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PHYS ED

Lobes of Steel

By GRETCHEN REYNOLDS

The Morris water maze is the rodent equivalent of an I.Q. test: mice are placed in a tank filled with water dyed an opaque color. Beneath a small area of the surface is a platform, which the mice can't see. Despite what you've heard about rodents and sinking ships, mice hate water; those that blunder upon the platform climb onto it immediately. Scientists have long agreed that a mouse's spatial memory can be inferred by how quickly the animal finds its way in subsequent dunkings. A "smart" mouse remembers the platform and swims right to it.

In the late 1990s, one group of mice at the Salk Institute for Biological Studies, near San Diego, blew away the others in the Morris maze. The difference between the smart mice and those that floundered? Exercise. The brainy mice had running wheels in their cages, and the others didn't.

Scientists have suspected for decades that exercise, particularly regular aerobic exercise, can affect the brain. But they could only speculate as to how. Now an expanding body of research shows that exercise can improve the performance of the brain by boosting memory and cognitive processing speed. Exercise can, in fact, create a stronger, faster brain.

This theory emerged from those mouse studies at the Salk Institute. After conducting maze tests, the neuroscientist Fred H. Gage and his colleagues examined brain samples from the mice. Conventional wisdom had long held that animal (and human) brains weren't malleable: after a brief window early in life, the brain could no longer grow or renew itself. The supply of neurons — the brain cells that enable us to think — was believed to be fixed almost from birth. As the cells died through aging, mental function declined. The damage couldn't be staved off or repaired.

Gage's mice proved otherwise. Before being euthanized, the animals had been injected with a chemical compound that incorporates itself into actively dividing cells. During autopsy, those cells could be identified by using a dye. Gage and his team presumed they wouldn't find such cells in the mice's brain tissue, but to their astonishment, they did. Up until the point of death, the mice were creating fresh neurons. Their brains were regenerating themselves.

All of the mice showed this vivid proof of what's known as "neurogenesis," or the creation of new neurons. But the brains of the athletic mice in particular showed many more. These mice, the ones that scampered on running wheels, were producing two to three times as many new neurons as the mice that didn't exercise.

But did neurogenesis also happen in the human brain? To find out, Gage and his colleagues had obtained brain tissue from deceased cancer patients who had donated their bodies to research. While still living, these people were injected with the same type of compound used on Gage's mice. (Pathologists were hoping to learn more about how quickly the patients' tumor cells were growing.) When Gage dyed their brain samples, he again saw new neurons. Like the mice, the humans showed evidence of neurogenesis.

Gage's discovery hit the world of neurological research like a thunderclap. Since then, scientists have been finding more evidence that the human brain is not only capable of renewing itself but that exercise speeds the process.

"We've always known that our brains control our behavior," Gage says, "but not that our behavior could control and change the structure of our brains."

The human brain is extremely difficult to study, especially when a person is still alive. Without euthanizing their subjects, the closest that researchers can get to seeing what goes on in there is through a functional M.R.I. machine, which measures the size and shape of the brain and, unlike a standard M.R.I. machine, tracks blood flow and electrical activity.

This spring, neuroscientists at Columbia University in New York City published a study in which a group of men and women, ranging in age from 21 to 45, began working out for one hour four times a week. After 12 weeks, the test subjects, predictably, became more fit. Their VO2 max, the standard measure of how much oxygen a person takes in while exercising, rose significantly.

But something else happened as a result of all those workouts: blood flowed at a much higher volume to a part of the brain responsible for neurogenesis. Functional M.R.I.'s showed that a portion of each person's hippocampus received almost twice the blood volume as it did before. Scientists suspect that the blood pumping into that part of the brain was helping to produce fresh neurons.

The hippocampus plays a large role in how mammals create and process memories; it also plays a role in cognition. If your hippocampus is damaged, you most likely have trouble learning facts and forming new memories. Age plays a factor, too. As you get older, your brain gets smaller, and one of the areas most prone to this shrinkage is the hippocampus. (This can start depressingly early, in your 30's.) Many neurologists believe that the loss of neurons in the hippocampus may be a primary cause of the cognitive decay associated with aging. A number of studies have shown that people with Alzheimer's and other forms of dementia tend to have smaller-than-normal hippocampi.

