Exercise or snack? How our brain decides

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Should I go and exercise, or would I rather go to the café and enjoy a delectable strawberry milkshake? Until now, what exactly happens in our brain when we make this decision has been a mystery to science, but researchers at ETH Zurich have found the solution. They have deciphered which brain chemical and which nerve cells mediate this

decision: the messenger substance orexin and the neurons that produce it.

These neuroscientific fundamentals are relevant because many people don't get enough exercise. Most of us have probably already decided once or even several times to skip exercising in favor of one of the numerous alternative temptations of daily life. According to the World Health Organization, 80% of adolescents and 27% of adults don't get enough exercise. And obesity is increasing at an alarming rate not only among adults but also among children and adolescents.

Focus on orexin

"Despite these statistics, many people manage to resist the constantly present temptations and get enough exercise," says Denis Burdakov, Professor of Neuroscience at ETH Zurich. "We wanted to know what it is in our brain that helps us make these decisions."

In their experiments with mice, the researchers were able to show that orexin plays a key role in this process. It's one of over a hundred messenger substances that are active in the brain. Other chemical messengers, such as serotonin and dopamine, were discovered a long time ago and their role has largely been decoded. The situation for orexin is different: Researchers discovered it relatively late, around 25 years ago, and they are now clarifying its functions step by step. Burdakov is one of the scientists who have devoted their efforts to studying orexin.

Existing knowledge can't explain the choice

"In neuroscience, dopamine is a popular explanation for why we choose to do some things but avoid others," says Burdakov. This brain

messenger is critical for our general motivation. "However, our current knowledge about dopamine does not easily explain why we decide to exercise instead of eating," the scientist continues. "Our brain releases dopamine both when we eat and when we exercise, which does not explain why we choose one over the other."

To find out what does explain this, the researchers devised a sophisticated behavioral experiment for mice, which were able to choose freely from among eight different options in ten-minute trials. These included a wheel they could run on and a "milkshake bar" where they could enjoy a standard strawberry-flavored milkshake.

"Mice like a milkshake for the same reason people do: It contains lots of sugar and fat and tastes good," says Burdakov.

Less time at the milkshake bar

In their experiment, the scientists compared different groups of mice: one made up of normal mice and one in which the mice's orexin systems were blocked, either with a drug or through genetic modification of their cells.

The mice with an intact orexin system spent twice as much time on the running wheel and half as much time at the milkshake bar as the mice whose orexin system had been blocked. Interestingly, however, the behavior of the two groups didn't differ in experiments in which the scientists only offered the mice either the running wheel or the milkshake.

"This means that the primary role of the orexin system is not to control how much the mice move or how much they eat," Burdakov says. "Rather, it seems central to making the decision between one and the other, when both options are available." Without orexin, the decision was

strongly in favor of the milkshake, and the mice gave up exercising in favor of eating.

Helping people who do little exercise

The ETH Zurich researchers expect that orexin may also be responsible for this decision in humans; the brain functions involved here are known to be practically the same in both species.

"It will now be a matter of verifying our results in humans," says Daria Peleg-Raibstein, group leader at ETH Zurich. She led the study together with Denis Burdakov. This could involve examining patients who have a restricted orexin system for genetic reasons—this is the case in around one in two thousand people. These people suffer from narcolepsy (a sleeping disorder). Another possibility would be to observe people who receive a drug that blocks orexin. Such drugs are authorized for patients with insomnia.

"If we understand how the brain arbitrates between food consumption and physical activity, we can develop more effective strategies for addressing the global obesity epidemic and related metabolic disorders," says Peleg-Raibstein.

In particular, interventions could be developed to help overcome exercise barriers in healthy individuals and those whose physical activity is limited. However, Burdakov points out that these would be important questions for scientists involved in clinical research in humans. He and his group have dedicated themselves to basic neuroscientific research. Next he wants to find out how the orexin neurons interact with the rest of the brain when making decisions like the one between exercise and snacking.

More information: Orexin neurons mediate temptation-resistant

voluntary exercise, *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01696-2