Medical Xpress

New genetic form of obesity and diabetes discovered

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This is an image of a weight scale. Credit: CDC/Debora Cartagena

Scientists have discovered a new inherited form of obesity and type 2 diabetes in humans.

A large number of genes are involved in regulating body weight, and there are now over 30 genes known in which people with harmful changes in DNA sequence become extremely overweight. Similarly,

there are a number of genes that can, when altered, cause type 2 diabetes . These conditions are inherited through families in exactly the same way as disorders such as cystic fibrosis or Huntington's disease.

It is unclear what proportion of severe obesity and type 2 diabetes is caused by genetic disease.

Researchers at Imperial College London discovered the new defect by sequencing the DNA of an extremely obese young woman and members of her family. In addition to an increased appetite leading to severe weight problems from childhood, she had type 2 diabetes, learning difficulties, and reproductive problems.

They found that she had inherited two copies of a harmful genetic change that meant she could not make a protein called carboxypeptidase-E (CPE). This is an enzyme that is important in the proper processing of a number of hormones and brain transmitters controlling appetite, insulin and other hormones important in the reproductive system.

Studies have previously shown that CPE deficiency causes obesity, diabetes, and impaired memory in mice, but no humans with the condition have been found before. CPE deficiency is a recessive condition, so a person would need to inherit the altered genetic sequence from both parents to be affected.

The study, published in the journal PLOS ONE, was funded by the NIHR Imperial Biomedical Research Centre and Diabetes UK.

Professor Alex Blakemore from the Department of Medicine at Imperial College London, who led the study, said: "There are now an increasing number of single-gene causes of obesity and diabetes known. We don't know how many more have yet to be discovered, or what proportion of the severely obese people in our population have these diseases - it is not

possible to tell just by looking.

"These are serious disorders that affect the body's ability to regulate hunger and fullness signals. They are inherited in the just same way as other genetic diseases and the sufferers should not be stigmatised for their condition. They should be offered genetic counselling and specialised lifelong support to allow them as healthy a life as possible."

The patient was clinically evaluated by consultant endocrinologist Dr Tony Goldstone, who runs a specialist genetics obesity clinic at Hammersmith Hospital. The patient's parents are cousins, giving her a relatively high likelihood of inheriting the same genetic change from both parents. She had an older brother with similar symptoms who died aged 21.

The first author Dr Sanne Alsters, also in the Department of Medicine, who carried out the genetic tests, said: "Finding a genetic cause for the patient's problems has helped her and her family to understand and manage her condition better. We can also look at members of her family with one abnormal copy of the gene, to see they are affected in more subtle ways that could increase their risk of obesity."

Professor Blakemore said genetic tests should be widely available for patients with severe obesity. "If people are diagnosed with a genetic condition like this one, we can look for other possible symptoms, and offer genetic advice to other family members if they want this. Diagnosis is very valuable to the patient. It helps to set realistic expectations, and can help them get the best possible treatment," she said.

More information: "Truncating homozygous mutation of carboxypeptidase E (CPE) in a morbidly obese female with type 2 diabetes mellitus, intellectual disability and hypogonadotrophic

hypogonadism." *PLOS ONE*, 29 June 2015. DOI: 10.1371/journal.pone.0131417

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