CALORIES

IS FASTING GOOD FOR YOU?

Intermittent fasting might improve health, but clinical data are thin

By David Stipp

IN THE BELOVED NOVEL *CHARLOTTE'S Web,* by E. B. White, an old sheep advises the gluttonous rat Templeton that he would live longer if he ate less. "Who wants to live forever?" Templeton sneers. "I get untold satisfaction from the pleasures of the feast."

It is easy to empathize with Templeton, but the sheep's claim has some merit. Studies have shown that reducing typical calorie consumption, usually by 30 to 40 percent, extends life span by a third or more in many animals, including nematodes, fruit flies and rodents. When it comes to primates and people, however, the picture is unclear. One long-term study of calorie-restricted rhesus monkeys showed that the stringent diets increased survival; another such study, published in 2012, surprisingly failed to show that. Yet a 2014 report suggested that the control monkeys in the latter study, which supposedly were not calorie-restricted, were actually on diets tantamount to mild calorie restriction. That may account for the study's failure to show a significant longevity difference between its controls and experimental animals. Even if calorie restriction does not help anyone live longer, a large portion of the data supports the idea that limiting food intake reduces the risks of diseases common in old age and lengthens the period of life spent in good health.

If only one could claim those benefits without being hungry all the time. There might be a way. In recent years researchers have focused on a strategy known as intermittent fasting as a promising alternative to continuous calorie restriction.

Intermittent fasting, which includes everything from periodic multiday fasts to skipping a meal or two on certain days of the week, may promote some of the same health benefits that uninterrupted calorie restriction promises. The idea of intermittent fasting is more palatable to most people because, as Templeton would be happy to hear, one does not have to renounce the pleasures of the feast. Studies indicate that rodents that feast one day and fast the next often consume fewer calories overall than they would normally and live just as long as rodents eating calorie-restricted meals every single day.

In a 2003 mouse study overseen by Mark P. Mattson, head of the National Institute on Aging's neuroscience laboratory, mice that fasted regularly were healthier by some measures than mice subjected to continuous calorie restriction; they had lower levels of insulin and glucose in their blood, for example, which signified increased sensitivity to insulin and a reduced risk of diabetes.

THE FIRST FASTS

RELIGIONS HAVE LONG maintained that fasting is good for the soul, but its bodily benefits were not widely recognized until the early 1900s, when doctors began recommending it to treat various disorders—such as diabetes, obesity and epilepsy.

Related research on calorie restriction took off in the 1930s, after Cornell University nutritionist Clive McCay discovered that rats subjected to stringent daily dieting from an early age lived longer and were less likely to develop cancer and other diseases as they aged, compared with animals that ate at will. Research on calorie restriction and periodic fasting intersected in 1945, when University of Chicago scientists reported that alternate-day feeding extended the life span of rats as much as daily dieting in McCay's earlier experiments. Moreover, intermittent fasting "seems to delay the development of the disorders that lead to death," the Chicago researchers wrote.

In the next decades research into antiaging diets took a backseat to more influential medical advances, such as the continued development of antibiotics and coronary artery bypass surgery.

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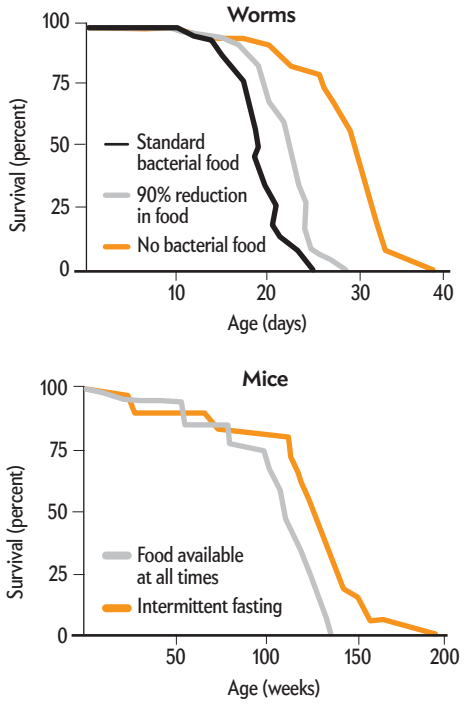
LIFE EXTENSION



FASTING BOOSTS SURVIVAL: Fasting has extended life span in post–larval stage worms (*top*) and mice (*bottom*). Such studies have also provided evidence that intermittent fasting staves off common age-related diseases in animals.

