manitoba neuroscience network

How ghrelin is a hormone that is important for coping with chronic stressors

SEMINAR & VISITING SPEAKER SERIES

DATE Tuesday, February 20th, 2024

TIME 12:00 PM to 1:00 PM

LOCATION BSMB THEATRE C

SPEAKER

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BIO

Dr. Alfonso Abizaid completed his BA, MA, and PhD in Psychology at Concordia University, where he received the Governor General Medal for his PhD work and was the valedictorian for the class of 2002. He then completed an NSERC-funded postdoctoral fellowship at Yale University School of Medicine. The Abizaid Lab is interested in the brain processes that integrate information from the environment to regulate feeding and energy balance. Their research focuses include the following:

-How metabolic hormones like ghrelin influence reward-seeking behaviours via actions on the mesolimbic reward system

-How the hormone ghrelin influences feeding as a coping mechanism to reduce the effects of chronic social stress

-How prenatal exposure to endocrine disruptors influences the development of brain systems implicated in the regulation of feed and energy balance

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ABSTRACT

Ghrelin, a peptide hormone primarily produced by the stomach and upper intestinal tract, binds to receptors in the central nervous system to modulate behaviors associated with increased feeding in response to negative energy balance states including chronic stress. The sites of action for these effects include the ventral tegmental area (VTA), a region that contains dopamine neurons linked to affective behavioral responses including reward seeking behaviors. Within the VTA, about 50-60 of these dopamine neurons express the only known ghrelin receptor, the growth hormone secretagogue receptor (GHSR), and these cells respond to GHSR stimulation by increasing their firing frequency and by releasing dopamine at terminal regions like the nucleus accumbens. Direct ghrelin infusions in the VTA also result in increased food intake and food motivation in rodents. Here we present data showing that the GHSR is present in several cell types within midbrain structures like the VTA and including dopamine producing neurons in mice and rats. Moreover, in some structures the GHSR is co-expressed with CB-1R in non- dopaminergic cells. We also show that alterations in GHSR signaling result in alterations in cannabinoid signalling within the VTA, and that blocking the cannabinoid receptor-1 subtype (CB-1R) attenuates the effects of ghrelin on food intake and motivation when infused into the VTA. Electrophysiological experiments demonstrate that ghrelin increases dopamine cell excitability in part through an increase in pre-synaptic excitatory tone, and that this increase is prevented by CB-1R antagonists. All of these data together point to a multilayered effect of ghrelin on VTA neurons that promotes excitatory tone on dopamine cells and that is dependent on the release of endocannabinoids to enhance food motivation.

OBJECTIVES

1. To show show evidence that ghrelin, a metabolic hormone produced by the stomach, is important for the regulation of motivated behaviors by acting on the mesolimbic dopaminergic system.

2. To demonstrate cellular and molecular mechanisms of ghrelin action on dopamine cells in the VTA.

3. To demonstrate how ghrelin acts on the VTA may be important to maintain homeostasis in the face of chronic stress.

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