

Newsweek March 19, 2007

Exercise does more than build muscles and help prevent heart disease. New science shows that it also boosts brainpower--and may offer hope in the battle against Alzheimer's.

By Mary Carmichael

The stereotype of the "dumb jock" has never sounded right to Chuck Hillman. A jock himself, he plays hockey four times a week, but when he isn't body-checking his opponents on the ice, he's giving his mind a comparable workout in his neuroscience and kinesiology lab at the University of Illinois. Nearly every semester in his classroom, he says, students on the women's cross-country team set the curve on his exams. So last year he started wondering if there was a vital and overlooked link between brawn and brains--if long hours at the gym could somehow build up not just muscles, but minds. With colleagues, he rounded up 259 Illinois third and fifth graders, measured their body-mass index and put them through classic PE routines: the "sit-and-reach," a brisk run and timed push-ups and sit-ups. Then he checked their physical abilities against their math and reading scores on a statewide standardized test. Sure enough, on the whole,

the kids with the fittest bodies were the ones with the fittest brains, even when factors such as socioeconomic status were taken into account. Sports, Hillman concluded, might indeed be boosting the students' intellect--and also, as long as he didn't "take a puck to the head," his own.

Hillman's study, which hasn't yet been published, isn't definitive enough to stand alone. But it doesn't have to: it's part of a recent and rapidly growing movement in science showing that exercise can make people smarter. Last week, in a landmark paper, researchers announced that they had coaxed the human brain into growing new nerve cells, a process that for decades had been thought impossible, simply by putting subjects on a three-month aerobic-workout regimen. Other scientists have found that vigorous exercise can cause older nerve cells to form dense, interconnected webs that make the brain run faster and more efficiently. And there are clues that physical activity can stave off the beginnings of Alzheimer's disease, ADHD and other cognitive disorders. No matter your age, it seems, a strong, active body is crucial for building a strong, active mind.

Scientists have always suspected as much, although they haven't been able to prove it. The idea of the "scholar-athlete" isn't just a marketing ploy dreamed up by the NCAA; it goes back to the culture of ancient Greece, in which "fitness was almost as important as learning itself," says Harvard psychiatrist John Ratey. The Greeks, he adds, were clued into "the mind-body connection." And they probably intuited a basic principle that Western researchers also figured out long ago: aerobic exercise helps the heart pump more

blood to the brain, along with the rest of the body. More blood means more oxygen, and thus better-nourished brain cells. For decades, that has been the only link between athletic and mental prowess that science has been able to demonstrate with any degree of certainty. "People have been slow to grasp that exercise can really affect cognition," says Hillman, "just as it affects muscles."

Now, however, armed with brain-scanning tools and a sophisticated understanding of biochemistry, researchers are realizing that the mental effects of exercise are far more profound and complex than they once thought. The process starts in the muscles. Every time a bicep or quad contracts and releases, it sends out chemicals, including a protein called IGF-1 that travels through the bloodstream, across the blood-brain barrier and into the brain itself. There, IGF-1 takes on the role of foreman in the body's neurotransmitter factory. It issues orders to ramp up production of several hormones, including one called brain-derived neurotrophic factor, or BDNF. Roney, author of the upcoming book "Spark: The Revolutionary New Science of Exercise and the Brain," calls this chemical "Miracle-Gro for the brain." It fuels almost all the activities that lead to higher thought.

With regular exercise, the body builds up its levels of BDNF, and the brain's nerve cells start to branch out, join together and communicate with each other in new ways. This is the process that underlies learning: every change in the junctions between brain cells signifies a new fact or skill that's been picked up and stowed away for future use. BDNF makes that process possible. Brains with more of it have a greater capacity for knowledge. On the other hand, says UCLA neuroscientist Fernando Gómez-Pinilla, a brain that's low on BDNF shuts itself off to new information. In his experiments, rats were put through weeks of running on a wheel, a workout that increased their BDNF levels. Gómez-Pinilla left half of the animals alone; in the other half, he blocked the hormone's effects with a drug. Then he subjected both groups of athletic rats to a test of wits, encouraging them to find an object that was hidden underwater. The first group easily pinpointed its location, but the second, BDNF-deprived group wasn't nearly as quick or sharp. Nature has conducted a similar experiment on humans. In unlucky people with a faulty variant of the gene that makes BDNF, the brain has trouble both creating new memories and calling up old ones.

