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Of fidgets and food

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When you're hungry, your thoughts go towards food. Without the urge to get up and find some, you're in trouble. It's a basic rule. Yet when transgressed one way or another, you can end up either overweight or underweight. It may sound silly because we feel – as humans – that we can decide for ourselves when to open the fridge or not. As it happens, we tend to an awful lot because eating is one of our pleasures. Consequently, we gather a surplus of energy which we stock around our buttocks and stomachs. However, given a little thought, moving for a meal is not so straightforward. Imagine a chicken whose organism needs fuel. If deprived of the sense of hunger, it may well do nothing about it, and starve. So there must be some underlying mechanism which pushes it to hunt down a grain or two; a mechanism which actually drives it to move elsewhere in pursuit of the calories it needs. Naturally, such a mechanism is always very complex. Yet scientists have discovered a protein – known as Bsx protein – which seems to be at the heart of both fidgeting and food intake, and hence of the propensity to be either stout or slim.

Old Woman Eating Peas, Jeannette Langmead

Courtesy of the artist

Movement or not, some people seem to stay lean whatever their calorie intake. This could be because they are the carriers of a 'fidget' gene, which makes them shuffle and shift more than necessary – as far as energy balance goes. Bsx – or Brain specific homeobox – is the fidget gene. Mice that carry the wild type version were recently shown to be ten times more active than those who carry the mutated form. As a consequence, in an environment where food is plentiful, the laid back mice will tend to stock fat whereas their more active counterparts will keep trim. So far, nothing new. We are all aware that a lack of exercise is not ever going to help you lose weight. But if you take it one step further, what would be the point of a protein that is there to make you move with regard to energy homeostasis?

Such proteins are likely to be the product of a proposed complex gene network, known as the thrift gene network. The thrift gene theory made its first appearance in the 1960s. It hypothesizes that animals carry a set of genes where the act of overfeeding coincides with food abundance, and stocks are made with the future prospect of famine. In our day and age though, there is so little famine in some parts of the world that, in many instances, there is a lot of overeating. Subsequently, many people are overweight. The thrift gene theory is an elegant attempt to explain obesity which is spreading worldwide. However, like all theories, it has met with some distaste and a number of scientists have suggested that being overweight is less a question of fat collected in the event of future starvation, than humans who are less faced – if not at all – with problems linked to predation, which are not only the source of stress but also get you moving.

It remains that Bsx certainly seems to be a protein involved both in locomotion and food intake. It is one of over a hundred homeoproteins isolated in mice. They are

transcription factors and Bsx, in particular, is largely expressed in the hypothalamus, the part of the brain involved in many important activities, including appetite, or the lack of it. Furthermore, Bsx not only seems to be important for the correct development of the embryonic brain as well as its adult function, but is also involved in the formation and maintenance of the mammary glands.

The hypothalamus organises two major networks of neurons, one of which encloses the NPY/AgRP hypothalamic neurons which regulate feeding behaviour and body weight. Bsx is not only expressed in NPY/AgRP neurons but is also required for their expression. As a consequence, Bsx not only affects the hypothalamus itself but also distant target organs – such as the mammary glands, for instance. So far, Bsx has been found in vertebrates as diverse as humans, mice, chicken, zebrafish and frogs. Hence, it is a little surprising to discover that Bsx has a role in mammary gland formation. This implies that, over time, the protein has acquired an additional function in mammals. A function still linked to food, nevertheless…

Involved in the molecular regulation of not only feeding but also locomotion, Bsx protein proves to be at the heart of an exceptional behavioural response: one related to food and movement. Without it, calorie intake is upset, leading to weight problems. This could prove to be a drug target for future therapies that would help people who suffer from obesity, for example, which is the source of health problems that kill millions of people every year. Once again, Bsx cannot be held as the sole culprit. Weight imbalances are always due to labyrinthine molecular networks and, obviously, the environment plays a role too. Nevertheless, Bsx could prove to be a novel and precious drug target to help people shed fat.

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