HUNGER – IT'S ALL IN THE MIND

TEXT: NORA LESSING

Feel hungry, grab a pudding, enjoy it, and have another. Many different electrical and chemical signals ensure that the body and the brain cooperate in the area of nutrition. Marc Tittgemeyer and his team at the Max Planck Institute for Metabolism Research in Cologne are studying the implications of such coordination.

Balance is essential in all things: this philosophy is the heart of Aristotle's Ethics, but we see the same principle at play in our body's efforts to maintain metabolic homeostasis. Ideally, behavior and metabolism are precisely attuned to avoid excessive fluctuation in blood sugar, oxygen saturation, and other physiological needs. Until now, however, little research has been done on how regulatory processes operate in humans and on the role of the brain in controlling bodily homeostasis. Neuroscientist and metabolism specialist Marc Tittgemeyer and his working group at the Max Planck Institute for Metabolism Research are on a mission to change this situation. Their approach: give study volunteers different foods, have them complete intricate behavioral tasks before eating, and measure serum blood levels together with nerve cell activity in the brain.

Tittgemeyer is looking at a photo on the computer screen in his office, taken on Brighton Beach in 1976. Hundreds of people in bikinis and swim shorts enjoying the sunshine. "This photo impressed me; you notice immediately how thin everyone is. This picture would look very different if it you took it now, 50 years later."

Six times more people are obese nowadays than in the 1970s. In the OECD countries, roughly half of adults and one in six children are overweight, and the trend is rising. The consequences are anything but harmless, ranging from shortness of breath and joint problems to high blood pressure, diabetes, and cardiovascular disease. What has gone wrong?

Metabolism in balance

Maintaining balance is crucial for keeping our bodies healthy. Various signals tell the body whether energy and hydration levels are still stable, and those signals are reported to the brain by a variety of distinct sensors. For in-

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Sweet and fatty: a combination that rarely occurs naturally in foods. Modern diets are full of such foods, however, which has grave health consequences.

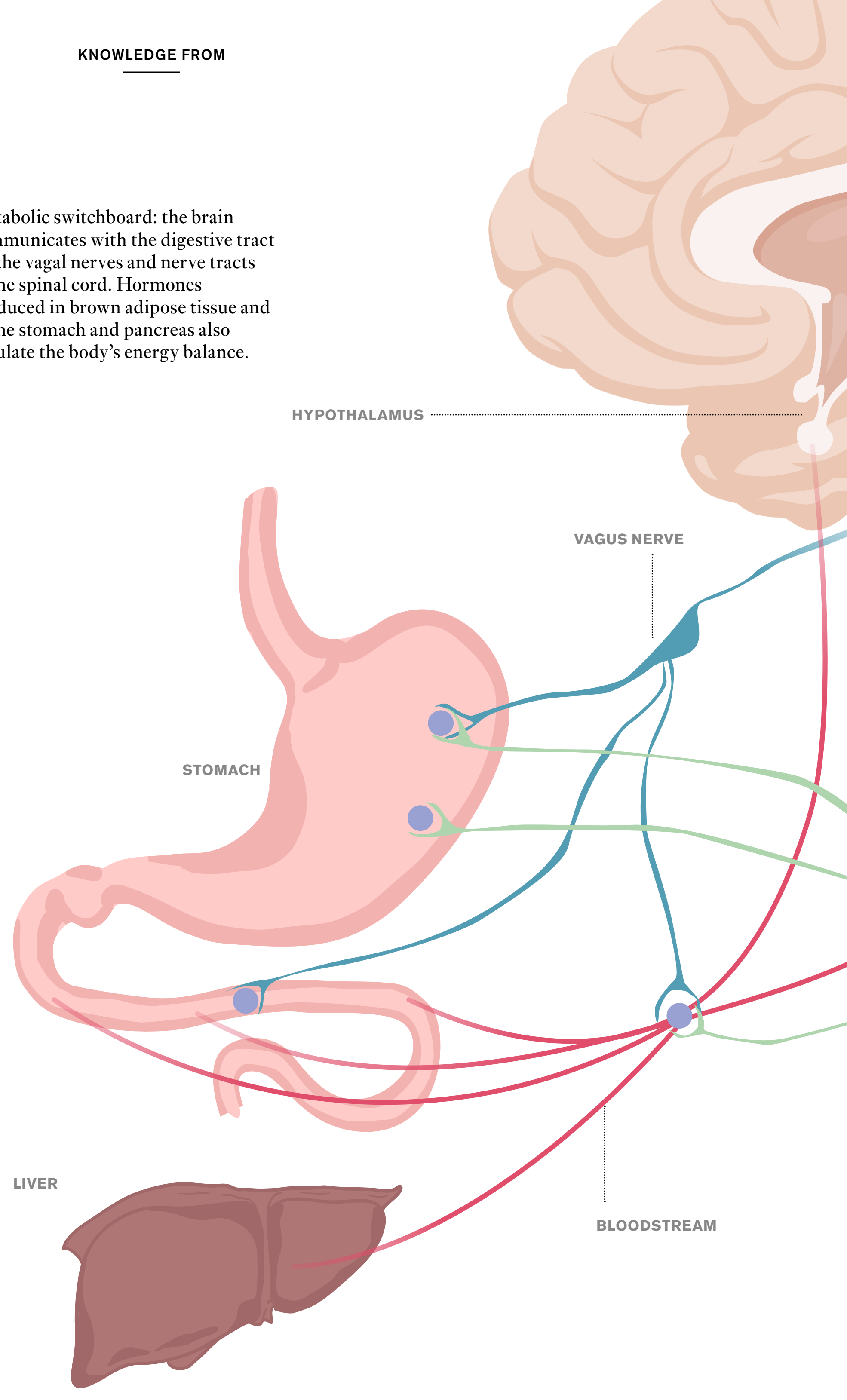
stance, if there is an imbalance between energy intake and expenditure, the body reacts with hunger. Then, pressure-sensitive cells in the stomach signal when the stomach is full, and the brain creates a feeling of satiety to keep us from overeating. The purpose of other signals, however, is to create reserves. These signals can outwit the forces striving for balance, pushing us to take in more calories than we need.