Most people maintain fairly constant levels of BDNF in adulthood. But as they age, their individual neurons slowly start to die off. Until the mid-'90s, scientists thought the loss was permanent--that the brain couldn't make new nerve cells to replace the dead ones. But animal studies over the last decade have overturned that assumption, showing that "neurogenesis" in some parts of the brain can be induced easily with exercise. Last week's study, published in *Science*, extended that principle to humans for the first time. After working out for three months, all the subjects in the study sprouted new neurons; those who gained the most in cardiovascular fitness also grew the most nerve cells. This, too, was the work of BDNF. Its second job is to transform stem cells into full-grown, functional neurons; more BDNF equals a bigger brain. "It was extremely exciting to see this in humans because it defied dogma," says Scott Small, a Columbia University neurologist who co-authored the study with Salk Institute neurobiologist Fred Gage. "In terms of trying to understand what it means, the field is just exploding."

The first step toward that understanding is to figure out exactly where the new brain cells are growing--and whether that is a part of the brain that needs to be rejuvenated. In Small and Gage's experiment, the new neurons created by exercise cropped up in only one place: the dentate gyrus of the hippocampus, an area that controls learning and memory. This region, tucked under the frontal lobes, is especially key to a type of higher thought called "executive functioning," which mainly entails decision-making, multitasking and planning ahead. Those are some of the first skills to erode as we age. The hippocampus also helps the brain match names to faces, another task that all too many people find harder as they get older. Fortunately, exercise seems to restore the hippocampus to a healthier, "younger" state. "It's not just a matter of slowing down the aging process," says Arthur Kramer, a psychologist at the University of Illinois. "It's a matter of reversing it." In dozens of studies of men and women in their 60s and 70s, brisk walking and other aerobic workouts have yielded improvements in executive functioning. Subjects have fared better on psychological tests that engage the hippocampus, answering questions more accurately and quickly. With the publication of the *Science* paper, researchers can now explain why.

As far as scientists know, adults can grow new neurons only in the hippocampus. But other parts of their brains benefit from exercise in many secondary ways. Last year Kramer found that exercise caused overall brain volume to increase in older men and women. The same is true for blood volume, says Small: "Wherever you have the birth of new brain cells, you have the birth of new capillaries." Active adults have less inflammation in the brain. They also have fewer "little bitty strokes that can impair cognition without the person even knowing," says University of California, San Francisco, neurologist Kristine Yaffe. Still other scientists have found that athletes have more astrocytes, or cells that support neurons and mop up neurotransmitters after they're used to send messages from cell to cell. And even the levels of those neurotransmitters are higher in people who exercise frequently. "Dopamine, serotonin, norepinephrine, all of these are elevated after a bout of exercise," says Ratey. "So having a workout will help with focus, calming down, impulsivity--it's like taking a little bit of Prozac and a little bit of Ritalin."

Unlike neurogenesis, which can take weeks to occur, most of these additional effects appear almost immediately. Get off the treadmill after a half-hour workout, says Hillman, and "within 48 minutes" your brain will be in better shape. But alas, these benefits are somewhat transient. Like weight, mental fitness has to be maintained. New neurons, and the connections between them, will stick around for years, but within a month of inactivity, "the astrocytes shrink down again, and then the neurons don't function as well anymore," says William Greenough, a psychologist at the University of Illinois. Let your body go, then, and your brain will follow.

To keep the effects, you've got to keep working out. "If you're thinking that by exercising at age 20 you're going to have some effect on what you're like at age 70," Greenough adds, you'd better be willing to commit to 50 years of hit-ting the gym.

