

Study offers new hope for the fight against genetically determined obesity

June 3 2018



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Around 2 to 6 percent of all people with obesity develop the condition in early childhood. Obesity-causal mutations in one of the 'appetite genes' gives them a strong genetic predisposition for developing obesity, also called monogenic obesity. Their experience of hunger is overruling and their feeling of satiety limited.

In addition, this group of people with [obesity](#) respond less well to existing treatments than others. Diets and surgery can help them lose weight, but the long-term effect is poor, as they are unable to maintain the weight loss.

Now, there is hope for this group of people. In a new study published in the scientific journal *Cell Metabolism* researchers at the University of Copenhagen have discovered that people with such a [genetic predisposition](#) can lose weight with the help of liraglutide, a modified form of the appetite-inhibiting hormone GLP-1, naturally secreted from the intestines when eating.

"These people develop obesity because they are genetically programmed to do so. That is, they are struggling with what is probably the strongest human drive: the desire to eat and thus to survive. However, the appetite-inhibiting drug liraglutide has a positive effect on them. They feel less hungry and lose six percent of their body weight within four months," says the study leader, Associate Professor Signe Sørensen Torekov from the Department of Biomedical Sciences and the Novo Nordisk Foundation Center for Basic Metabolic Research.

Receptor Confusion

In this study the researchers have examined 14 persons with obesity caused by pathogenic mutations in the so-called MC4R gene and 28 persons with obesity without the mutations. Both groups were treated with the medicine for four months; no changes were made to their diet and level of exercise in this period.

The individuals with this most common form of monogenic obesity lost 7 kg of their body weight compared to 6 kg for the people with common obesity.

"We are positively surprised to see that the treatment has a good effect on this group of people. Many researchers have believed that the function of the medicine was mainly to inhibit the appetite by stimulating this specific appetite receptor in the brain which does not work in this particular group of people with obesity. However, our study shows that the medicine still has an appetite-inhibiting effect and thus must affect the appetite in a different way," says Signe Sørensen Torekov.

Medicine acting as an analogue to our natural GLP-1 hormone is already available, as it has been FDA and EMA licensed for the treatment of obesity and type 2 diabetes. The new study thus makes it possible to treat cases of the most common form of genetically caused obesity in which patients respond poorly to existing treatments.

"People who have suffered from obesity all their lives probably are not aware that it is caused by this mutation. It can therefore be a huge relief for many to learn why they have developed obesity and that there is actually a treatment that works," says first-author of the study, Ph.D. Student Eva Winning Iepsen at the Department of Biomedical Sciences and the Novo Nordisk Foundation Center for Basic Metabolic Research.

She also points out that the medicine makes it easier for people with this monogenic form of obesity to control their blood sugar. The [medicine](#) can thus also have an effect on diabetes and pre-diabetes often seen in this particular group of individuals with genetically determined obesity.

As MC4R mutations cause obesity already in early childhood, the researchers hope the results can pave the way for new studies on young people in the future. If they are able to prevent this condition before the young people reach adulthood, it will have a great positive effect on their health and perhaps also social stigmatization, the researchers believe.

More information: Eva W. Iepsen et al, Patients with Obesity Caused by Melanocortin-4 Receptor Mutations Can Be Treated with a Glucagon-like Peptide-1 Receptor Agonist, *Cell Metabolism* (2018). [DOI: 10.1016/j.cmet.2018.05.008](https://doi.org/10.1016/j.cmet.2018.05.008)

Provided by University of Copenhagen

Citation: Study offers new hope for the fight against genetically determined obesity (2018, June 3) retrieved 9 April 2024 from <https://medicalxpress.com/news/2018-06-genetically-obesity.html>

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