

## **Everybody Dance! The Energy You Use Won't Shorten Your Life**

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The theory that animals die when they've expended their lifetime allotment of energy may be reaching the end of its own life, according to a study presented at The American Physiological Society conference, Comparative Physiology 2006. However, the longitudinal study leaves open a newer form of the theory -- that antioxidants help prolong life by limiting the damage that oxidative stress can cause to cells.

"These findings join a growing body of evidence suggesting that lifetime energy expenditure per se does not underlie senescence," wrote Lobke Vaanholt, Serge Daan, Theodore Garland Jr. and G. Henk Visser in a summary of the study presented at Comparative Physiology 2006: Integrating Diversity. Vaanholt, Daan and Visser are from the University of Groningen, The Netherlands. Garland is from the University of California at Riverside. The conference takes place Oct. 8-11 in Virginia Beach, Virginia.

A bit of background: One early theory, the rate of living theory, held that every organism has a set amount of energy to expend. Once the animal expended that number of calories, the grim reaper was on the doorstep. Over the years, the theory has become much more sophisticated, but metabolic rate and aging have remained linked, Vaanholt explained.

Decades ago, physiologists discovered that during metabolism, oxygen  $(O_2)$  can split into single oxygen atoms, known as free radicals. These rogue oxygen atoms can remain on their own or combine with hydrogen atoms to form reactive oxygen species (ROS), which wreak havoc with



enzymes and proteins and adversely affect cell function. The faster the metabolism, the more ROS produced, the modern theory goes.

## **Energy expenditure not the key**

In this study the researchers divided the mice into three groups of 100 mice each. Two groups were "runner" mice, that is, mice that loved to run on the running wheels placed in their cages. One group of runner mice had access to running wheels, but the second group of runner mice did not. The third group consisted of regular laboratory mice that had a running wheel.

Vaanholt's team followed 60 mice from each of the three groups throughout their natural lives, nearly three years. They measured wheel running activity and took periodic measurements of body mass.

They found:

• Runner mice that had access to a wheel expended 25% more energy over the course of their lives compared to both the runner group that did not have a wheel and the regular mice

• Both groups of mice bred for running, one group with the wheel and one without, lived about 90 days less than the regular mice

• The regular (non-runner) mice lived longest, 826 days, compared to the runners with a wheel, 735 days and runners without a wheel, 725 days

The rate of living theory would have predicted that the running group that expended more energy would die earlier than the two groups that did not, Vaanholt said. This was not the case. There was no difference in life span between the two runner groups, even though one expended more energy.

In addition, the rate of living theory would have predicted that the runner



mice without the wheel and the normal mice would live approximately the same life span because there was no difference in energy expenditure between the two. This was not the case. The runner mice without the wheel died sooner.

"The shorter life span cannot, therefore, be explained by a difference in metabolism," Vaanholt concluded. "There must be something else going on that causes these animals to age and die."

## More activity = higher metabolism = more antioxidants?

A second portion of the experiment involved the remaining 40 mice in each of the three groups. The researchers periodically used mice from these three groups to determine energy expenditure, body composition and the antioxidant enzyme levels and protein synthesis in the heart and liver tissues. The researchers selected mice, at two months, 10 months, 18 months and 26 months for this analysis.

Since the group of runner mice that expended more energy lived as long as the runner group that was less active, the researchers tested whether there was a difference in antioxidant production between the two groups. Since metabolic rate rises with activity level and oxidative stress rises with metabolic rate, perhaps the runner mice that expended more energy also produced more antioxidants, the body's defense against oxidative stress, Vaanholt said.

However, the study found no difference in antioxidant levels among the groups, at least in the heart and the liver, regardless of energy expenditure. "We would have expected additional antioxidants among the group of mice that expended 25% more energy, but that was not the case," Vaanholt said.



"We can conclude that the presence of a running wheel resulted in increased daily energy expenditure without a change in lifespan or in antioxidant enzyme activity in the heart and liver," Vaanholt explained.

Further research must examine whether tissues in other areas of the body generated additional antioxidants to help cope with the increased oxidative stress brought on with increased activity and metabolic rate, she said. In addition, future studies may examine whether other mechanisms are at work, including whether activity level is connected to DNA repair rates.

Source: American Physiological Society

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