New study finds strong link between obesity and 'carb breakdown' gene

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Juan Carreño de Miranda?'s "La monstrua desnuda" (The Nude Monster) painting.

Researchers at King's College London and Imperial College London have discovered that people with fewer copies of a gene coding for a carb-digesting enzyme may be at higher risk of obesity. The findings, published in *Nature Genetics*, suggest that dietary advice may need to be more tailored to an individual's digestive system, based on whether they have the genetic predisposition and necessary enzymes to digest different foods.

Salivary amylase plays a significant role in breaking down carbohydrates in the mouth at the start of the digestion process. The new study suggests that people with fewer copies of the AMY1 gene have lower levels of this enzyme and therefore will have more difficulty breaking down carbohydrates than those with more copies.

Previous research has found a genetic link between obesity and food behaviours and appetite, but the new discovery highlights a novel genetic link between metabolism and obesity. It suggests that people's bodies may react differently to the same type and amount of food, leading to weight gain in some and not in others. The effect of the genetic difference found in the latest study appears much stronger link than any of those found before.

Researchers first measured gene expression patterns in 149 Swedish families with differences in the levels of obesity and found unusual patterns around two amylase genes (AMY1 and AMY2), which code for salivary and pancreatic amylase. This was suggestive of a variation in copy numbers relating directly to obesity.

The finding was replicated strongly in 972 twins from TwinsUK, the biggest UK adult twin registry, which found a similar pattern of expression. The researchers then estimated the precise copy numbers of the amylase gene in the DNA of a further 481 Swedish subjects, 1,479 subjects from TwinsUK and 2,137 subjects from the DESIR project.

The collaborative team found that the number of copies of the AMY1 gene (salivary amylase) was consistently linked to obesity. Further replication in French and Chinese patients with and without obesity showed the same patterns.

A lower estimated AMY1 copy-number showed a significantly increased risk of obesity in all samples and this translated to an approximate eight-fold difference in the risk of obesity between those subjects with the highest number of copies of the gene and those with the lowest.

Standard Genome wide mapping methods (GWAS) had missed this strong association as the area is technically hard to map. This variation in copy numbers, also known as 'copy number variants'

(CNV) has been underestimated as a genetic cause of disease, but the link between CNV in the amylase gene and obesity provides an indication that other major diseases may be influenced by similar mechanisms.

Professor Tim Spector, Head of the Department of Twin Research and Genetic Epidemiology at King's College London and joint lead investigator said: "These findings are very exciting. While studies to date have mainly found small effect genes that alter eating behaviour, we discovered how the digestive 'tools' in your metabolism vary between people – and the genes coding for these – can have a large influence on your weight.

"The next step is to find out more about the activity of this digestive enzyme, and whether this might prove a useful biomarker or target for the treatment of obesity.

"In the future, a simple blood or saliva test might be used to measure levels of key enzymes such as amylase in the body and therefore shape dietary advice for both overweight and underweight people. Treatments are a long way away but this is an important step in realising that all of us digest and metabolise food differently – and we can move away from 'one-size fits all diets' to more personalised approaches."

More information: Low copy number of the salivary amylase gene predisposes to obesity, *Nature Genetics*, DOI: 10.1038/ng.2939

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