

Feeding behavior is modulated by hypothalamic activation of cholinergic receptor $\alpha 7$ nAChR in model of maternal obesity during gestation and lactation

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Abstract

Activation of cholinergic receptor ($\alpha 7$ nAChR) in hypothalamus can modulates inflammatory response and they are colocalized with POMC and NPY neurons. Activation of hypothalamic nAChR modulated NPY and POMC expression and reduced food intake. Maternal obesity promoted reduction of nAChR in hypothalamus of the offspring and increased food intake. Thus, the reduction of hypothalamic $\alpha 7$ nAChR in offspring may be related to obesity development induced by maternal consumption of high fat diet during pregnancy and lactation.

Key words: $\alpha 7$ nAChR, Hypothalamus, Food Intake.

Introduction

Nicotinic cholinergic receptor $\alpha 7$ ($\alpha 7$ nAChR) has important role in the inflammatory response. Inflammatory pathways have been associated to obesity and insulin resistance development. The literature has shown that cholinergic receptors may modulate the excitability of POMC and NPY neurons and energy homeostasis. Objective: To evaluate the colocalization of $\alpha 7$ nAChR receptors in POMC and NPY neurons and the modulation of energy expenditure by pharmacological activation.

Results and Discussion

Methods: Male Swiss mice of 8 weeks were used and offspring mice, 28 days old (SC-O), and offspring mice of high fat diet (HFD) dams fed with HFD during pregnancy and lactation (HFD-O). The hypothalamic expression of $\alpha 7$ nAChR was evaluated by, western blot, immunofluorescence. Energy expenditure and expression POMC and NPY by qPCR was evaluated after stimulus with saline or PNU (specific agonist of the $\alpha 7$ nAChR) in previously cannulated mice.

Results and Discussion: Pharmacological activation of $\alpha 7$ nAChR with PNU (ICV) in adult mice resulted in reduced food intake (Figure 1A) that accompanied by increased hypothalamic expression of POMC (Figure 1B) and decreased expression of NPY (Figure 1C). In offspring mice $\alpha 7$ nAChR receptor was detected by immunofluorescence in both, POMC and NPY neurons (Figure 2A and 2B). In a model metabolic programming HFD offspring mice presented reduced hypothalamic expression of $\alpha 7$ nAChR (Figure 2E), higher milk intake, higher body weight (Figure 2C) and reduced energy expenditure (2D).

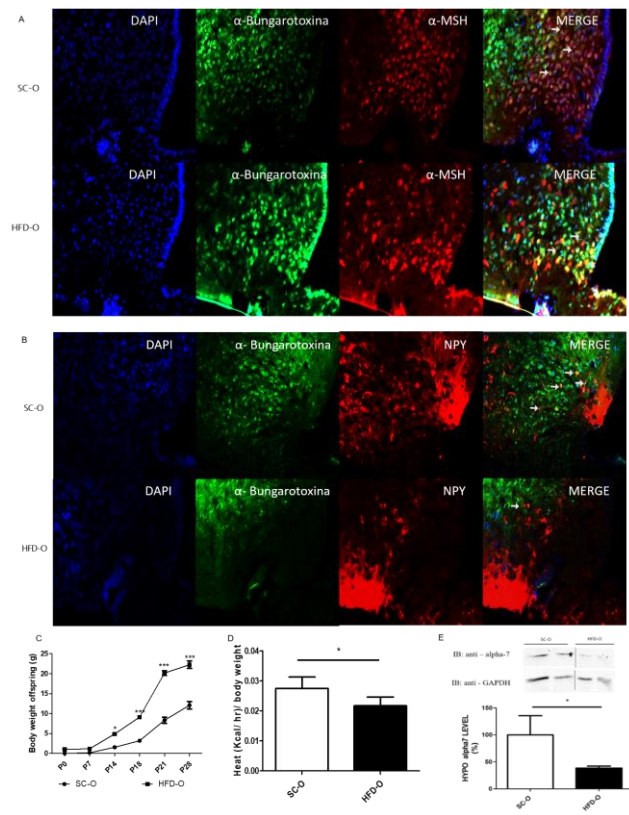


Figure 2. SC-O and HFD-O offspring at 28 days Hypothalamic immunofluorescence **A.** DAPI (blue), α -bungarotoxin-Alexa/fluor488 (antagonist of AchR $\alpha 7$ receptor) (green) and α -MSH neurons (red). **B.** DAPI (blue), α -bungarotoxin-Alexa/fluor488 (green) and NPY neurons (red). **C:** Body weight, **D:** Heat, **E:** Protein content of $\alpha 7$ AChR. * $p < 0.05$

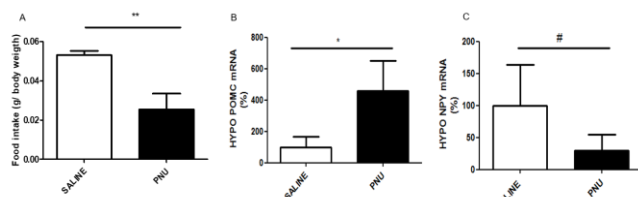


Figure 1. Evaluation of food intake (A), POMC expression (B), and NPY expression (C) in mice (8 weeks old) after fasting (16 hour) and stimulation with 45uMol PNU/ mice during 40 minutes. The amount of mRNA was normalized by the amount of GAPDH. * $p < 0.05$, # $p = 0.07$

Conclusions

Neurons responsible to control energy homeostasis express $\alpha 7$ nAChR. Pharmacological activation of $\alpha 7$ nAChR modulates feeding behavior and expression of neuropeptides. Maternal exposition to HFD during pregnancy and lactation impaired hypothalamic expression of $\alpha 7$ nAChR. This modification may be related to increased food intake and obesity development in the adult life.

Acknowledgement