**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 89031

**Manuscript Type:** LETTER TO THE EDITOR

**Epinephrine also acts on beta cells and insulin secretion**

Zabuliene L *et al*. EPI and insulin

Lina Zabuliene, Ioannis Ilias

**Lina Zabuliene,** Faculty of Medicine, Vilnius University, Vilnius LT-03101, Lithuania

**Ioannis Ilias,** Department of Endocrinology, “Hippokration” General Hospital, Athens GR-11527, Greece

**Author contributions:** Zabuliene L and Ilias I researched for this work; Zabuliene L and Ilias I wrote the manuscript. Both authors agree to this publication.

**Corresponding author: Ioannis Ilias, MD, PhD, Director,** Department of Endocrinology, “Hippokration” General Hospital, No. 63 Evrou Street, Athens GR-11527, Greece. iiliasmd@yahoo.com

**Received:** October 18, 2023

**Revised:** January 30, 2024

**Accepted:** March 4, 2024

**Published online:**

**Abstract**

In a recent review examining neurotransmitter modulation of insulin secretion, the significant impact of epinephrine was not addressed. Its primary action involves inhibiting insulin release *via* alpha-adrenergic receptors, thereby reducing the response to insulin secretion stimulators, through the activation of K+ channels and resulting in membrane hyperpolarization in beta cells.

**Key Words:** Epinephrine; Insulin; Islets; Glucose; Human

Zabuliene L, Ilias I. Epinephrine also acts on beta cells and insulin secretion. *World J Clin Cases* 2024; In press

**Core Tip:** Among the neurotransmitters influencing insulin secretion, the role of epinephrine (EPI) might be underestimated. EPI mainly inhibits insulin release through alpha-adrenergic receptors, thereby attenuating the response to insulin secretion stimulators.

**TO THE EDITOR**

We have reviewed with interest the concise examination by Kong *et al*[1] of neurotransmitter influence on insulin secretion. While the authors extensively cover norepinephrine (NEPI), the role of epinephrine (EPI) is overlooked. Both EPI and NEPI, acting as neurotransmitters and hormones, are synthesized and released in the central and peripheral nervous systems and the adrenal medulla[2]. Despite NEPI's primary role as a neurotransmitter, the significance of EPI, which also functions as a hormone, should not be disregarded for its neurotransmitter functions. Hence, EPI's impact closely parallels that of NEPI, though with more pronounced peripheral effects[2].

EPI can prompt insulin release *via* beta-adrenergic receptor activation, involving adenylate cyclase, cAMP generation, and the cAMP Response Element-Binding Protein pathway[3]. However, its primary effect, mediated by alpha-adrenergic receptor activation, inhibits insulin secretion through the Protein kinase A pathway. This inhibition significantly moderates the response to insulin's strongest stimulants[4]. EPI achieves this by activating K+ channels, leading to hyperpolarization of pancreatic beta cell membranes[5,6].

The above concise overview of EPI's impact on insulin secretion complements the excellent and comprehensive review of neurotransmitter effects on insulin secretion[1].

**REFERENCES**

1 **Kong CC**, Cheng JD, Wang W. Neurotransmitters regulate β cells insulin secretion: A neglected factor. *World J Clin Cases* 2023; **11**: 6670-6679 [PMID: 37901031 DOI: 10.12998/wjcc.v11.i28.6670]

2 **Kapalka GM.** Chapter 4-Substances Involved in Neurotransmission. Kapalka GM, editor. Nutritional and Herbal Therapies for Children and Adolescents. 2010; 71-99. Available from: https://www.sciencedirect.com/book/9780123749277/nutritional-and-herbal-therapies-for-children-and-adolescents

3 **Belgardt BF**, Stoffel M. SIK2 regulates insulin secretion. *Nat Cell Biol* 2014; **16**: 210-212 [PMID: 24576898 DOI: 10.1038/ncb2925]

4 **Hiatt N**, Davidson MB, Chapman LW, Sheinkopf JA. Epinephrine enhancement of potassium-stimulated immunoreactive insulin secretion. Role of beta-adrenergic receptors. *Diabetes* 1978; **27**: 550-553 [PMID: 206480 DOI: 10.2337/diab.27.5.550]

5 **Zhang Y**, Shumilina E, Häring HU, Lang F, Ullrich S. Epinephrine-induced hyperpolarization of pancreatic islet cells is sensitive to PI3K-PDK1 signaling. *FEBS Lett* 2009; **583**: 3101-3106 [PMID: 19716369 DOI: 10.1016/j.febslet.2009.08.027]

6 **Rorsman P**, Ashcroft FM. Pancreatic β-Cell Electrical Activity and Insulin Secretion: Of Mice and Men. *Physiol Rev* 2018; **98**: 117-214 [PMID: 29212789 DOI: 10.1152/physrev.00008.2017]

**Footnotes**

**Conflict-of-interest statement:** Authors report that they have no conflict of interest to declare.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** October 18, 2023

**First decision:** January 30, 2024

**Article in press:**

**Specialty type:** Medicine, research and experimental

**Country/Territory of origin:** Greece

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Jovandaric MZ, Serbia **S-Editor:** Qu XL **L-Editor:** A **P-Editor:**