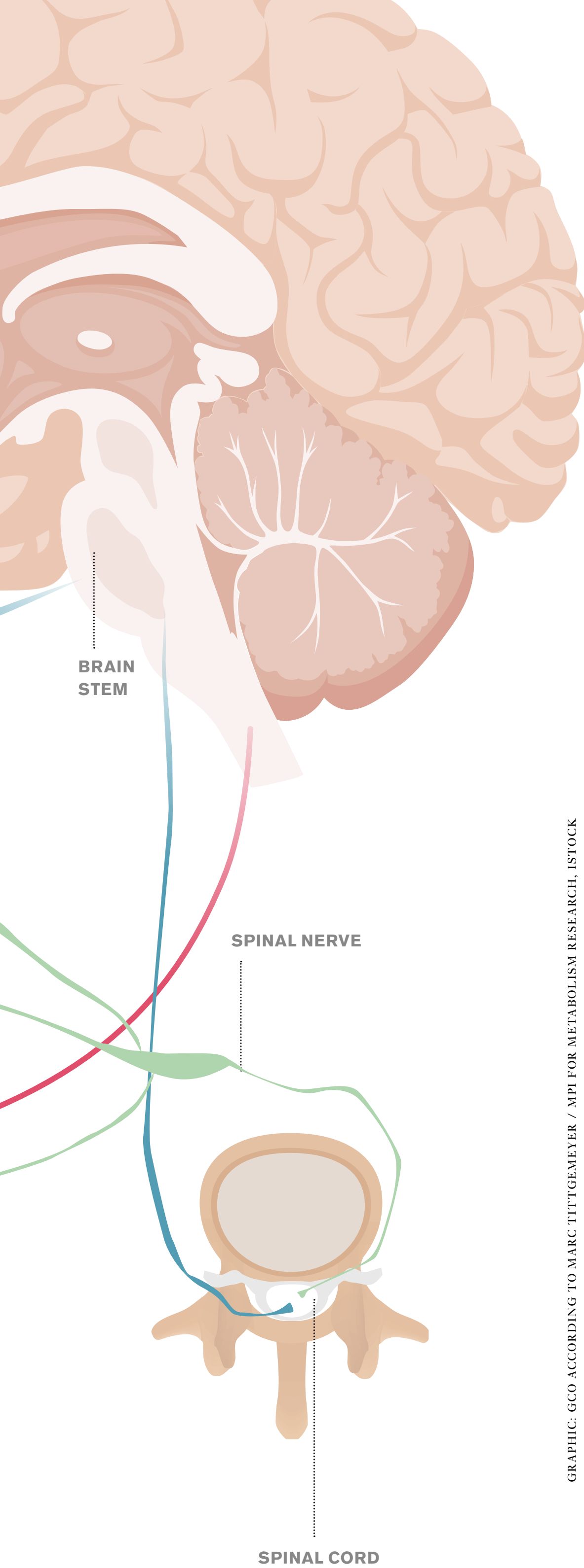
Adaptation to insufficiency

To understand the widespread problem of obesity today, one has to consider the past – more precisely, the evolutionary history of human metabolism. Our brains and bodies, after all, work the same way they did for our ancestors. They did not swim in lakes of sugar or pick chocolate bars from trees; instead, food was often meager, and people often suffered from starvation. Our metabolism adapted to these living conditions over the course of centuries. "Evolution taught the brain and body that food is not always available. Whenever there is an abundance of food, we learned to fill our stomachs in order to be prepared for lean times," explains Tittgemeyer. Signals of satiety may be overridden, for example, by activating our reward system even if the stomach is already full. The neurotransmitter dopamine plays an important role in this. Another signaling system estimates the energy content of a meal and prepares the body accordingly before your mouth takes the first bite. Nerve cells located in the hypothalamus of the brain, called "hunger neurons," are involved in this process. "These cells only fire a little bit when we are full. But when we are hungry, they become very active," Tittgemeyer elaborates.

Research has shown that the hunger neurons of mice calm down immediately when they start nibbling on a piece of chocolate. These nerve cells also mute themselves when the mice can merely smell chocolate, but are unable to eat it. The neurons will resume activity after a while if the snack does not end up in the mouse's stomach, however. "This indicates that the body, be it of mice or of humans, anticipates that foods will have a certain calorie content and prepares itself accordingly."

Metabolic switchboard: the brain communicates with the digestive tract via the vagal nerves and nerve tracts in the spinal cord. Hormones produced in brown adipose tissue and in the stomach and pancreas also regulate the body's energy balance.





GRAPHIC: GCO ACCORDING TO MARC TITTGEMEYER / MPI FOR METABOLISM RESEARCH, ISTOCK

What role do these metabolic signals, which have come about through the course of evolution, play in today's rising bodyweight worldwide? "There were several speculations about this, ranging from society's moving away from physical work to the idea that we eat more today than in ages past," Tittgemeyer explains. "We now know that the primary factor behind the dramatic rise in obesity is that we eat differently today than we used to." Ultra-processed products, for example, trick the body's hunger signals in several ways. These are often calorie-packed foods, such as ready-made pizza, 100 grams of which contains roughly five times more calories than 100 grams of apples. But there's no metabolic signal that tells us to reduce portion sizes accordingly. And the mechanoreceptors (a sort of "pressure sensor") in our digestive tract are of no help here either because they do not differentiate whether fullness is due to apples or pizza. What is more, the combination of proteins, sugars, and fats characteristic of processed products stimulates multiple signal paths simultaneously that activate the reward system in different ways. This results in a strongly felt increase in reward stimuli.