More recently, however, Mattson and other researchers have championed the idea that intermittent fasting probably lowers the risks of degenerative brain diseases in later life. Mattson and his colleagues have shown that periodic fasting protects neurons against various kinds of damaging stress, at least in rodents. One of his earliest studies revealed that alternate-day feeding made the rats' brains resistant to toxins that induce cellular damage akin to the kind cells endure as they age. In follow-up rodent studies, his group found that intermittent fasting protects against stroke damage, suppresses motor deficits in a mouse model of Parkinson's disease and slows cognitive decline in mice genetically engineered to mimic the symptoms of Alzheimer's disease. A decidedly slender man, Mattson has long skipped breakfast and lunch except on weekends. "It makes me more productive," he declares. The 57-year-old researcher, who has a Ph.D. in biology but not a medical degree, has written or co-authored more than 700 articles.

Mattson thinks that intermittent fasting acts in part as a form of mild stress that continually revs up cellular defenses against molecular damage. For instance, occasional fasting increases the levels of "chaperone proteins," which prevent the incorrect assembly of other molecules in the cell. Additionally, fasting mice have higher levels of brain-derived neurotrophic factor (BDNF), a protein that prevents stressed neurons from dying. Low levels of BDNF have been linked to everything from depression to Alzheimer's, although it is still unclear whether these findings reflect cause and effect. Fasting also ramps up autophagy, a kind of garbage-disposal system in cells that gets rid of damaged molecules, including ones that have been previously tied to Alzheimer's, Parkinson's and other neurological diseases.

One of intermittent fasting's main effects seems to be increasing the body's responsiveness to insulin, the hormone that regulates blood sugar. Decreased sensitivity to insulin often accompanies obesity and has been linked to diabetes and heart failure; long-lived animals and people tend to have unusually low insulin, presumably because their cells are more sensitive to the hormone and therefore need less of it. A 2012 study at the Salk Institute for Biological Studies in La Jolla, Calif., showed that mice that feasted on fatty foods for eight hours a day and subsequently fasted for the rest of each day did not become obese or show dangerously high insulin levels.

The idea that periodic fasting may offer some of the same health benefits as continuous calorie restriction—and allows for some feasting while slimming down—has convinced an increasing number of people to try it, says Steve Mount, a University of Maryland genetics professor who has moderated a Yahoo discussion group on intermittent fasting for more than nine years. Intermittent fasting "isn't a panacea—it's always hard to lose weight," adds Mount, who has fasted three days a week since 2004. "But the theory [that it activates the same signaling pathways in cells as calorie restriction] makes sense."

ON THIN GROUND

DESPITE THE GROWING enthusiasm for intermittent fasting, researchers have conducted few robust clinical trials, and its long-term effects in people remain uncertain. Still, a 1956 Spanish study sheds some light, says Louisiana-based physician James B. Johnson, who co-authored a 2006 analysis of the study's results. In the Spanish study, 60 elderly men and women fasted and feasted on alternate days for three years. The 60 participants spent 123 days in the infirmary, and six died. Meanwhile 60 nonfasting seniors racked up 219 infirmary days, and 13 died.

In 2007 Johnson, Mattson and their colleagues published a clinical study showing a rapid, significant alleviation of asthma symptoms and various signs of inflammation in nine overweight asthmatics who near-fasted every other day for two months.

Detracting from these promising results, however, the literature on intermittent fasting also includes several red flags. A 2011 Brazilian study in rats suggests that long-term intermittent fasting increases blood glucose and tissue levels of oxidizing compounds that could damage cells. Moreover, in a 2010 study co-authored by Mattson, periodically fasting rats mysteriously developed stiff heart tissue, which in turn impeded the organ's ability to pump blood.

And some weight-loss experts are skeptical about fasting, citing its hunger pangs and the possible dangers of compensatory gorging.

Still, from an evolutionary perspective, three meals a day is a strange modern invention. Volatility in our ancient ancestors' food supplies most likely brought on frequent fasting—not to mention malnutrition and starvation. Yet Mattson believes that such evolutionary pressures selected for genes that strengthened brain areas involved in learning and memory, which increased the odds of finding food and surviving. If he is right, intermittent fasting may be both a smart and smartening way to live. SA

David Stipp is a Boston-based science writer who focuses on aging research. He is author of *The Youth Pill: Scientists at the Brink of an Anti-Aging Revolution* (Current, 2010).

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