Mouse study: When it comes to living longer, it's better to go hungry than go running

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A study investigating aging in mice has found that hormonal changes that occur when mice eat significantly less may help explain an already established phenomenon: a low calorie diet can extend the lifespan of rodents, a benefit that even regular exercise does not achieve.

“We know that being lean rather than obese is protective from many diseases, but key rodent studies tell us that being lean from eating less, as opposed to exercising more, has greater benefit for living longer. This study was designed to understand better why that is,” said Derek M. Huffman, the study’s lead author.

The study applies only to rodents, which are different in some key ways from humans, cautions Huffman. However, at least two studies which examined people who engage in high-volume exercise versus people who restricted their calorie intake, had a similar outcome: caloric restriction has physiological benefits that exercise alone does not. Researchers expect that clues to the physiology of longevity in mice will eventually be applied to people, Huffman said.

The study, “Effect of exercise and calorie restriction on biomarkers of aging in mice,” appears in the May issue of the American Journal of Physiology published by The American Physiological Society (APS; www.The-APS.org). The study was carried out by Huffman, Douglas R. Moellering, William E. Grizzle, Cecil R. Stockard, Maria S. Johnson and Tim R. Nagy, all of the University of Alabama-Birmingham (UAB) and funded by the UAB Center for Aging. Dr. Huffman is now at the Albert

Einstein College of Medicine in New York.

The study built upon previous studies that showed:

-- Rats that exercise regularly will, on average, live longer compared to a group that eats the same amount but does not exercise. This is because exercise prevents some diseases, which allows more individual animals to live out their expected life span.

-- However, when comparing the rats in these two groups that eat the same amount, the longest-lived animals in the exercise group don't live any longer than the longest-lived rats in the non-exercise group. Taken together, these findings indicate that exercise can prevent an early death from disease in some rats, but does not extend the maximal lifespan of any of the rats.

-- When comparing rats that exercise to those that don't exercise but eat much less, the longest-lived rats are from the group that ate less.

Two theories

Taken together, these findings indicate that caloric restriction protects against disease better than exercise does, and has the added benefit of extending the life span of some rats. Physiologists have been trying to unravel the reasons for this, and two major theories have emerged.

One theory is that exercise places stress on the body, which can result in damage to the tissues and DNA. Another theory is that caloric restriction leads to physiological changes which benefit the body.

Huffman and his colleagues designed a study to examine the roles of exercise and caloric restriction, singly and combined. They controlled for factors such as weight and the amount of energy expended versus the

calories consumed.

They found:

-- Mice allowed to eat as much as they wanted had higher insulin levels, regardless of whether they exercised. That is, how much the mice ate determined their insulin level, while exercise did not have much effect. High insulin levels are associated with a risk of diabetes.

-- The animals that ate as much as they wanted and did not exercise had the highest levels of insulin-like growth factor (IGF-1), which plays a key role in regulating cell growth and cell death. The animals on caloric restriction had the lowest levels of IGF-1. Exercise also seemed to play an important role in regulating IGF-1 levels.

-- There were some elevated levels of heat shock proteins, a measure of oxidative stress and possible tissue damage among the exercising mice. But total protein carbonyls, another stress measure, were not significantly different.

-- Both exercise and caloric restriction moderated the level of 8-hydroxyguanosine (8-OHdG), a marker of DNA damage. Among the animals that ate all they wanted, those that did not exercise had the highest levels of 8-OHdG and those that exercised had much lower levels. The researchers concluded that DNA damage increases with age and is accelerated by obesity but could be slowed by caloric restriction and/or exercise. The researchers noted, however, that the results may differ if they had used older mice or subjected them to greater caloric restriction than the mild (9% fewer calories) or moderate (18%) restriction this study employed.

Overall, these findings indicate that the physiological stress of exercise did not produce enough damage to tissues or DNA to explain why

exercise does not lengthen life span. Instead the study suggests that caloric restriction creates beneficial changes in the body's hormone levels which exercise does not. The researchers concluded that these metabolic changes play a role in extending life.

A handful of studies comparing calorie restricted people to people who are avid exercisers, found similar hormonal benefits among those eating less. However, calorie restriction studies are difficult to carry out in people because participants often complain of feeling hungry, lethargic, and cold.

Huffman also emphasized that the benefits of exercise may be greater for humans than for mice because people are more prone to develop cardiovascular diseases, and exercise is particularly good at warding off those diseases. Mice tend to die of kidney disease and cancer, Huffman said.

"I wouldn't say this study has direct implications for people right now," Huffman said. "But it shows what physiological changes caloric restriction and exercise produce. We can continue to build upon these findings until we can get a better understanding of how this works in people."

Source: American Physiological Society

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