Sweeteners can make you hungry

Sweeteners are another potential problem. Though they are intended to save calories by replacing sugar, our internal calorie forecasting program throws a wrench into the works: "When the body is used to sugar in your coffee, it expects to get a certain number of calories. The body prepares accordingly, for example, by increasing the insulin level," says Tittgemeyer. "When there is no sugar at all, contrary to expectations, the body reacts with a feeling of hunger. This is how sweeteners can lead to increased calorie consumption, when really, they should accomplish the opposite."

Another example of how modern foods can throw our metabolism off kilter is the intoxicating effect of sugar and fats in combination. Tittgemeyer and his team have found out why we find it particularly difficult to resist foods like ice cream, buttered noodles, and cream cake. The researchers showed test subjects pictures of foods with the same calorie count but with differing macronutrient content. Some of the foods were particularly high in sugar, others in fat, and some in both. The test subjects were asked to assign a monetary value to the respective foods based on their degree of preference. The subjects assigned the highest values to foods rich in both sugar and fat.

The reason for this is that the reward stimuli our brain releases when we consume sugar or fat are irresistible. The respective signal paths run on differing routes from the digestive tract to the brain. The Cologne-based researchers were able to show that both of these pathways end in the site of reward processing – the midbrain, where they have tremendous impact through the release of dopamine. "Foods containing either sugar or fat cause a release of dopamine in the midbrain. When a food contains both at the same time, the effect is amplified," says Tittgemeyer. "This effect is referred to as 'super-additive.'" Pasta alone or a cream sauce on its own will make the brain happy, but pasta in a cream sauce creates a real sense of euphoria. Why this is so remains a mystery. Only very few foods occur in nature containing large amounts of sugar and fat at the same time — breast milk, for example. This is the first food we consume, and is of major social significance to us, which could be what exhibits the necessary evolutionary pressure and makes us so receptive to that combination of nutrients. This theory is not easily proven, however.

