

Learning more about the endocrine system could lead to fewer cases of type 2 diabetes and obesity

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Nurse Anna Hellman measures the blood pressure of a participant in a treatment study where researchers are investigating how the hormone vasopressin is affected by how much water we drink. Credit: Kennet Ruona

How much water do we need to drink to stay healthy? How do different diets affect our metabolism? Studies of various hormones in the body

are providing diabetes researchers with new answers to these questions. The goal is to develop individualized treatments and dietary recommendations that could lower the risk of developing obesity and diseases such as type 2 diabetes.

The endocrine system and the nervous system work together to control a lot of what happens in the body, for example regulating our metabolism. Neurotensin and vasopressin are two of the hormones that are being studied by [diabetes](#) researchers at Lund University. By learning more about these hormones, researchers can discover who is at risk of developing obesity and type 2 diabetes.

Neurotensin is released from the gastrointestinal tract after we have consumed fat. Research at Lund University has shown that neurotensin can be used as a biomarker to predict the risk of developing [cardiovascular disease](#), type 2 diabetes, and [fatty liver disease](#).

Olle Melander heads a research group that has published several studies about neurotensin's importance when it comes to the risk of developing disease.

"During the stone age, when access to food was limited, there were survival benefits in being able to store high-fat foods. This ability is not so good today when there is an abundance of food in many parts of the world. Our studies have shown that there is an association between raised levels of the hormone after fat consumption and the risk of developing type 2 diabetes, cardiovascular disease, and fatty liver," says Olle Melander, professor of internal medicine at Lund University and affiliated with the strategic research area EXODIAB (Excellence of Diabetes Research in Sweden).

Preventive treatments

Could a reduced intake of fat help individuals with high levels of neurotensin in the blood? Perhaps, but it could also potentially lead to an increased concentration of neurotensin in the blood due to compensatory mechanisms. Therefore, Olle Melander and his research group are planning to start treatment studies where they investigate if an already approved drug can reduce the production of neurotensin.

"Unfortunately, type 2 diabetes can cause many different types of complications, such as myocardial infarction, stroke, and other diseases. The main goal of our research is to find ways to prevent type 2 diabetes and its most serious complications," says Olle Melander.

Studies of increased water intake

Drugs can treat certain hormonal disturbances effectively, but in some cases, it may be better to look at the effect natural products have on the endocrine system. Olle Melander's research group is currently studying the vasopressin hormone in a treatment study with participants who don't usually drink a lot of water.

Vasopressin is released when the body is dehydrated, or when the concentration of salts in the blood is high. Researchers measure the stable part of vasopressin, called copeptin, in their studies and have found that there is a connection between high levels of copeptin and the development of diseases such as type 2 diabetes, myocardial infarction, and renal failure.

"A [pilot study](#) that we carried out on healthy people showed that increased water intake reduced the levels of copeptin and fasting blood glucose concentrations. Now, we are carrying out a larger treatment study where we investigate if we can reduce the risk of type 2 diabetes in people with raised levels of the hormone."

To date, almost 700 participants have been recruited into the study, in which they drink one and a half liters of water extra a day in addition to their normal consumption over the course of a year. In connection with the study treatment, participants' blood glucose, blood pressure, and BMI (body mass index) values are measured regularly.

"The most important question we seek to answer is if an increased intake of water could reduce blood glucose levels in participants. We are also investigating if the intervention could lead to a reduction in BMI. We hope that the treatment results in a reduced incidence of diabetes in individuals with low water intake. It's probably easier to get people to drink more water than to change their dietary habits. This method is also easy to implement and would have a great impact at a population level," says Olle Melander.

Individualized diets

What happens with the two important hormones insulin and glucagon when we eat meals that are high in either fat or sugar? This is a question that another research group at Lund University are looking into.

Research group leader Peter Spéjel and his colleagues recently published a study in the journal *Acta Physiologica* that maps how different meals affect the relationship between the two hormones. Insulin is a hormone that builds muscles and fatty tissue, whilst glucagon breaks down the body's energy reserves.

"We need to better understand how the two hormones interact to develop individualized diets that suit people at different stages of life. An older person may need to gain weight to maintain [good health](#), whilst an overweight younger person may need to lose weight to prevent type 2 diabetes," says Peter Spéjel, corresponding author of the scientific article.

Carbohydrates have the most effect

The research team wanted to find out how the relationship between insulin and glucagon is affected by different nutrients using a value called the insulin glucagon ratio (IGR). Previous research on diabetes drugs have shown that drugs that lead to a high IGR, that is a lot of insulin in relation to glucagon, result in weight gain. Drugs that instead lead to a reduction in IGR, that is more glucagon in relation to insulin, result in weight loss. How the ratio is affected by diet has not yet been established.

The research team began by studying how the value was affected in the islets of Langerhans in mice. They saw an increase in the value when sugar was added, but the value remained unchanged when the cells were fed fat. In the next step, the team examined what happened in 20 people with type 2 diabetes and 20 people without the disease when they ate meals with different amounts of fat and carbohydrate. All participants ate one meal high in carbohydrates and one high in fat a couple of months apart. The levels of insulin and glucagon in the blood were measured after each meal and it was discovered that the meal high in carbohydrates resulted in a much higher IGR than the meal high in fat.

"Our study shows that carbohydrates have a bigger effect than fat on metabolism at group level, regardless of if the individual has type 2 diabetes or not. Results indicate that a diet low in carbohydrates could be good for people who want to lose weight. A diet low in fat and high in carbohydrates does however not seem to have the same effect. We need more studies in this field before we can develop new dietary recommendations. Here, we have studied what happens at a hormonal level and therefore we can't make assumptions about long-term effects of diets," says Peter Spégel, docent in molecular metabolism at Lund University and involved in the strategic research area EXODIAB.

In future studies, Peter Spégel will include other common nutrients, such as protein and fiber, to get a more complete picture. The journal *Acta Physiologica* highlights this study as an interesting example of how this type of research can make way for individually tailored dietary recommendations.

"It's very positive that our study was noticed and that we are acknowledged for the work we do on insulin and glucagon to gain a better understanding of metabolism. As a researcher, I'm interested in investigating how we can improve our health through what we eat. Drugs that contribute to weight loss are expensive in some parts of the world so it would be good if we could develop tailored diets to help people who need to lose weight," says Peter Spégel.

More information: Klinsmann Carolo dos Santos et al, The impact of macronutrient composition on metabolic regulation: An Islet-Centric view, *Acta Physiologica* (2022). [DOI: 10.1111/apha.13884](https://doi.org/10.1111/apha.13884)

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