You are when you eat: Limiting flies to specific eating hours protected their hearts against aging

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Drosophila. Credit: Wikipedia

If you're looking to improve your heart health by changing your diet, when you eat may be just as important as what you eat. In a new study published today in *Science*, researchers at San Diego State University and the Salk Institute for Biological Studies found that by limiting the time span during which fruit flies could eat, they could prevent aging- and

diet-related heart problems. The researchers also discovered that genes responsible for the body's circadian rhythm are integral to this process, but they're not yet sure how.

Previous research has found that people who tend to eat later in the day and into the night have a higher chance of developing heart disease than people who cut off their food consumption earlier.

"So what's happening when people eat late?" asked Girish Melkani, a biologist at SDSU whose research focuses on cardiovascular physiology. "They're not changing their diet, just the time."

Melkani, one of the paper's senior authors, teamed up with Satchidananda Panda, a circadian rhythms expert at the Salk Institute, to address whether changing the daily eating patterns of fruit flies could affect their heart health. Fruit flies have long been used as model organisms to identify the genetic basis of human disease, including cardiovascular disease.

Shubhroz Gill, a postdoctoral researcher in Panda's lab and now at the Broad Institute in Boston, was the lead author on this study. Hiep D. Le of the Salk Institute also contributed to the study.

Time flies

In their experiments, one group of 2-week-old fruit flies was given a standard diet of cornmeal and allowed to feed all day long. Another group was allowed access to the food for only 12 hours a day. Over the course of several weeks, Melkani and Gill recorded how much food the flies were eating and tested a battery of health measures related to their sleep, body weight and heart physiology.

After three weeks, the results were clear: Flies on the 12-hour time-

restricted feeding schedule slept better, didn't gain as much weight and had far healthier hearts than their "eat anytime" counterparts, even though they ate similar amounts of food. The researchers observed the same results after five weeks.

"In very early experiments, when we compared 5-week-old flies that were fed for either 24 hours or 12 hours, the hearts of the latter were in such good shape that we thought perhaps we had mistaken some young 3-week-old fruit flies for the older group," Gill said. "We had to repeat the experiments several times to become convinced that this improvement was truly due to the time-restricted feeding."

What's more, another set of experiments revealed that the benefits of a time-restricted diet weren't exclusive to young flies. When the researchers introduced these dietary time restrictions to older flies, their hearts became healthier, too. (The average lifespan of a fruit fly is about 30 days.)

"Even if you introduce time-restricted feeding very late, you still have some benefit," Melkani said.

Some degree of heart protection persisted even for flies that went back to eating whenever they wanted, he added.

Key genes

Next, the researchers sequenced the RNA of the flies at various points in the experiment to find which of their genes had changed as a result of time-restricted feeding. They identified three genetic pathways that appear to be involved: the TCP-1 ring complex chaperonin, which helps proteins fold; mitochondrial electron transport chain complexes (mETC); and a suite of genes responsible for the body's circadian rhythm.

Melkani and Gill repeated their experiments using mutant strains of flies with nonfunctional versions of the TCP-1 and circadian rhythm genes. In these flies, time-restricted feeding granted no health benefits, strengthening the case that these genetic pathways play key roles.

Conversely, in mutant flies with altered mETC genes, the flies showed increased protection against cardiac aging.

"If and how these three pathways all work together, we don't yet know entirely," Melkani said.

Nix the late-night snacks

The results complement earlier research from Panda's lab showing benefits of time-restricted feeding for obesity, metabolic diseases and type-2 diabetes in rodents.

"All together, these results reinforce the idea that the daily eating pattern has a profound impact on both the body and the brain," Panda said.

Gill noted that there are some hurdles to clear before extrapolating this research to humans.

"Humans don't consume the same food every day," he said. "And our lifestyle is a major determinant of when we can and cannot eat. But at the very minimum, our studies offer some context in which we should be pursuing such questions in humans."

Melkani is optimistic that the results could one day translate into cardiac- and obesity-related health benefits for humans. "Time-restricted feeding would not require people to drastically change their lifestyles, just the times of day they eat," Melkani said. "The take-home message then would be to cut down on the late-night snacks."

More information: Time-restricted feeding prevents age-related cardiac decline in Drosophila, *Science*, www.sciencemag.org/lookup/doi/… 1126/science.1256682

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