'Wrong'-time eating reduces fertility in fruit flies

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Dieticians will tell you it isn't healthy to eat late at night: it's a recipe for weight gain. In fruit flies, at least, there's another consequence: reduced fertility.

That's the conclusion of a new study this week in Cell Metabolism by researchers at the Perelman School of Medicine at the University of Pennsylvania, in which they manipulated circadian rhythms in fruit flies and measured the affect on egg-laying capacity.

Lead author Amita Sehgal, PhD, John Herr Musser Professor of Neuroscience, stresses, though, that what is true in flies grown in a lab does not necessarily hold for humans, and any potential link between diet and reproduction would have to be independently tested.

"I wouldn't say eating at the wrong time of the day makes people less fertile, though that is the implication," says Sehgal, who is also a Howard Hughes Medical Institute Investigator. "I would say that eating at the wrong time of the day has deleterious consequences for physiology."

It's All Connected

Many aspects of animal biology cycle over the course of a day. Sleep and wakefulness, activity and rest, body temperature, and more, all fluctuate in a pattern called a circadian rhythm. Disruption of these rhythms has been shown to negatively affect physiology. Shift workers, for instance,

often suffer from psychological and metabolic issues that colleagues on normal hours do not. Rodents with disrupted circadian rhythms are more likely to develop obesity.

For a while, Sehgal explains, researchers believed animals had a single master molecular clock, located in the brain, that controlled activity throughout the body. In recent years, however, they have come to understand that some individual organs also have their own, independent clocks, like townspeople who wear a wristwatch and keep it synchronized with the clock in city hall.

The mammalian liver is one organ that has its own independent clock. In 2008, Sehgal's team discovered that the fruit fly equivalent of the liver, called the fat body, has its own clock, which controls eating and food storage. They wanted to know what would happen if the fat body clock became desynchronized from the master clock in the brain.

Decoupling Clocks

First, her team asked which fly genes are controlled specifically by the fat body clock. Using gene chip microarrays, they identified 81 genes related to lipid and carbohydrate metabolism, the immune system, and reproduction that fit those criteria.

Next, the researchers attempted to decouple the fat body and central clocks by keeping the flies in constant darkness (to eliminate effects of light on these clocks) and feeding them at times when they don't normally eat. They found the two clocks could be desynchronized: disrupting the animals' feeding cycles altered the cycling of genes controlled by the fat-body clock, but not those regulated by the central clock itself itself.

Finally, the team addressed the functional consequences of this

desynchronization, by counting the number of eggs the flies laid under different conditions. Flies fed at the "right" time of the day deposited about 8 eggs per day, compared to about 5 when they fed at the "wrong" time.

"Circadian desynchrony caused by feeding at the 'wrong' time of day leads to a defect in overall reproductive capacity," the authors wrote.

The next question to pursue, Sehgal says, is finding the molecular mechanism that controls this phenomenon: How does the fat body communicate with the ovaries. And, more importantly, is this effect restricted to fruit flies, or does it also occur in higher organisms, including humans.

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