

A new insight of the protective role of estrogens in diabetes

April 5 2018





Estrogens influence the entire metabolism at stake, acting both on pancreatic cells producing GLP1 and on so-called L cells the gut harbors, whose main function is also to produce GLP1. Credit: UNIGE

Epidemiological data indicate an explosion of type 2 diabetes cases for women after menopause. What is responsible for that? The surprisingly protective role of oestrogens, highlighted by the fact that a woman undergoing hormone replacement therapy has up to 35 percent less risk of developing type 2 diabetes than a woman without treatment. By elucidating how oestrogen affects two of the hormones involved in glucose homeostasis, glucagon and GLP1, researchers at the University of Geneva (UNIGE), Switzerland, and at the Geneva University Hospitals (HUG) proved the value of oestrogen supplementation from the onset of menopause.

This research, published in *JCI Insight*, also shows that only one of the three oestrogen receptors seems to be involved in this mechanism. This could ultimately provide much more targeted therapies with a specific molecule that would prevent patients the sometimes embarrassing side effects when treated with a too-powerful hormone regimen.

Diabetes experts know that pre-menopausal women are less likely than men to develop type 2 diabetes. However, after menopause, the trend reverses very clearly, highlighting the protective role of women's sexual hormones and especially oestrogens. But what is their specific <u>effect</u> on metabolism? This question was answered by the team led by Jacques Philippe, Diabetes specialist at UNIGE Faculty of Medicine and Head of the HUG Department of Endocrinology, Diabetes, Hypertension and Nutrition.

"A number of scientists are working on the effect of oestrogens on



pancreatic insulin-producing cells," says Sandra Handgraaf, a researcher at the Faculty of Medicine and the first author of this work. "But its effect on glucagon-producing cells, another hormone regulating blood sugar, had never been explored before. Indeed, if the pancreas secretes insulin, it also secretes glucagon, a hormone with the opposite effect—insulin captures sugar, while glucagon releases it. Diabetes is therefore due to an imbalance between these two hormones controlling the sugar level in the blood."

Pancreatic cells, but also intestinal ones

Oestrogen administration to post-menopausal female mice led the Geneva scientists to identify an increased tolerance to glucose, which is correlated to a lower risk of diabetes. However, if the effect on insulin was expected, the effect on glucagon—and especially on GLP1, an intestinal and pancreatic hormone that increases insulin production—was much less so. These results confirmed the sensitivity to <u>oestrogen</u> of pancreatic alpha cells, which then secrete less hyperglycemic glucagon, but more GLP1. Also released by the intestine during the absorption of meal, this <u>hormone</u> stimulates the secretion of insulin, inhibits the secretion of glucagon and induces the feeling of satiety. The lack of GLP1 is therefore an essential and little-understood marker of the onset of diabetes. The role played by GLP1 represents a major explanation of the protection of women regarding diabetes onset before menopause.

"This first observation was already interesting," explains Sandra Handgraaf. "But we went a step further. The gut harbours cells called the L cells that are very similar to pancreatic alpha cells and whose main function is precisely to produce GLP1. We also observed a strong increase in the production of GLP1 in the gut cells, thus proving the crucial role of the intestine in the control of carbohydrate balance and the influence of oestrogens on the entire metabolisms at stake." These results were also confirmed on human <u>cells</u> and tissue samples.



Interesting substitution treatments

Hormonal substitution treatments are often subject to negative publicity, mainly because of the cardiovascular risks associated with them. "It is important to remember that hormonal substitution, when taken at the beginning of menopause and for a few years only, does not cause any particular risk of cardiovascular events," stresses Jacques Philippe. "However, if hormonal treatment is taken more than 10 years after menopause, the cardiovascular risk is effectively increased. In the context of diabetes, an oestrogenic treatment allows to avoid, in all cases, the explosion of female <u>diabetes</u> cases. These treatments, well administered, can really add value for women's health."

In their study, the Geneva researchers were also able to dissect the fine cellular mechanisms involved: Of the three oestrogens receptors, only one is mainly involved in this protective effect. It would therefore be possible to develop a molecule that only activates the interesting receptor, with a much more targeted effect. "One could imagine a treatment that, without the side effects of a little too powerful hormonal therapy, would also address men," concludes Sandra Handgraaf.

More information: JCI Insight, DOI: 10.1172/jci.insight.98569

Provided by University of Geneva

Citation: A new insight of the protective role of estrogens in diabetes (2018, April 5) retrieved 6 May 2024 from <u>https://medicalxpress.com/news/2018-04-insight-role-estrogens-diabetes.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.