

Explorations

Research and
Discovery



Can exercise delay
or prevent
Alzheimer's?
/ BY ELIZABETH
DOUGHERTY

Work It
Out

When Karin Schon enrolled in a 12-week fitness training program during her doctoral studies in cognitive neuroscience at BU, she expected it to improve her health. She had no idea that it would also shape her research.

BEFORE SCHON TOOK A SINGLE STEP, HER TRAINERS gave her a fitness test that measured body fat, weight, and cardiovascular fitness. That first test provided a baseline; another test three months later would determine if the program had made a difference. “I liked it from a scientific perspective,” says Schon (GRS’05), a School of Medicine assistant professor of anatomy and neurobiology and a BU Alzheimer’s Disease Center faculty member, who studies the effects of physical activity on the aging brain. “It felt like I was participating in a study.”

The program worked. Schon lost about 20 pounds, her

▲ Researcher Karin Schon uses a functional magnetic resonance imaging machine to study the connection between physical fitness and memory performance. Her work may lead to interventions for Alzheimer’s disease.

cardiovascular fitness improved, and she was able to hold plank (the upper position of a push-up and a test of core strength and endurance) for nearly seven minutes.

“This program had such an impact on me physically,” says Schon. “I thought that it must have an effect on the brain if it has an effect on the body.”

She decided to study the effects of exercise on memory, and in 2010 won a Pathway to Independence Award from the National Institute on Aging, which provided five years of funding for her research.

In the United States today, cognitive decline is a serious concern. One in three senior citizens dies with Alzheimer’s disease or another form of dementia and the number of cases is

rising, according to the Alzheimer's Association. The costs of caring for people with Alzheimer's are expected to reach approximately \$1 trillion by 2050.

As a graduate student at BU, Schon joined the lab of neuroscientist Chantal Stern, a College of Arts & Sciences professor of psychological and brain sciences, and learned to use functional magnetic resonance imaging (fMRI) to study the hippocampus, a seat of memory in the brain.

To measure memory capabilities, Schon showed study participants pictures in a series. She presented one image, then another, then a test picture, with delays between each presentation. The participants determined if they had seen the test picture before, as in the game Concentration.

She found that the fMRI patterns during the delays predict whether someone remembers the picture 15 minutes later.

Schon continues to use this method to study the relationship between fitness and memory. She recruited a group of students to take a fitness test and then look at pictures in the fMRI scanner. She discovered an indirect connection between fitness and memory performance. A growth hormone called BDNF appears to connect the two. "There's greater memory accuracy with greater levels of BDNF in more fit individuals," explains Rachel Nauer (GRS'15,'20), a graduate student in Schon's Brain Plasticity and Neuroimaging Laboratory.

BDNF is also known to play a role in the growth of new neurons in the brain, a factor that provided Schon with the first of several connections between her research and Alzheimer's disease.

Making a connection to Alzheimer's in any research program is difficult. The disease is mysterious. It occurs when a protein called amyloid forms plaques in the brain. Tangles, caused by tau, a different protein, follow, as does neurodegeneration, the loss of brain cells.

It isn't clear yet what causes plaques to form in the first place, or if those plaques directly cause tangles to appear. Also, plaques may begin forming in the brain 20 years before a person begins to misplace car keys or forget names. This long lead time makes it extremely difficult to study the progression of the disease and especially difficult to show that an intervention slows progression.

Enter Jake Gyllenhaal

So instead of focusing on Alzheimer's disease directly, Schon is focusing on links to it in the brain. One link is BDNF, which helps the brain grow new neurons. In the hippocampus, that neurogenesis occurs in a subregion called the dentate gyrus, which, animal studies have shown, is enlarged by exercise.

A second link to Alzheimer's disease is in the entorhinal cortex, which is connected to the dentate gyrus. Schon's team found that the entorhinal cortex is bigger in people with higher fitness levels. Animal studies suggest that these two regions of the brain—the dentate gyrus and the entorhinal cortex—malfunction first in Alzheimer's disease.

Schon plans to study the effects of exercise on the entorhinal cortex, pending funding from the National Institutes of Health. She is now studying an exercise intervention focusing on the dentate gyrus. To do this, she and Nauer had to develop a method to specifically stimulate the dentate gyrus. They needed an extremely sensitive test to detect changes in



► Rachel Nauer (GRS'15,'20) and Matt Dunne, a research team from Karin Schon's Brain Plasticity and Neuroimaging Laboratory at the School of Medicine, are studying the effects of exercise on memory. They spend several hours at FitRec assessing the fitness of each participant in their exercise intervention study. They also guide them through experiments in the fMRI machine to assess memory capabilities and capture brain images.

this tiny brain region, and, potentially, to connect them to subtle behavior changes that other cognitive tests miss.

