Being obese and a couch potato may have a biological basis in the brain

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Some brains may be wired to encourage fidgeting and other restless behaviors that consume calories and help control weight, according to new research published by The American Physiological Society.

The study found that the brains of rats bred to be lean are more sensitive to a chemical produced in the brain, orexin A, which stimulates appetite and spontaneous physical activity such as fidgeting and other unconscious movements. Compared to rats bred to be obese, the lean rats had a far greater expression of orexin receptors in the hypothalamus.

"The greater expression of orexin receptors suggests the lean rats' brains were more sensitive to the orexin the brain produces," said Catherine M. Kotz, the study's senior researcher. "The results point to a biological basis for being a couch potato."

This line of research suggests that frequent minor unconscious movements such as fidgeting and other behaviors associated with restlessness burn calories and help control weight, Kotz said. Further, it suggests a strategy to reduce weight gain and could lead to the development of a drug to stimulate minor activity.

The study "Elevated hypothalamic orexin signaling, sensitivity to orexin A and spontaneous physical activity in obesity resistant rats," appears in the online edition of the *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* published by The American Physiological Society. The study was done by Jennifer A. Teske and

Allen S. Levine of the University of Minnesota and the Minnesota Obesity Center, St. Paul; Michael Kuskowski, VA Medical Center, Minneapolis; James A. Levine, Mayo Clinic, Rochester, Minnesota; and Catherine M. Kotz, the VA Medical Center, University of Minnesota, and the Minnesota Obesity Center.

Study looks at obese versus lean rats

"Many people focus on diet, but it may be more feasible for some people to stand or move more throughout the day" as a way to control their weight, Kotz said. Contrary to common belief, metabolism rates don't vary greatly from person to person and weight gain usually results from eating too much, burning too few calories, or both, she said.

The researchers drew their conclusions after performing a series of experiments with obesity-prone and obesity-resistant rats. The obesity-prone strain was developed for obesity research by breeding obese rats with other obese rats. The obesity-resistant rats were developed by breeding lean rats with lean rats, Kotz noted. The study also employed a control group of normal laboratory rats.

Each rat consumed the same number of calories each day. The researchers took baseline measurements of each rat's activity using sensors to measure even minor movements, such as grooming and standing.

They found that the lean group moved significantly more during this baseline period than the obese group, Kotz said. This was true even though the rats were young and both groups weighed the same -- eliminating the obesity itself as the cause of the decreased movement. After the baseline data gathering, the researchers moved to the experimental part of the study.

Lean rats have elevated expression of orexin receptors

"We knew from previous studies that orexin stimulated physical activity, and so we wanted to find out whether it enhances activity more in lean rats than in obese rats, Kotz explained. The researchers injected orexin into the lateral hypothalamus area of the brains of both groups and found that the lean rats became even more active, while the obese rats didn't respond much at all. "Not only do the lean rats have a higher base activity rate but they respond more to orexin," she said.

Orexin must bind to receptors in the brain to produce increased activity, so the researchers reasoned that the lean rats must have more orexin receptors. When they did a blind analysis of the brains of obese and lean rats of various ages, they found that the lean rats had double the gene expression level of orexin receptors compared to the obese rats, Kotz explained.

The greater gene expression of orexin receptors does not conclusively prove that there are more orexin receptors, but it is highly suggestive of that finding. Kotz and her fellow researchers are now looking to see if the lean rats have a greater number of orexin receptors in their brains.

Activity level important to weight control

Because the rats in this study ate the same amount of food, the researchers concluded that the weight gain of the obese rats comes more from expending too few calories than from consuming too many. Other studies have shown that disabling the orexin system of lean rats causes them to eat less and move less, which leads them to become obese, Kotz said. When the orexin system is working optimally, the increase in eating which orexin causes is believed to be offset by increased physical activity, she said.

It would be impossible to do a similar study of the brain in humans. But one of the researchers, James Levine, found in a previous study with humans that lean individuals move about two hours per day more than obese individuals. What does this mean for those who are overweight?

"If we can get obese individuals to a slightly higher level of activity, that would be very beneficial," Kotz concluded.

Source: American Physiological Society