00:06

Have you ever wondered why a pair of siblings living in the same house with the same parents, with the same food, sometimes end up in opposite sides of the weight spectrum? My name is Mads and for the last 25 years, I've been studying what we eat, when we eat and how much we eat. And probably more importantly, I've been studying how each of our unique bodies responds differently to the same food and the same environment. To be more precise, I study obesity.

00:40

During my training as an MD, PhD, I was very fascinated by a series of experiments done by Barry Levin. He took 100 rats and subjected them to high-fat feeding. After months of feeding, he ended up with a bell-shaped curve and a weight distribution with some skinny rats and some obese rats and some in the middle. What he then did was to take the skinny rats and breed them among themselves, and the heavy rats. And he bred those among themselves. And after rounds of breeding, he ended up with two distinct populations: a diet-resistant rat and an obesity-prone rat. And here's the really interesting part. Then he took the skinny or the obese, and either massively over- or underfed them. And their weight would, of course, go up and down depending on the dietary regimen. But it was as if the little bodies would remember the same old weight trajectory. So once the dietary regimen was stopped, the rats went right back to the initial weight trajectory. It was like as if you could dress up the obese rat in a skinny sheep's clothing. But the obese rat nature was still scratching to get out.

02:01

The same thing applies to humans. If you take a thousand kids and weigh them, their weight will also be distributed in a bell-shaped curve. Some skinny, some in the middle and some heavy. We know that some of the skinny kids will remain skinny throughout life, and some of the obese kids will stay obese throughout life. You could argue that their weight, to some degree, has been predetermined. You could also argue that obesity is a disease. Wait, did I just say that obesity a disease? Yes. There's actually data and science that shows that. And I've made it my audacious life goal to come up with a solution to prevent, treat or even cure obesity. Let me explain.

02:53

In the early 1980s and 1990s, obesity was considered a potential global problem, a global problem of a magnitude that led WHO in the end of 1990s to declare obesity a global pandemic. And I probably don't have to tell you why. Higher rates of diabetes, hypertension, cardiovascular disease, even some cancers, osteoarthritis and a clear link to mental conditions such as depression. So as the number of obese individuals grew, so did the number of people suffering from these diseases. Today, more than 50 percent of the US adult population are living with

obesity or overweight. From a health perspective, that is devastating. But it's not only a US problem. The obesity surge has made obesity a global health problem.

03:50

Many inside and outside the medical community believe obesity is not a disease. They believe that obesity is a condition, a condition brought about by too much eating and too little exercise. As a matter of fact, a lot of people living with obesity think that too. They believe that their weight is 100 percent their own fault, which can lead to self-blame and low self-esteem, and perhaps even shame or stress eating, which is both heartbreaking, as well as counterproductive.

04:25

But where is the scientific proof that obesity is a disease? Well, medically speaking, there's many ways to define disease, but let me give you just three examples. As a process that impairs your functionality and reduces life expectancy -- obesity, check. You can define disease as a process that leaves you more susceptible to other diseases or causes disease. Obesity, check. Or you can define disease as a genetic impairment that leads to functional impairment, like, for instance, a duplication of genes on chromosomes. There is clear evidence that a single gene mutation can lead to obesity, such as, for instance, leptin deficiency and POMC deficiency. We also have two-three genes leading to obesity. And it's my prediction that we, by the year 2030, will be able to explain most obesity by the genetic makeup of the individual. So obesity as a disease by this measure, check.

05:34

Let me be clear. We humans have had the same genes for decades. And just recently, obesity has become a bigger problem. How do we then explain that? One obvious thing is actually food, especially calorie-rich food, which is much more readily available. It's relatively easy and also relatively cheap to eat your entire daily need of calories by a fast food or big soft drinks. So genes do play a role, but the environment also plays a huge role. The overabundance of calories in certain communities is a relatively new thing, and our genes haven't quite adapted yet. In the history of feast and famine, genetic selection has prepared us much better for famine, and for good reason. Starvation is bad, but you could also argue obesity is bad. And if obesity is a disease, how do we then prevent, treat or even cure it? I believe that the brain holds the key.

06:44

I have always been fascinated with how small electrical signals in discrete parts of the brain lead to big behavioral changes. And my study of the brain led me to Glucagon-Like Peptide 1, or GLP-1 for short. GLP-1 is a hormone and a signal molecule that is produced both in the gut and

in the brain. The brain speaks to the gut and the gut speaks to the brain. Yes, that's right. Your belly and your brain are literally connected.

07:19

Our research led us to see that GLP-1 has an effect on nerve cells sitting in areas that control whether we eat or not. So, for instance, if we increase the level of GLP-1, the body's desire to eat or overeat food gets turned off. GLP-1 serves as the full signal in your car's gas tank. I've spent years and decades mapping the circuitry of GLP-1 and how GLP-1 interacts with other signal molecules and hormones. All of these things go together and control food intake, body weight and the control of eating behavior. And what does that all mean? Well, today, we have engineered and studied the molecule, so we now have a molecule that can lead to a significant weight loss.

08:11

Obviously, GLP-1 is not the whole answer. We and others have discovered numerous hormones and other signal molecules that are also pivotal for the regulation of food intake and body weight. And it may end up that these signal molecules and hormones are even more important than GLP-1. So ... There's plenty for us to do. There's still plenty for us to explore. So this is not the end. It's not even the beginning to the end. But perhaps this may be the end to the beginning.

08:49

We may have a massive weight crisis on the planet today, but the good news is we are on the right path. We now have solutions for people living with obesity, and the next steps will be to understand even better the problems people living with obesity are facing. To understand even better how genes and environment play together. And understand, finally, how all these things come together and determine our body weight. Then, and maybe just then, we will be able to come up with a prevention, a treatment or even a cure for people living with obesity, like we strive for with any other chronic disease. And this -- this still remains our audacious life’s goal.

09:39

Thank you.