Why some people are lean and others fat

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Venus de Willendorf, Natural History Museum, Vienna. Credit: Georgi Nemtzov, Flickr

With an abundance of food available, it's not surprising that people are getting fatter. But why do some people remain lean? A Cambridge University scientist suggests that the reason is rooted deep in our DNA.

There are few healthcare topics as emotive or contentious as obesity, a condition that currently affects 24 per cent of women and 23 per cent of men in the UK and is rapidly increasing. What we eat and how we eat, what shape and weight we are, and how we view ourselves and our bodies, is the outcome of a complex web of physiological, psychological, cultural and social factors.

Yet people who are fat, let alone clinically obese, are often dismissed by

their leaner peers as greedy, lazy and stupid. "Eat less and move more," they are repeatedly told. But it is not nearly as simple as that, says Professor Stephen O'Rahilly, Co-Director of the Institute of Metabolic Research, University of Cambridge, and one of the country's leading obesity researchers.

Professor O'Rahilly is a man with a mission: to share his belief that to tackle the epidemic of obesity in the developed world requires a nuanced and multi-stranded approach. He will be giving a public talk at the Cambridge Science Festival (comms.group.cam.ac.uk/sciencefestival/) on 18 March to bring some key facts to the attention of his audience and counteract some of the prejudices that overweight people face.

At the core of the problem lies one immutable fact: this is the abundance of cheap food now available to almost everyone in the developed world, an "unnatural" situation that has evolved over the past 50 years, a period that is the merest blip in terms of human evolutionary history.

"Human beings are not genetically geared up to limitless high-calorie food being available to them 24/7. We evolved as hunter gatherers. If we all reverted to the lifestyle of our ancestors, the problem of obesity would disappear," said Professor O'Rahilly. "But we live in the real world where you can purchase a takeaway meal, containing enough calories for a day, for less than £2 - so we need to look at the whole picture."

As well as presenting the big picture, he will outline the latest genetic research, which looks not just at why so many people are fat but also at why many others remain lean, even when food is equally available.

The most exciting recent hypothesis adjusts the notion of "thrifty genes", genetic variants that promote the acquisition and storage of calories, to that of "drifty genes", genetic variants that have not been selected for or

against during most of human evolution and which are somewhat randomly distributed throughout human populations, but which now, in the face of abundant food availability, strongly influence why some people are predisposed to becoming fat while others effortlessly remain lean.

"Everyone has views about obesity and views are often rather fixed and based on personal experience or anecdote. Obese people are significantly discriminated against. Research tracking the careers of large numbers of US teenagers has shown that those who are fat go on to earn substantially less as adults than those who are not fat, and that is even when factors such as education, parental income and scholastic aptitude are accounted for," he said.

"To be blunt, in today's society it's definitely not ok to be racist or sexist and it's increasingly not ok to be ageist which is all to the good - but it still seems to be quite ok to be fattist even, and perhaps especially, in highly educated circles. This isn't helping us with the serious science that will help provide some answers."

Heading a team of scientists looking at the underlying reasons for obesity and its adverse consequences, O'Rahilly describes himself as being on the "nerdy end" of metabolic research. While other colleagues in the Institute of Metabolic Science institutes are investigating environmental contributions to obesity and diabetes, his own particular expertise is in exploring the biological systems that control human body weight and metabolism and how genetic variation influences how well, or badly, these systems work in one person vs. another

"We know for sure that a propensity for obesity - or its opposite, a propensity for leanness - is rooted in the genes. Some 70 per cent of the variation between people in terms of their amount of body fat is explained by inherited differences that are built into our genetic make-

up and passed from generation to generation," he said.

"What our work has shown is that, rather unexpectedly, a lot of these genes primarily influence appetite and satiety, i.e. how hungry we get and/or how satisfied by a particular amount of food we are, rather than how fast or slow we burn off calories."

In the 1960s, the American geneticist James Neel developed what became known as the "thrifty gene" theory to explain the increase in obesity that lay behind a rise in diabetes. According to his hypothesis, the thrifty genotype would have been advantageous for early humans allowing them to store fat in times of abundance and survive in times of food scarcity. In modern societies with an abundance of food, this genotype prepares individuals for a famine that never comes. The result is obesity and diabetes.

The thrifty gene argument begs the question: in the face of the abundance of cheap food present in most modern societies, why isn't everyone fat? "The biologist John Speakman from Aberdeen University has re-examined the thrifty gene theory and suggested that it doesn't necessarily add up. He has suggested that famines weren't a huge threat before the advent of farming - about 15000 years ago - and could not have had sufficient a differential impact on survival of the lean and obese as to have had such a powerful selective effect," said Professor O'Rahilly.

Speakman has come up with an alternative theory, nicknamed the 'drifty gene' hypothesis. He argues that the modern distribution of obesity stems from a genetic drift in the genes encoding the system that regulates metabolism and controlling an upper limit on our body fatness. Such a drift may have started because around 2 million years ago when ancestral humans ceased to be prey, which was probably a key factor maintaining the upper boundary of the regulation system.

"The drifty gene theory provides a more satisfying explanation of why, even in places where obesity is very common, a large proportion of the population remains lean," said Professor O'Rahilly.

Such debates about the biology of obesity and its origins are not merely of theoretical and academic interest. A better understanding of how body weight and fatness are controlled will be critical if we are to come up with effective strategies to reduce the adverse health consequences of obesity through improvements in our approaches to prevention and treatment.

Provided by University of Cambridge

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