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Eat Smart

Foods may affect the brain as well as the body

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This is part two of a two-part series on lifestyle and brain fitness. Part I: "Buff and Brainy," is available at http://www.sciencenews.org/articles/20060225/bob10.asp.

At family dinner tables around the globe, prodding mothers have dished out the same refrain for decades: "Eat your fish," they say. "It's brain food!" For children picking at crusty fish sticks or blobs of pink poached salmon, the statement raises suspicions. But the message is turning out to be more than just an attempt to get children to clean their plates. Recent research is suggesting that what you eat can influence the function of your brain.

Scientists are providing hints that what you choose to consume or avoid in your daily diet can have consequences on the brain's resiliency in the face of injury or disease. Studies suggest that foods such as fish and a curry spice called curcumin, for example, can give the brain an added edge to stay healthy.

On the other hand, a steady diet of high-fat and starchy foods, such as that double cheeseburger from a favorite fast-food joint, may eventually do the brain a serious disservice. On the extreme end of dieting, some research indicates that paring food intake to the bare minimum may protect the brain from a lifetime of everyday insults.

Taken together, these results point in a direction that any kid could have seen coming: Once again, Mom was right.

Fish curry

Besides a mother's goading, there are plenty of reasons to eat a succulent fillet of fish. The strongest incentive, neuroscientists say, may lie in the growing number of benefits attributed to nutrients known as omega-3 fatty acids, found in small amounts in some plants and in abundance in oily, cold-water fish such as salmon.

Neurosurgery professor Fernando Gómez-Pinilla operates a traumatic brain-injury center at the University of California, Los Angeles (UCLA). Because his past studies suggested that exercise affects how well brains function (SN: 2/25/06, p. 122: http://www.sciencenews.org/articles/20060225/bob10.asp), he wondered whether diet might also change how his patients coped with brain injuries.

Working with rats, Gómez-Pinilla and his colleagues compared the effects of two diets. Both included healthy, low-fat chow. However, one diet contained 8 percent fish oil—the amount people would receive by eating fish about twice a week. After 4 weeks, Gómez-Pinilla's team subjected some of the rats to a mild percussion injury—a knock on the head in a machine specially designed to standardize the force of its blows.

The researchers tested all the animals a week later in a water maze to see how quickly the rats could learn the location of a platform hidden beneath the water's milky surface. They found that brain-injured rats fed the fish oil-supplemented diet found the platform's location in about two-thirds of the time it took the injured rats that ate the standard rat chow to do so. Surprisingly, Gómez-Pinilla says, the injured rats fed the fish oil mastered the maze almost as quickly as rats that weren't injured did.

He and his colleagues found that rats that had eaten unsupplemented chow had lower brain concentrations of a protein called brain-derived neurotrophic factor (BDNF). This compound encourages nerve cells to grow and make new connections. BDNF concentrations are typically low after the type of injury that the rats had

experienced. In contrast, BDNF concentrations in rats fed fish oil were much like those in rodents that hadn't received brain injuries.

Gómez-Pinilla and other scientists have shown in previous studies that nerve cells produce BDNF when animals exercise. This protein may be a prime player in the neurological benefits that animals get from exercise.

Researchers aren't yet sure how the components of fish oil change BDNF amounts in the brain. However, Gómez-Pinilla says, "eating a diet rich in omega-3 fatty acids could have some of the same [neurological] effects as exercise."

Neuroscientist Greg M. Cole, working in another laboratory at UCLA and also at the Veterans Administration Medical Center in Sepulveda, Calif. is finding that supplementing food with just the omega-3 fatty acid DHA—rather than the complex blend of fish-oil ingredients—can dramatically slow neurodegenerative symptoms in mice bred to develop an Alzheimer's-like disease.

In a study published in the March 23, 2005 *Journal of Neuroscience*, Cole's team peered into the brains of Alzheimer's-susceptible mice that had been fed diets either high or low in DHA for about 3 months. They found that mice on the high-DHA diet had only about 30 percent as many deposits of a waxy protein called beta-amyloid—a hallmark of Alzheimer's disease—compared with mice that ate little or no DHA.

Curcumin, a yellow polyphenol that's a component of the curry spice turmeric, has similar effects in reducing the amount of beta-amyloid in Alzheimer's-susceptible mice. Cole's team fed mice a daily dose of curcumin that was similar, in proportion to food intake, to the amount that a person in India typically eats each day. Those mice had about half as many beta-amyloid deposits as did mice that weren't given the spice.

In a study published in the Feb. 18, 2005 *Journal of Biological Chemistry*, Cole and his colleagues reported that curcumin binds to bits of amyloid-beta protein, discouraging them from aggregating into the waxy clumps associated with Alzheimer's symptoms.

He says that both fish oil and curcumin may eventually become widely used in preventing neurodegenerative diseases, while causing few side effects. On the other hand, recently created drugs for treating neurodegenerative diseases are expensive and often have troubling side effects.

Cole notes that people have been eating fish and curries safely for centuries. "We're interested in these approaches that have cost-effectiveness and safety built into them," he says.

Fat attack

Just as fish oil and curcumin seem to aid the brain, other foods—such as those in the typical high-fat, sugary U.S. diet—could take brain health down a notch.

Four years ago, Gómez-Pinilla and his colleagues tested how the typical diet of people in industrialized Western countries affected brain function in rats. The researchers fed half of a group of rats a regular lab diet composed of about 13 percent fat and 59 percent complex carbohydrates, among other nutrients. The other animals received a high-fat and high-sugar (HFS) diet made with 39 percent fat, primarily from lard and corn oil, and 40 percent refined white sugar.

