

Mark Mattson

Mark Mattson's vigor as a researcher matches his strict physical regime. Here he talks about how limiting calories might protect the aging brain—and help create a healthy researcher.

If there's one thing everyone agrees on about Mark Mattson, it's that he's thin. At 5 feet 9 inches and 125 pounds, Mattson is so scrawny that some colleagues say they fear for his health. "We're worried as hell," says Caleb Finch, an expert in aging research at the University of Southern California in Los Angeles. "This guy has no reserves."

Mattson, who religiously exercises and monitors his diet, has no such qualms about his wellbeing. Indeed, his own research at the US National Institute on Aging backs up the benefits of his lifestyle. As chief of the institute's Laboratory of Neurosciences, he has most recently carved out a niche exploring why animals placed on a drastic diet defy aging and the brain's associated decay.

Mattson traces his interest in aging back to his ninth-grade classroom. Asked then to write an essay on a scientific topic of his choice, he picked cryopreservation—the futuristic concept that humans can be resurrected after being suspended in the deep freeze for years. "I was grabbed with the idea of putting aging on hold," he now says.

The budding scientist took a circuitous academic route before returning to his childhood passion. After completing a PhD and a postdoctoral position investigating aspects of neurodegeneration, he landed a job at the University of Kentucky College of Medicine, where he scaled the ranks to professor. It was there that Mattson became intrigued by medical literature showing that mice whose normal calorie intake is slashed by one-third live around 30% longer, to as many as 40 months—equivalent to 100 human years or more.

After mulling over the findings, Mattson and his colleagues waded into the field of 'caloric restriction' in the late 1990s. They soon produced the first studies showing that a low-calorie diet protects the brain, as it does other organs, from the ravages of age-associated disorders such as Alzheimer and Parkinson diseases. "No one anticipated that," says Dennis Choi, executive vice-president for neuroscience at Merck Research Laboratories in West Point, Pennsylvania. "It was really a provocative finding."

Mattson's biggest public splash came from a study published last year, showing that regular fasting confers the same health benefits as total caloric restriction. The team showed that mice starved every other day, but allowed to gorge in between, consume only 10% fewer calories than normal, but still have healthier blood glucose levels and recover better from brain injury (*PNAS* 100, 6216–6220; 2003). This supports the idea that semistarvation boots up stress-response proteins, which then protect cells from aging and disease. Mattson is now hunting for those protective molecules.

Far from being inspired by caloric restriction, Mattson maintains that his strict dietary habits stem from his family's medical history. As a 21-year-old undergraduate student at the University of Iowa, the news that his grandfather had died of a heart attack shocked him into cleaning up his fast-food habits. Today, he says, both his lifestyle and research are driven by the desire to achieve a healthy old age rather than everlasting youth. "I'm not interested in

figuring out how to reach 200," he says. "I'm interested in figuring out how everyone can live to be 80 or 90 without any disease."

Whatever his motivation, Mattson's lifestyle takes self-control. He limits himself to 2,000 to 2,200 calories a day and runs four miles every day. Breakfast is often nonexistent, lunch is light, and dinner—which is different from his family's—is typically a bowl of steamed broccoli, carrots and cabbage with some salmon or yogurt. Mattson says he indulges himself on special occasions and, often before bed, gulps down a bowl of oatmeal and raisins. "My daughter said, 'Why do you eat breakfast before you go to sleep?'" he says.

Mattson's self-discipline also extends to other parts of his life. He routinely arrives for work at 5 a.m. and, by all accounts, is extremely dedicated and hardworking. If there is one thing Mattson is criticized for, says his former postdoctoral researcher Steven Barger, now at the University of Arkansas in Little Rock, it is Mattson's expectation that others show the same single-minded dedication. "It's the biggest source of friction of anyone who's worked for [Mattson]," Barger says.

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Mattson routinely tests his students' minds, but Barger recounts one incident where Mattson also challenged their fitness. At a 1995 lab meeting, he asked if anyone wanted to participate with him in a 10-kilometer race in Lexington, Kentucky, then added that he did not expect anyone to be able to keep up with him. "It's not bragging," says Barger, who indeed trailed in behind his boss. "As a scientist, [Mattson] was stating the cold, hard facts."

On the diet front at least, Mattson is well aware that other people find it tough to match his self-control. One of his goals is to find ways in which people can reap the potential benefits of caloric restriction without abandoning food. As part of this, he plans to launch the first human intervention trial of intermittent fasting this summer. To mimic the laboratory animals' fasting regimen, subjects recruited to the trial will eat only one big meal a day for two months, while researchers monitor their blood cholesterol, blood sugar and other health indicators.

Some people don't need clinical trials to coax them into calorie restriction, however. Mattson says he receives frequent inquiries from members of the Calorie Restriction Society, an international group keen to be included in studies and already pursuing a long life through meager diets. Though Mattson does not adhere to such a strict routine, some colleagues view his dietary habits with skepticism and amusement. "[The field] is driven by some unusual personalities," says Finch.

Helen Pearson, Bethesda