Session 595 - Neuroimmunology: Behavioral Effects

Add To Itinerary

595.10 / AAA4 - Hypothalamic lipotoxicity leads to microglia activation and ghrelin signaling disruption in rats

November 6, 2018, 1:00 PM - 5:00 PM | SDCC Halls B-H

Presenter at Poster
Tue, Nov. 6, 2018, 2:00 PM - 3:00 PM

Grant Support
CONACYT-255317

Grant Support
CONACYT-573686

Authors
*R. MALDONADO[1], M. RODRIGUEZ PADILLA[2], A. CAMACHO[3];
[1]Autonomous Univ. of Nuevo Leon, Santa Catarina, Mexico; [2]Fac. of Biol. Sciences, Univ. Autonoma de Nuevo Leon., San Nicolas de los Garza, Mexico; [3]Univ. Autónoma de Nuevo León, Nuevo León, Mexico

Disclosures
R. Maldonado: None. M. Rodriguez Padilla: None. A. Camacho: None.

Abstract
Obesity associates with chronic systemic inflammation and insulin resistance. Hypothalamic microglia activation by lipids oversupply has been shown to negatively regulate energy-sensing processes at central and peripheral sites. Here we used an ***in vitro*** and ***in vivo*** model to address whether lipid-induced toxicity correlates with an increase in inflammatory cytokine profile and changes in food intake during hypothalamic ghrelin stimulation. Primary microglia cultures and SIM-A9 cell line were incubated by 100 mM palmitic acid, palmitoleic acid, linoleic acid, stearic acid, N-Hexanoyl-D-sphingosine, or 0.1 µg/mL LPS (0111: B4) for 24h. IL-1β, IL-6 and TNF-α production were quantified by ELISA assays. ***In vivo*** lipotoxicity was performed by i.c.v. administration of LPS (0.1 µg/mL) or palmitic acid (32.4 mM) or artificial cerebrospinal fluid (ACSF) for 5 days following by ghrelin administration. Inflammatory activation was identified by TBK1-NFkbeta protein expression using western blot and ghrelin effects was analyzed by food intake quantification. Our results show that primary microglia and SIM-A9 stimulation by palmitic acid, palmitoleic acid or N-Hexanoyl-D-sphingosine promotes IL-1β, IL-6 and TNF-α and TNF-α release, respectively. Palmitic acid stimulation partially correlates with TBK1 activation evidenced by western blot. Also, we identified that lipotoxic stimulus by i.c.v. palmitic acid administration for 5 days does not disrupt plasma glucose homeostasis, however, it sensitizes

ghrelin signaling pathway promoting positive food intake following ghrelin administration when compare to rats i.c.v. administered with ACSF. Food intake sensitive to palmitic acid administration correlates with inflammatory activation evidenced by NF-κB whereas a reduction in TBK1 activation in the arcuate nucleus of hypothalamus. In summary, central lipotoxic insult by i.c.v. palmitic acid administration exacerbates the orexigenic effect of ghrelin promoting food intake stimulation which potentially correlates with TBK1-NF-κB pathway activation in arcuate nucleus.

Support
This work was funded by National Council of Science and Technology in Mexico (CONACYT-255317) and 573686 for Maldonado-Ruiz R.

Abstract Citation