After just 2 months, Gómez-Pinilla's team found that animals on the standard diet learned the water-maze task faster than did rats on the HFS diet. When the scientists dissected the animals' brains after a year on the special diets, they found that rats on the HFS diet had less than half as much BDNF as mice on the healthy diet did. The HFS rats also had reduced amounts of several other proteins associated with learning and memory.

In another experiment published 2 years later, Gómez-Pinilla tested how rats on the two diets fared after a mild brain injury such as the one that the rats on the fish oil diets had been subjected to. Animals ate their assigned diet for 4 weeks then received a mild brain injury. In the water maze, both sets of animals had performed equally well before being injured. However, rats fed the HFS diet showed greater deficits in learning the maze a week after their percussion injuries than did rats fed the regular diet.

When the scientists examined the animals' brains, they found that rats on the HFS diet had lower amounts of BDNF than those on the healthy diet did. A shortage of BDNF could underlie the animals' inability to recover from their neurological injuries as well as the other rats did, says Gómez-Pinilla.

"A lot of the problems of consuming this diet become more obvious when animals are exposed to some insult,

like a traumatic brain injury," he adds.

Gómez-Pinilla suggests another possible reason for the HFS rats' poor performance: damage in the brain caused by a chemical process called oxidation. Diets high in fat and sugar are also usually high in calories. The more calories an animal eats, the more its body generates free radicals: negatively charged molecular particles that cause oxidation damage in cells, particularly those in the nervous system.

The HFS rats may also have had less brain power because a steady fare of fat and sugar can change how the body responds to insulin, says Carol E. Greenwood, who studies nutrition and aging at the University of Toronto. Animals eating such food can become less sensitive to insulin, the compound that signals cells to take up glucose from the blood for processing into energy.

Low insulin sensitivity effectively starves these animals' cells, including brain cells. Numerous studies by Greenwood's lab and others indicate that a steady diet of such food can decrease an animal's ability to learn and remember.

Furthermore, Greenwood and her colleague Gordon Winocur report in a supplement to the December 2005 *Neurobiology of Aging* that the already poor learning and memory abilities of insulin-resistant people get even worse after they consume a sugary snack, which raises glucose concentrations.

The researchers aren't sure why high glucose concentrations have such a detrimental effect on brain function. "Our instinct at this point is that when glucose gets too high in the blood, it launches a cascade of oxidative reactions. Various components of that cascade may contribute to cognitive deficits," says Greenwood.

Ascetic eater

Since taking in calories generates damaging free radicals, some researchers have hypothesized that simply eating less may protect the brain from harm. Recent studies support this hypothesis. For example, teams led by neuroscientist Mark Mattson of the National Institute on Aging in Baltimore have shown that cutting back calories in lab animals can reduce the symptoms seen in Huntington's- and Parkinson's-like diseases.

In one experiment, Mattson and his colleagues worked with mice that carried a mutant form of the human *huntingtin* gene. People who have this mutation show a variety of emotional and physical symptoms, such as mood swings and loss of muscle control, generally starting in adulthood. They eventually die of the disease.

Mattson's team gave the Huntington's mice a normal diet for 8 weeks. Then, the researchers began to feed some of the animals only every other day to cut by about 20 percent the number of calories consumed. Other mice were permitted to eat as much as they wanted.

Those eating fewer calories showed their first symptoms of the Huntington's-like disease an average of 12 days later than the other group did. Mice eating restricted diets also lived longer. At 21 weeks, all the free-eating mice had died from the disease. However, 60 percent of those on the restricted diets were still alive.

When researchers dissected the animals' brains, they found that the animals on the every-other-day diets had less atrophy and fewer clumps of the mutant huntingtin protein than the free-eaters did.

Mattson has had similar success by decreasing the calorie intake of monkeys with a Parkinson's-like disease.

After feeding some of the monkeys 30 percent less food over 6 months, Mattson's team found that those animals had fewer symptoms of the disease, such as muscle tremors and rigidity, compared with monkeys that ate as much as they wanted. Examination of the animals' brains showed that those that ate fewer calories had higher concentrations of dopamine, even though the majority of their dopamine-producing neurons had died.

Use your brain

Mattson says that the reason calorie restriction seems to save neurons probably extends beyond simply protecting them from free radicals. Eating less cuts energy to all the body's cells, including those in the brain.

This mild stress makes brain cells more active and triggers production of protective proteins, such as BDNF and heat-shock protein. Mattson suggests that the lightly stressed neurons tend to cope better with more-severe stress—such as that imposed by neurological disease—than cells of animals on a steady diet do.

"When you put animals on dietary restriction, some studies suggest that their brains are more active because

they're apparently looking for food," says Mattson.

While caloric restriction seems to protect animals from neurological diseases, Mattson notes that people rarely want to cut back so stringently. So, should they just eat fish curries every night while conscientiously avoiding fast-food fare?

"That's the kind of talk that raises the hair on the backs of nutritionists," says Greenwood. Different foods have different benefits, and studies show that patterns of food consumption influence health. "Everything we see out there suggests that variety is what we need in our diets," she concludes.

She argues that in laboratory studies, it's difficult to separate effects of different diets on the brain from the diets' effects on the rest of the body. Nevertheless, a healthy diet seems to be good all around. "The idea is that by taking care of your body, your brain also benefits," she says.

Now, that's an idea that any mom would approve.

Part I of this series: "Buff and Brainy," appeared in last week's issue. Available at http://www.sciencenews.org/articles/20060225/bob10.asp.

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