

Researchers note differences between people and animals on calorie restriction

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Calorie restriction, a diet that is low in calories and high in nutrition, may not be as effective at extending life in people as it is in rodents, according to scientists at Washington University School of Medicine in St. Louis.

Previous research had shown that laboratory animals given 30 percent to 50 percent less food can live up to 50 percent longer. Because of those findings, some people have adopted calorie restriction in the hope that they can lengthen their lives. But the new research suggests the diet may not have the desired effect unless people on calorie restriction also pay attention to their protein intake.

In an article published online this month in the journal *Aging Cell*, investigators point to a discrepancy between humans and animals on calorie restriction. In the majority of the animal models of longevity, extended lifespan involves pathways related to a growth factor called IGF-1 (insulin-like growth factor-1), which is produced primarily in the liver. Production is stimulated by growth hormone and can be reduced by fasting or by insensitivity to growth hormone. In calorie-restricted animals, levels of circulating IGF-1 decline between 30 percent and 40 percent.

"We looked at IGF-1 in humans doing calorie restriction," says first author Luigi Fontana, M.D., Ph.D., assistant professor of medicine at Washington University and an investigator at the Istituto Superiore di Sanità in Rome, Italy. "For years, we have been following a cohort of people from the CR Society who have been on long-term calorie restriction. We found no difference in IGF-1 levels between people on calorie restriction and those who are not."

The CR Society members, who call themselves CRONies (Calorie Restriction with Optimal Nutrition), had been on a calorie-restriction diet for an average of seven years when Fontana did the

measurements, but their IGF-1 levels were virtually identical to sedentary people who ate a standard, Western diet.

Because calorie restriction is linked to extraordinary increases in maximal lifespan in rats and mice, Fontana and colleagues at Washington University, including principal investigator John O. Holloszy, M.D., professor of medicine, have been involved in a scientific study that compares calorie restriction to exercise and measures many biological factors linked to longevity and health. Called the CALERIE study (Comprehensive Assessment of the Long term Effects of Reducing Intake of Energy), the project randomly divided 48 people into three groups: Eighteen cut their caloric intake by 25 percent for one year. Another 18 started exercising to increase their energy expenditure by 25 percent for a year. A third group of 10 people didn't change anything.

At the end of that year, the investigators measured IGF-1 levels in all three groups. Again they found no reductions in the group on calorie restriction.

"That was puzzling because it was the first time we hadn't seen agreement between mice and rats on calorie restriction and humans on calorie restriction," Fontana explains. "But we know there are two major influences on IGF-1 levels: calorie intake and protein intake. So we decided to look at the influence of protein."

Again, Fontana had a ready-made study group. His team has been following a population of strict vegans for several years. They tend to eat less protein than the CRONies from the CR Society, so he compared IGF-1 levels between the two groups.

"The vegans had significantly less circulating IGF-1, even if they were heavier and had more body fat than CRONies," he says. "Protein in the diet seemed to correlate with the lower levels of IGF-1. The strict vegans took in about 10 percent of their

total calories from protein, whereas those on calorie restriction tended to get about 23 or 24 percent of calories from protein." too much protein, but these findings suggest perhaps they should.

Source: Washington University

The investigators wanted to take one more look at the relationship between dietary protein and IGF-1, so Fontana asked a group of CRONies to eat less protein for a few weeks. He says it was not easy to cut protein because those on calorie restriction have to do a lot of calculating and juggling to ensure they take in very few calories and still get adequate nutrition. Increasing dietary protein is one way many CRONies guard against becoming malnourished.

"But six of them agreed to lower their protein intake," Fontana explains, "and after three weeks their circulating IGF-1 declined dramatically."

Previous research from Fontana's group had found that a diet lower in protein might protect against some cancers. These more recent findings suggest lowering protein also might be important to longevity. Fontana admits his evidence is preliminary, but the findings suggest that when people adjust their diets to improve health and lengthen life, they should control not only calories and fat but also keep an eye on protein.

Fontana isn't proposing radical low-protein diets. Instead, he is suggesting the current recommended daily allowance (RDA) for protein, which is 0.82 grams of protein per kilogram of body weight, or about 56 grams of protein for an average, adult man and 46 grams for an average, adult woman. Most people, including CRONies, consume much more protein than the RDA recommendation.

"It's much easier to restrict protein than to restrict calories," he says. "If our research is on the right track, maybe humans don't need to be so calorie restricted. Limiting protein intake to .7 or .8 grams per kilogram per day might be more effective. That's just a hypothesis. We have to confirm it in future studies."

Until then, Fontana suggests people might want to look at protein consumption and tailor it to RDA recommendations. Traditionally, he says, nutritionists have not worried about people eating

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