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Tara Parker-Pope on Health

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Can Exercise Keep You Young?

By GRETCHEN REYNOLDS

We all know that physical activity is beneficial in countless ways, but even so, Dr. Mark Tarnopolsky, a professor of pediatrics at McMaster University in Hamilton, Ontario, was startled to discover that exercise kept a strain of mice from becoming gray prematurely.

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But shiny fur was the least of its benefits. Indeed, in heartening new research published last week in The Proceedings of the National Academy of Sciences, exercise reduced or eliminated almost every detrimental effect of aging in mice that had been genetically programmed to grow old at an accelerated pace.

In the experiment, Dr. Tarnopolsky and his colleagues used lab rodents that carry a genetic mutation affecting how well their bodies repair malfunctioning mitochondria, which are tiny organelles within cells. Mitochondria combine oxygen and nutrients to create fuel for the cells — they are microscopic power generators.

Mitochrondria have their own DNA, distinct from the cell's own genetic material, and they multiply on their own. But in the process, mitochondria can accumulate small genetic mutations, which under normal circumstances are corrected by specialized repair systems within the cell. Over time, as we age, the number of mutations begins to outstrip the system's ability to make repairs, and mitochondria start malfunctioning and dying.

Many scientists consider the loss of healthy mitochondria to be an important underlying cause of aging in mammals. As resident mitochondria falter, the cells they fuel wither or die. Muscles

shrink, brain volume drops, hair falls out or loses its pigmentation, and soon enough we are, in appearance and beneath the surface, old.

The mice that Dr. Tarnopolsky and his colleagues used lacked the primary mitochondrial repair mechanism, so they developed malfunctioning mitochondria early in their lives, as early as 3 months of age, the human equivalent of age 20. By the time they reached 8 months, or their early 60s in human terms, the animals were extremely frail and decrepit, with spindly muscles, shrunken brains, enlarged hearts, shriveled gonads and patchy, graying fur. Listless, they barely moved around their cages. All were dead before reaching a year of age.

Except the mice that exercised.

Half of the mice were allowed to run on a wheel for 45 minutes three times a week, beginning at 3 months. These rodent runners were required to maintain a fairly brisk pace, Dr. Tarnopolsky said: “It was about like a person running a 50- or 55-minute 10K.” (A 10K race is 6.2 miles.) The mice continued this regimen for five months.

At 8 months, when their sedentary lab mates were bald, frail and dying, the running rats remained youthful. They had full pelts of dark fur, no salt-and-pepper shadings. They also had maintained almost all of their muscle mass and brain volume. Their gonads were normal, as were their hearts. They could balance on narrow rods, the showoffs.

But perhaps most remarkable, although they still harbored the mutation that should have affected mitochondrial repair, they had more mitochondria over all and far fewer with mutations than the sedentary mice had. At 1 year, none of the exercising mice had died of natural causes. (Some were sacrificed to compare their cellular health to that of the unexercised mice, all of whom were, by that age, dead.)

The researchers were surprised by the magnitude of the impact that exercise had on the animals’ aging process, Dr. Tarnopolsky said. He and his colleagues had expected to find that exercise would affect mitochondrial health in muscles, including the heart, since past research had shown a connection. They had not expected that it would affect every tissue and bodily system studied.

Other studies, including a number from Dr. Tarnopolsky’s own lab, have also found that exercise affects the course of aging, but none has shown such a comprehensive effect. And precisely how exercise alters the aging process remains unknown. In this experiment, running resulted in an upsurge in the rodents’ production of a protein known as PGC-1alpha, which regulates genes involved in metabolism and energy creation, including mitochondrial function. Exercise also sparked the repair of malfunctioning mitochondria through a mechanism outside the known repair pathway; in these mutant mice, that pathway didn’t exist, but their mitochondria were nonetheless being repaired.

Dr. Tarnopolsky is currently overseeing a number of experiments that he expects will help to elucidate the specific physiological mechanisms. But for now, he said, the lesson of his experiment and dozens like it is unambiguous. “Exercise alters the course of aging,” he said.

Although in this experiment, the activity was aerobic and strenuous, Dr. Tarnopolsky is not convinced that either is absolutely necessary for benefits. Studies of older humans have shown that weightlifting can improve mitochondrial health, he said, as can moderate endurance exercise. Although there is probably a threshold amount of exercise that is necessary to affect physiological aging, Dr. Tarnopolsky said, “anything is better than nothing.” If you haven’t been active in the past, he continued, start walking five minutes a day, then begin to increase your activity level.

The potential benefits have attractions even for the young. While Dr. Tarnopolsky, a lifelong athlete, noted with satisfaction that active, aged mice kept their hair, his younger graduate students were far more interested in the animals’ robust gonads. Their testicles and ovaries hadn’t shrunk, unlike those of sedentary elderly mice.

Dr. Tarnopolsky’s students were impressed. “I think they all exercise now,” he said.