Medical Xpress

# Slim people have a genetic advantage when it comes to maintaining their weight

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In the largest study of its kind to date, Cambridge researchers have looked at why some people manage to stay thin while others gain weight easily. They have found that the genetic dice are loaded in favour of thin

people and against those at the obese end of the spectrum.

More than six in ten adults in the UK are overweight, and one in four adults is obese. By age five, almost one in four children is either overweight or obese. Excess weight increases the risk of related health problems including type 2 diabetes and heart disease.

While it is well known that changes in our environment, such as easy access to high calorie foods and sedentary lifestyles, have driven the rise in obesity in recent years, there is considerable individual variation in weight within a population that shares the same environment. Some people seem able to eat what they like and remain thin. This has led some people to characterise overweight people as lazy or lacking willpower.

With support from Wellcome and the European Research Council, a team led by Professor Sadaf Farooqi at the Wellcome-MRC Institute of Metabolic Science, University of Cambridge, established the Study Into Lean and Thin Subjects - STILTS - to examine why and how some people find it easier to stay thin than others. Studies of twins have shown that variation in body weight is largely influenced by our genes. To date studies have overwhelmingly focused on people who are overweight. Hundreds of genes have been found that increase the chance of a person being overweight and in some people faulty genes can cause severe obesity from a young age.

Professor Sadaf Farooqi's team were able to recruit 2,000 people who were thin (defined as a body mass index (BMI) of less than 18 kg/m2) but healthy, with no medical conditions or eating disorders. They worked with general practices across the UK, taking saliva samples to enable DNA analysis and asking participants to answer questions about their general health and lifestyles. It is thought to be the only cohort of its kind in the world and the researchers say that the UK's National Institute

for Health Research—the National Health Service's research infrastructure—strongly enabled and supported their research.

In a study published today in the journal *PLOS Genetics*, Professor Farooqi's team collaborated with Dr. Inês Barroso's team at the Wellcome Sanger Institute to compare the DNA of some 14,000 people -1,622 thin volunteers from the STILTS cohort, 1,985 severely obese people and a further 10,433 normal weight controls.

Our DNA comprises of a sequence of molecules known as base pairs, represented by the letters A, C, G and T. Strings of these base pairs form genetic regions (which include or make up our genes). Our genes provide the code for how our body functions and changes in the spelling—for example, a C in place of an A—can have subtle or sometimes dramatic changes on features such as hair colour and eye colour but also on a person's weight.

The team found several common genetic variants already identified as playing a role in obesity. In addition, they found new genetic regions involved in severe obesity and some involved in healthy thinness.

To see what impact these genes had on an individual's weight, the researchers added up the contribution of the different genetic variants to calculate a genetic risk score.

"As anticipated, we found that obese people had a higher genetic risk score than normal weight people, which contributes to their risk of being overweight. The genetic dice are loaded against them," explains Dr. Barroso.

Importantly, the team also showed that thin people, had a much lower genetic risk score—they had fewer genetic variants that we know increase a person's chances of being overweight.

"This research shows for the first time that healthy thin people are generally thin because they have a lower burden of genes that increase a person's chances of being overweight and not because they are morally superior, as some people like to suggest," says Professor Farooqi. "It's easy to rush to judgement and criticise people for their weight, but the science shows that things are far more complex. We have far less control over our weight than we might wish to think."

Three out of four people (74%) in the STILTS cohort had a family history of being thin and healthy and the team found some genetic changes that were significantly more common in thin people, which they say may allow them to pinpoint new genes and biological mechanisms that help people stay thin.

"We already know that people can be thin for different reasons" says Professor Farooqi. "Some people are just not that interested in food whereas others can eat what they like, but never put on weight. If we can find the genes that prevent them from putting on weight, we may be able to target those genes to find new weight loss strategies and help people who do not have this advantage."

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