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Timing of Food Consumption Activates Genes in Specific Brain Area

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Giving up your regular late-night snack may be hard, and not just because it's a routine. The habit may genetically change an area of the brain to expect the food at that time, researchers at UT Southwestern Medical Center have discovered.

By training mice to eat at a time when they normally wouldn't, the researchers found that food turns on body-clock genes in a particular area of the brain. Even when the food stopped coming, the genes continued to activate at the expected mealtime.

"This might be an entrance to the whole mysterious arena of how metabolic conditions in an animal can synchronize themselves with a body clock," said Dr. Masashi Yanagisawa, professor of molecular genetics and senior author of the study.

The UT Southwestern researchers report their findings in the Aug. 8 issue of the *Proceedings of the National Academy of Sciences*.

The daily ups-and-downs of waking, eating and other bodily processes are known as circadian rhythms, which are regulated by many internal and external forces. One class of genes involved in these cycles is known as Period or Per genes.

When food is freely available, the strongest controlling force is light, which sets a body's sleep/wake cycle, among other functions. Light acts on an area in the brain called the suprachiasmatic nucleus, or SCN.

But because destroying the SCN doesn't affect the body clock that paces feeding behavior, the circadian pacemaker for feeding must be somewhere else, Dr. Yanagisawa said.

To find the answer, his group did a simple but labor-intensive experiment. The scientists set the mice on a regular feeding schedule, then examined their brain tissue to find where Per genes were turned on in sync with feeding times.

The researchers put the mice on a 12-hour light/dark cycle, and provided food for four hours in the middle of the light portion.

Because mice normally feed at night, this pattern is similar to humans eating at inappropriate times. Dysfunctional eating patterns play a role in human obesity, particularly in the nocturnal eating often seen in obese people, the researchers note.

The mice soon fell into a pattern of searching for food two hours before each feeding time. They also flipped their normal day/night behavior, ignoring the natural cue that day is their usual time to sleep.

After several days, the researchers found that the daily activation cycle of Per genes in the SCN was not affected by the abnormal feeding pattern.

However, in a few different areas of the brain, particularly a center called the dorsomedial hypothamalic nucleus or DMH, the Per genes turned on strongly in sync with feeding time after seven days.

When the mice subsequently went two days without food, the genes continued to turn on in sync with the expected feeding time.

"They started to show the same pattern of anticipatory behaviors several hours before the previously scheduled time of feeding," said Dr. Yanagisawa, a Howard Hughes Medical Institute investigator. "So somewhere in the body, they clearly remembered this time of day."

Upcoming research will focus on how the centers that control various body clocks communicate with each other, Dr. Yanagisawa said.

Other UT Southwestern researchers involved in the study were: Dr. Michihiro Mieda, former postdoctoral fellow at the Howard Hughes Medical Institute and currently of Tokyo Medical and Dental University; S. Clay Williams, an HHMI research specialist; and Dr. James Richardson, professor of pathology. Dr. Kohichi Tanaka of Tokyo Medical and Dental University also participated.

Source: UT Southwestern Medical Center

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