The effect of insulin on excitatory synaptic transmission in the rat dorsomedial hypothalamus

by

Christelinda Laureijs

A thesis submitted to the
Department of Biology
Mount Allison University
in partial fulfillment of the requirements for the
Bachelor of Science degree with Honours
in Biology

April 10, 2024

This thesis was typeset in R Markdown and the text was set in EB Garamond. The data and code used to produce this document are available at *https://github.com/christelinda-laureijs/honours-thesis*.

Abstract

Insulin plays a key role in regulating blood glucose levels and it also acts in brain regions involved with appetite regulation. The dorsomedial hypothalamus (DMH) is one such brain region, and although it is a major site of insulin receptors, virtually nothing is known about the effect of insulin on neuronal activity and communication between DMH neurons. Since DMH neurons stimulate appetite and insulin is a satiety hormone, I hypothesized that insulin inhibits both neuronal activity and neuronal communication in the DMH. I used whole-cell patch clamp electrophysiology to record from living DMH neurons taken from young male and female Sprague-Dawley rats. I compared recordings before and after applying 500 nM of insulin (Labouèbe et al., 2013) to determine the effect of insulin on action potentials (a measure of neuronal excitability) and excitatory synaptic transmission (a measure of neuronal communication). Insulin significantly decreased action potential frequency and excitatory current amplitudes in both sexes, indicating that insulin decreases neuronal excitability and excitatory synaptic transmission in the DMH. Recordings taken with various insulin receptor blockers present suggested that insulin binds to insulin-like growth factor 1 receptors. Insulin signalling in the DMH is also independent of feeding state, suggesting that it is involved with regulating physiological processes beyond appetite regulation. This research contributes to our understanding of how insulin acts in the brain to influence energy metabolism, with direct applications to research on the pathophysiological effects of insulin resistance in obesity and diabetes.

Contents

List of Figures

List of Abbreviations

DMH	Dorsomedial hypothalamus
GABA	Gamma-aminobutyric acid
eEPSC	Evoked excitatory post-synaptic current
PPR	Paired pulse ratio
HNMPA	Hydroxy-2-naphthalenylmethylphosphonic acid
PPP	Picropodophyllotoxin

Labouèbe, G., Liu, S., Dias, C., Zou, H., Wong, J. C. Y., Karunakaran, S., Clee, S. M., Phillips, A., Boutrel, B., & Borgland, S. L. (2013). Insulin induces long-term depression of VTA dopamine neurons via an endocannabinoid-mediated mechanism. *Nature Neuroscience*, *16*(3), 300–308. https://doi.org/10.1038/nn.3321