÃO PRETO
Departamento de Clínica Médica

REUNIÃO CIENTÍFICA

ANO: 2019

Número: 11

Data: 29.05.2019 **Local:** Sala 640 – Departamento de Clínica Médica **Horário:** 11h00

Título: STAT3 but not ERK1/2 in VMH neurons is an Essential Mediator against Diet-Induced Obesity in a sex-specific manner.

Pesquisador: Gabriel Henrique Marques Gonçalves

Orientador: Profa. Dra. Margaret de Castro

INTRODUCTION: Leptin, an adipocyte-derived hormone, plays an important role in the control of energy homeostasis. Through its actions in the central nervous system, more specifically in the hypothalamus, leptin promotes a state of negative energy balance, decreasing food intake and increasing energy expenditure by activating different signaling pathways: STAT3 and ERK1/2. The ventromedial nucleus of the hypothalamus (VMH) is known to mediate some effects of leptin in the energy balance. However, little is known about the intracellular mechanisms which VMH neurons mediate these effects. OBJECTIVE: To assess the role of the STAT3 or ERK1/2 signaling in neurons that express the steroidogenic factor 1 (SF1) of the VMH on energy homeostasis. METHODOLOGY: We used cre-lox technology to generate mice with specific disruption of STAT3 or ERK1/2 in SF1 neurons of the VMH. Then, we evaluated the effects of the lack of STAT3 or ERK1/2 in this hypothalamic area on body weight, food intake and energy expenditure in mice with conditional deletion (SF1-cre; STAT3flox; or SF1-cre;ERK1/2flox) compared to control animals (STAT3flox; or ERK1/2flox) in both male and animals under regular chow diet or high fat diet (HFD). RESULTS: We demonstrated that the conditional knockout of STAT3 in SF1 neurons of the VMH (SF1-cre;STAT3flox) doesn't affect body weight, food intake or energy expenditure in animals on regular chow. However, when challenged with HFD, loss of STAT3 in SF1 neurons caused a significant increase in body weight and food intake that was more remarkable in females. Also, female but not male SF1-cre;STAT3flox mice on HFD showed decreased energy expenditure. In contrast, deletion of ERK1/2 in SF1 neurons of VMH didn't have any impact on energy homeostasis in male and female SF1-cre;ERK1/2flox mice compared to ERK1/2flox mice in both regular diet and high fat conditions. CONCLUSION: Disruption of STAT3 but not ERK1/2 signaling in SF1 neurons of VMH aggravates the body weight gain induced by diet-induced obesity in a sex-specific manner, indicating that this signaling pathway is required for the hypothalamic responses against obesogenic diet.