The researchers measure changes in metabolic processes via positron emission tomography to observe the reward reactions that foods trigger in the brain, such as a high-fat, high-sugar milkshake. Beverages of this kind give you a dopamine kick from the first sip. When the stomach then begins to digest the shake some 15 minutes later, the messenger substance is released a second time. “The signal from the stomach is transmitted via nerve cell networks in the brain that control motivation and learning behavior. These associate the milkshake with a reward, which leaves us inclined to have another shake next time around,” Tittgemeyer explains.

Thus, what we eat influences our preferences, which in turn influence what we eat – in a feedback loop that can turn into a vicious circle. This concept has also been shown in another experiment conducted by the Cologne-based researchers in which the study subjects added half a cup of high-fat, high-sugar pudding to their daily diet. After eight weeks it was evident that the subjects were neither gaining weight nor reacting any differently to the body’s messenger substances than at the start. The pudding did however give test subjects a stronger inclination toward fatty foods, and they also learned differently than the control group. The researchers conclude that regular consumption of foods rich in carbohydrates, fat, and sugar can rewire nerve cell networks in the brain without a change in body weight or metabolism.

Learning via the brain stem

Does eating high-fat pudding generally lead to mental decline? “Certainly not,” explains Tittgemeyer, “but it does seem to change the way people learn associations.” Importantly, learning to change our food preferences involves the brain stem – one of the oldest parts of the human brain.

SUMMARY

Changes in the foods we eat are partly behind the increasing prevalence of obesity worldwide. Added fats and sugars pack foods with calories, and moreover have a mutually amplifying effect on the brain’s reward center.

Fatty and sugary foods release lots of dopamine in the brain, which promotes learned behavior and a preference for such foods.

It has been observed in mice how poor eating habits and acquired preferences can be changed, but it remains unclear to what extent the same is possible for humans.

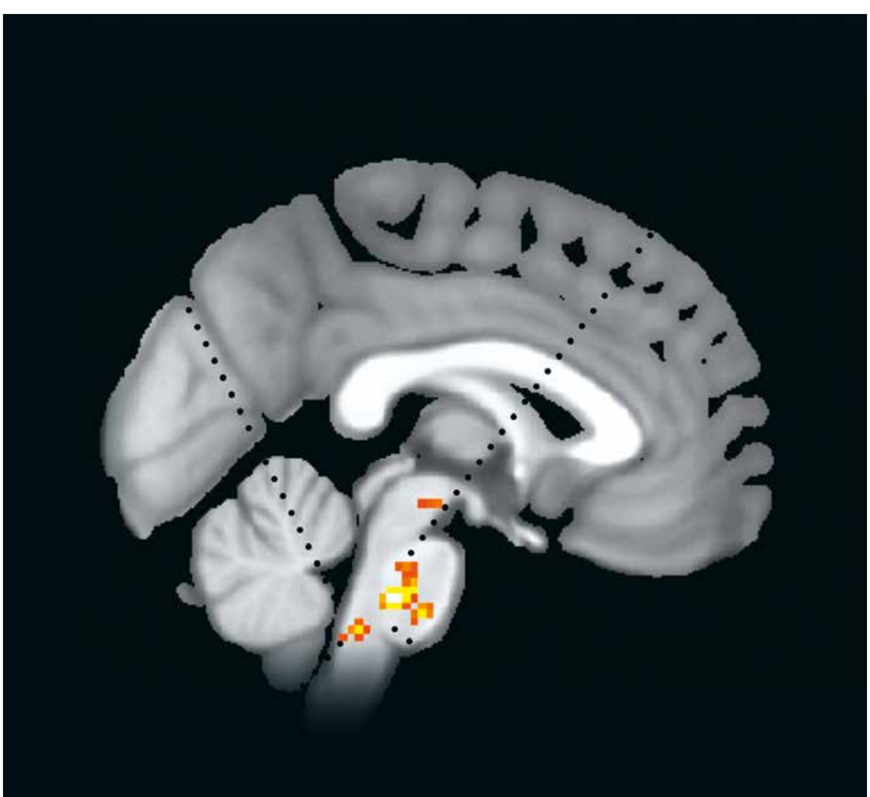
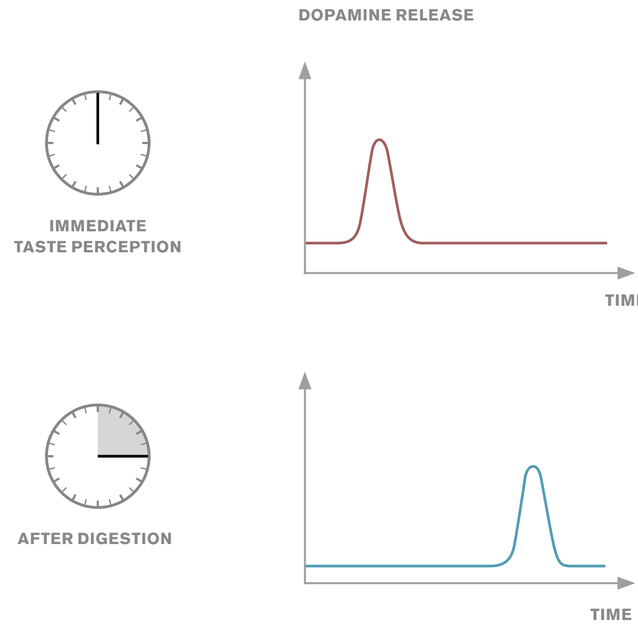