The Columbia study suggests that shrinkage to parts of the hippocampus can be slowed via exercise. The subjects showed significant improvements in memory, as measured by a word-recall test. Those with the biggest increases in VO2 max had the best scores of all.

"It's reasonable to infer, though we're not yet certain, that neurogenesis was happening in the people's hippocampi," says Scott A. Small, an associate professor of neurology at Columbia and the senior author of the study, "and that working out was driving the neurogenesis."

Other recent studies support this theory. At the University of Illinois at Urbana- Champaign, a group of elderly sedentary people were assigned to either an aerobic exercise program or a regimen of stretching.

(The aerobic group walked for at least one hour three times a week.) After six months, their brains were scanned using an M.R.I. Those who had been doing aerobic exercise showed significant growth in several areas of the brain. These results raise the hope that the human brain has the capacity not only to produce new cells but also to add new blood vessels and strengthen neural connections, allowing young neurons to integrate themselves into the wider neural network. “The current findings are the first, to our knowledge, to confirm the benefits of exercise training on brain volume in aging humans,” the authors concluded.

And the benefits aren’t limited to adults. Other University of Illinois scientists have studied school-age children and found that those who have a higher level of aerobic fitness processed information more efficiently; they were quicker on a battery of computerized flashcard tests. The researchers also found that higher levels of aerobic fitness corresponded to better standardized test scores among a set of Illinois public school students. The scientists next plan to study how students’ scores change as their fitness improves.

What is it about exercise that prompts the brain to remake itself? Different scientists have pet theories. One popular hypothesis credits insulin-like growth factor 1, a protein that circulates in the blood and is produced in greater amounts in response to exercise. IGF-1 has trouble entering the brain — it stops at what’s called the “blood-brain barrier” — but exercise is thought to help it to do so, possibly sparking neurogenesis.

Other researchers are looking at the role of serotonin, a hormone that influences mood. Exercise speeds the brain’s production of serotonin, which could, in turn, prompt new neurons to grow. Abnormally low levels of serotonin have been associated with clinical depression, as has a strikingly shrunken hippocampus. Many antidepressant medications, like Prozac, increase the effectiveness of serotonin. Interestingly, these drugs take three to four weeks to begin working — about the same time required for new neurons to form and mature. Part of the reason these drugs are effective, then, could be that they’re increasing neurogenesis. “Just as exercise does,”Gage says.

Gage, by the way, exercises just about every day, as do most colleagues in his field. Scott Small at Columbia, for instance , likes nothing better than a strenuous game of tennis. “As a neurologist,” he explains, “I constantly get asked at cocktail parties what someone can do to protect their mental functioning. I tell them, ‘Put down that glass and go for a run.’ ” .

This Is Your Brain on Something Other Than Exercise

The human brain undergoes neurogenesis — the creation of new cells — throughout a person’s life, although the amount depends on a variety of factors, not just exercise.

MARIJUANA: We just report the data; we don’t endorse it. A 2005 study on rats found that stimulation of the brain’s receptors for marijuana increased neurogenesis.

ALCOHOL: A 2005 study found that mice that swallowed a moderate amount of ethanol showed more neurogenesis than teetotalers. Other studies on mice have suggested that heavier drinking can be damaging to the brain.

SOCIABILITY: One study suggests that rats that live alone and have access to a run ning wheel experience less neurogenesis than those that have access to a running wheel and live in group housing. So go ahead and join that singles running club you've been avoiding.

DIET: A diet high in saturated fat and sugar sharply diminishes the brain's production of the proteins and nerve-growth factors necessary for neurogenesis. Exercise may mitigate that effect somewhat.

STRESS: Mice that are subjected to uncontrollable stress (like electric shock) suffer substantial deterioration in their ability to produce new neurons.

CHOCOLATE: In a study published this year, an ingredient in cocoa, epicatechin, was shown to improve spatial memory in mice, especially among those that exercised. Epicatechin can also be found in grapes, blueberries and black tea. "I plan to start ingesting more epicatechin," says Henriette van Praag, a neuroscientist at the Salk Institute, "as soon as I can't find my car keys anymore." **G.R.**