Fluoxetine Impairs Insulin Secretion without Modifying Extracellular Serotonin Levels in MIN6 beta-cells

Por: Cataldo, LR (Cataldo, L. R.)[1,2]; Cortes, VA (Cortes, V. A.)[1]; Mizgier, ML (Mizgier, M. L.)[1]; Aranda, E (Aranda, E.)[3];Mezzano, D (Mezzano, D.)[3]; Olmos, P (Olmos, P.)[1]; Galgani, JE (Galgani, J. E.)[1,4]; Suazo, J (Suazo, J.)[5]; Santos, JL(Santos, J. L.)[1]

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Resumen

Introduction: Pancreatic -cells synthetize and store Serotonin (5-Hydroxytriptamine, 5HT) which is co-released with insulin. It has been proposed that extracellular 5HT binds to specific cell surface receptors and modulate insulin secretion. On the other hand, Selective Serotonin Reuptake Inhibitor (SSRI) fluoxetine seems to reduce Glucose-Stimulated Insulin Secretion (GSIS). However, it is unknown whether this effect results from changes in extracellular 5HT concentration owed to the blockade of 5HT transporter (SERT) or from non-5HT dependent actions. The aims of this work were: 1) to quantify extracellular 5HT levels and GSIS in -cell lines, 2) to determine whether extracellular 5HT levels and GSIS are changed by fluoxetine or 5-Hydroxytryptophan (5HTP, the immediate 5HT biosynthetic precursor), and 3) to quantify the expression of Slc6a4 gene (encoding SERT) in -cell lines in relation to other genes involved in 5HT system.

Material and Methods: -cell lines MIN6 and RINm5f were subjected to GSIS protocols, after treatment with fluoxetine, 5HTP or 5HT. Insulin and 5HT were quantified by ELISA and HPLC, respectively. Relative mRNA expression was quantified by RT-qPCR.

Results: MIN6 -cells secretes 5HT in response to glucose, showing a sharp increase in 5HT release when cells were preloaded with 5HTP. Treatment with 5HT or fluoxetine reduces GSIS. Fluoxetine fails to further increases 5HTP-induced elevation of secreted 5HT. MIN6 -cells express both isoforms of Tryptophan Hydroxylase (Tph1 and Tph2), and have high expression levels of L-Dopa decarboxylase (Ddc), both enzymes involved in 5HT biosynthetic pathway, but do not express the 5HT transporters Slc6a4 or Slc6a3 (the Dopamine-5HT transporter) genes.

Conclusion: The inhibitory effect of fluoxetine on -cell glucose stimulated insulin secretion is not mediated by blockage of 5HT transporter through SERT.

Palabras clave

Palabras clave de autor:beta-cell; insulin secretion; serotonin; fluoxetine
KeyWords Plus:PERIPHERAL SEROTONIN; DIABETES-MELLITUS; TRANSPORTER; GLUCOSE; SENSITIVITY; METABOLISM;DEPRESSION; PREGNANCY; INSIGHTS; MASS

Información del autor

Dirección para petición de copias: Santos, JL (autor para petición de copias)

Pontificia Univ Catolica Chile, Sch Med, Dept Nutr Diabet & Metab, Ave Libertador Bernardo Higgins 340, Santia

Direcciones:

[1] Pontificia Univ Catolica Chile, Sch Med, Dept Nutr Diabet & Metab, Santiago, Chile

[2] Univ Los Andes, Fac Med, Santiago, Chile

[3] Pontificia Univ Catolica Chile, Sch Med, Lab Hemostasia, Santiago, Chile

[4] Pontificia Univ Catolica Chile, Sch Med, UDA Ciencias Salud Carrera Nutr & Dietet, Santiago, Chile

[5] Univ Chile, Fac Dent, Inst Res Dent Sci, Santiago, Chile

Direcciones de correo electrónico:jsantos@med.puc.cl

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JOHANN AMBROSIUS BARTH VERLAG MEDIZINVERLAGE HEIDELBERG GMBH, RUEDIGERSTR 14, D-70469 STUTTGART, GERMANY

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