IMAGE: MARC TITTGEMEYER / MPI FOR METABOLISM RESEARCH

The vagal nerves serve as a signal switchboard between the brain and the internal organs, transmitting information from the digestive tract to the brain, among other functions. Areas in the brain stem can be activated through artificial stimulation (yellow, red).

A milkshake releases dopamine: the release of this messenger substance in the brain is observable via positron emission tomography. Taste receptors in the mouth trigger the first dopamine wave immediately upon tasting, then higher brain areas release a second wave a short time later.



GRAPHIC: GCO ACCORDING TO MARC TITTGEMEYER / MPI FOR METABOLISM RESEARCH, ISTOCK

Changes in that area of the brain influence our perception and behavior across the board.

Is it possible to change eating habits once they have been acquired? Shrugging his shoulders, Tittgemeyer declares: “That’s the question, right there! At any rate, experiments with mice have shown that eating habits are not set in stone. Mice will switch to low-fat eating habits if a low-fat diet is imposed on them over an extended period of time.” More research will have to be conducted to find out how long a human being would need until mentally adopting an initially externally imposed diet.

Our brain rewards our surplus calorie intake – be it high-calorie ready-made meals, our love of sugar combined with fat, or other eating habits we hold so dear – with feelings of happiness. There can be serious consequences to this, as unhealthy eating and being overweight can lead to diseases like type 2 diabetes, which causes the body to become increasingly resistant to insulin. The primary purpose of this hormone is to maintain stable blood sugar levels. Insulin resistance means the cells of the body can no longer sufficiently absorb sugar from the bloodstream. Insulin also affects the brain’s reward center by inhibiting the release of dopamine. “As a result, more and more fat and sugar are needed to achieve the same reward effect,” Tittgemeyer explains.

Thus patients with type 2 diabetes have to consume more calories than healthy people in order to feel good, which causes them to gain even more weight. Being overweight in turn promotes the formation of inflammatory substances in the body that inhibit drive and motivation. It is difficult to get out of this vicious circle once caught in it.

Medication alone is not enough

Can modern drugs provide a solution? Active ingredients known as GLP-1 receptor antagonists have recently been hailed as a sensational new treatment for obesity. These drugs regulate blood sugar and insulin and restrain the appetite. The stomach empties more slowly, and thus a feeling of fullness come more quickly. Tittgemeyer and his research team have furthermore shown that such drugs also affect the brain’s reward system. “However, I do not believe that obesity can be cured solely through medication,” he elaborates. “Without changing one’s behavior and modifying eating habits, it just won’t work.”

In their research, Tittgemeyer and his associates have demonstrated how metabolic disorders are behind numerous other health conditions besides obesity and related diseases, including dementia and possibly Parkinson’s.

“The more I learn in this field, the more I come to understand how being overweight has nothing to do with lacking willpower or discipline,” says Tittgemeyer, “If the metabolism goes haywire, it is extraordinarily difficult to take control. Our body dictates what we eat.” A person who chooses to have a chocolate pudding rather than a salad, against their better judgment, has a midbrain addicted to dopamine to thank for that decision.