The new test her group developed builds on Schon's earlier fMRI methods for stimulating the hippocampus. The team presents special images that trigger the brain to perform a process called pattern separation, which deciphers subtle differences in images and—critically—which occurs in the dentate gyrus. So they believe the method triggers activity in a seat of neurogenesis in the brain, and a place of earliest vulnerability in Alzheimer's.

Nauer illustrates the types of images they show using familiar faces, such as actors Jake Gyllenhaal, Joseph Gordon-Levitt, and John Travolta, although in the actual experiments, the images are of unfamiliar scenes. In her example, she shows faces that have been morphed using computer software so that they have specific degrees of similarity. One face might be 90 percent Gyllenhaal and 10 percent Gordon-Levitt, for example, and another might be 90 percent Gordon-Levitt and 10 percent Gyllenhaal. As the degree of similarity increases, the images become harder to decipher.

The researchers are still recruiting sedentary participants in two age groups—18 to 35 and 55 to 85—who enroll in a fitness program like the one Schon took years ago. Each participant is given aerobic and muscle function tests as well as memory tests, including the pattern separation test in the fMRI. Researchers also sample BDNF levels.

The participants are then given an individualized exercise prescription—either an aerobic fitness routine or a resistance training routine—to follow three times a week for 12 weeks. Since animal studies indicate that cardiovascular fitness is the key to improved memory, the researchers consider the resistance training group to be a control.

For Nauer, this research isn't so much about whether exercise will make a difference, but rather what kind of exercise makes the most difference and how much is needed. "My focus moving forward is doing research that informs doctors," she says, "so they may someday prescribe an exercise program rather than a drug."

Schon is also working with Rhoda Au (Questrom'95), a MED professor of neuropsychology and a School of Public Health professor of epidemiology, on another exercise intervention that uses digital cognitive assessments to detect subtle memory changes. These assessments record answers to memory questions and track the thinking that goes on behind these tasks. Au hopes to identify changes in behavior that are more subtle than the symptoms a doctor would look for.

This distinction between disease treatment and disease prevention is a critical one. Exercise may help individuals with cognitive impairments slow the disease, but Au thinks Schon's work could have wider implications. The way she sees it, if exercise prevents cognitive decline, it could shrink the looming specter of Alzheimer's disease.

Since 1990, Au has been an investigator for the Framingham Heart Study, the nation's longest-running epidemiological study, supported by the National Heart, Lung, and Blood Institute, and run by BU since 1971. According to a study report, delaying Alzheimer's disease by five years reduces a person's risk of getting the disease by 50 percent. "Essentially, the disease is competing with mortality," she explains.

If fitness delays Alzheimer's disease enough to reduce the risk by any percentage, that puts a dent in the problem. With the number of Americans with Alzheimer's possibly reaching 7.1 million in the coming decade, any improvement is welcome.

Scientists unravel the mystery
of Jupiter's "energy crisis" /
BY KATE BECKER

Red Spot, Hot Spot

FIVE HUNDRED MILES ABOVE THE SWIRL of Jupiter's caramel-and-cream clouds lies a mystery. The atmosphere's top layer, which covers the whole planet like a gigantic orange rind, should be a frigid 200 Kelvin. Instead, it broils away at 850 Kelvin—more than 1,000 degrees Fahrenheit.

This hot layer is called the thermosphere, and for 40 years—since observations from NASA's *Voyager* spacecraft and ground-based telescopes first revealed its temperature—researchers have tried to understand the source of this extreme heat. They have even given the problem a name: the "energy crisis."

Now a team of astronomers from BU and the University of Leicester in England think they have found the solution to the mystery—in Jupiter's iconic Great Red Spot.

The Red Spot is the greatest storm on the grandest planet in the solar system, a colossal hurricane that makes Earth's worst gales look positively tranquil. Wider than our whole planet, lashed by 400-mile-per-hour winds, the Great Red Spot has been raging for at least 150 years—possibly centuries longer.

▲ Artist's concept of the heating mechanism from Jupiter's Great Red Spot. The storm in the Great Red Spot churns up the gas around it, sending waves traveling upward. Like ocean waves breaking on the shore, the waves of compressed gas "dump" their stored-up energy in the upper atmosphere.

