



Hypothalamic mechanisms of depression associated with diabetes (DAD)

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Abstract

Ample evidence indicates that depression is a common comorbid of diabetes, which represents a major health concern as its rates have been steadily increasing in the world. However, there are still no effective treatments to ameliorate the depression associated with diabetes, which might be attributable to our incomplete understanding of the implicated pathological processes. Agouti- related protein (AgRP) neurons in hypothalamic arcuate nucleus (ARC) play crucial roles in the regulation of glucose levels, and corticotropin-releasing hormone (CRH) neurons in hypothalamic paraventricular nucleus (PVN) modulates hypothalamus-pituitary-adrenal (HPA) functions by terminating the median eminence (ME), a brain region connected to the ARC. It is thus paramount important to define and characterize the AgRP to CRH axonal connections in the ME and potential alterations implicated in depressive-like behaviors associated with diabetes. Our photometry data show that the activity of GABAergic AgRP neurons and the level of AMPK in these neurons are increased in diabetes and depression, and AMPK orchestrates the activity of AgRP neurons. More interestingly, the GABA neurotransmitter exerts excitatory effects in the ME. Together, our results let us propose that sustained stimulated AgRP neurons in diabetes enhance the HPA functions via AgRP-CRH axon connections in the ME, resulting in hypercortisolemia and subsequent hippocampal dysfunctions and depression.

Biography

Yunlei Yang completed his MD/PhD in China, and received his postdoctoral training at The Rockefeller University, Icahn School of Medicine at Mount Sinai, and Janelia Research Campus Howard Hughes Medical Institute. In 2012, he started his laboratory at SUNY Upstate Medical University and then relocated to Albert Einstein College of Medicine in 2017. He has been investigating hypothalamic synaptic plasticity and neural circuit rewiring in both normal and pathological conditions including obesity and diabetes, and related animal behaviors. He has published around 30 research articles in high-profile journals.



22nd Annual Meet on Obesity and Diet | December 17-18, 2021

Citation: Yunlei Yang, Hypothalamic mechanisms of depression associated with diabetes (DAD), Obesity 2021, 22nd Annual Meet on Obesity and Diet | December 17-18, 2021,04