Unless, that is, you're a kid. Most studies of exercise and cognition have focused on older people--the folks who are just starting to worry that their minds aren't what they used to be--but the effects of physical exertion on the brain aren't limited to that group at all. In fact, in young children, they're even more potent. Exercise probably has "a more long-lasting effect on brains that are still developing," says Phil Tomporowski, a professor of exercise science at the University of Georgia. In kids, as in adults, the hippocampus reaps many benefits from exercise. This won't surprise parents of kids with ADHD, many of whom already use physical activity as a substitute or supplement for drugs. In children with the disorder, the hippocampus is enlarged, and it may be wired to the rest of the brain in abnormal ways that affect its function.

But a good workout, or for that matter a boisterous session of kickball, can also have much more widespread effects on children's brains. Until about age 20, kids don't have fully developed frontal lobes, so they "recruit" other parts of the brain to perform necessary functions, including those involved in learning. In Hillman's look at third- and fifth-grade PE students, exercise sped up not just executive functioning, but a broad variety of skills ranging from math to logic to reading, all of which rope in many regions of the brain. "In kids you have a tremendous amount of growing brain tissue, particularly in the frontal lobe," says Tomporowski. "So we can't just break it down to hippocampal function in them. Exactly what else is going on in there, I don't think anybody knows."

With that science in mind, many educators are now pushing for an overhaul of physical education in public schools. Teachers can ensure their students' success in other subjects, they argue, by making PE longer and more focused on brain-strengthening cardiovascular exercise. Inspired by Hillman's work, Kentucky state Sen. Katie Stine recently proposed a bill making a daily half hour of PE mandatory for kids up to eighth grade. It passed the Senate last month. And at schools in Naperville, Ill., students with poor verbal skills have started taking PE immediately before reading class. Their report cards, says Ratey, are already looking better.

The hope of educators isn't just that John-ny and Susie will do better on the SAT. There's a long-term goal as well. If kids develop a love of sport early in life, they're more likely to grow into active adults. And if they do, they may avoid a fate their grandparents are currently facing: a slow slide into mild cognitive impairment, followed by Alzheimer's. Gómez-Pinilla says that Americans' lazy lifestyles may be

contributing their high rates of the disease. Humans have evolved, he notes, to thrive on physical activity; without it, "our brains aren't doing what they're supposed to," and they go awry. Early studies suggest that people who exercise at least a few times a week tend to develop Alzheimer's less often and later than their more sedentary counterparts. There are clues at the level of the brain as well: one of the disease's first targets is the hippocampus.

More controversial is the proposal that exercise might slow the progression of Alzheimer's once it has taken hold. "By the time somebody has fairly well-developed Alzheimer's, it's probably too late," says Yaffe. "It's going to be difficult to get them into an exercise program at that point, and the damage may already be done." There's a grain of hope, however, to be found in animal studies. In mice engineered to develop an Alzheimer's-like disease, a type of "beta-amyloid" plaque, similar to what's found in people, builds up and prevents the brain from working properly. Researchers examined some of those mice in 2005 and found that those who spent more time running on wheels in their cages fared better on memory tests. Even more intriguing were the results from the pathology lab. It's unclear why, but the more active mice had lower levels of plaque in their brains.

That gives rise to the question: if exercise is such good medicine, could scientists someday distill its brain-powering effects into chemical form--a sort of "workout in a pill"? The result might end up resembling many of the drugs that scientists are currently developing to bolster memory in Alzheimer's patients. It would also surely appeal to people who aren't willing to drag themselves to the gym every other day. "There's a resistance to maintaining an exercise program, since it involves a lot of work. People just don't feel like it," says Ratey. "They're, like, 'I want it done fast, and I want it done now, and why should I have to labor over the treadmill?' " Small, the Columbia researcher, sheepishly admits to being in this group. "I exercise, but frankly, I'm not very good at it," he says. "I would much rather find that biochemical link and think about how we might be able to reproduce the effect for the couch potatoes among us."

Before that can happen--way before that can happen--scientists will have to answer a number of nagging questions that remain. Chief among them is why some forms of exercise affect the brain far more than others. Most researchers have focused on aerobic exercise, "and they've ignored strength training" in the process, says Carole Lewis, a physical therapist and coauthor of the new book "Age-Defying Fitness." So far, though, for reasons that no one really understands, the few studies that have examined stretching, toning and weight-lifting have found little to no effect on the brain. Researchers also don't have a clear idea of how much exercise is too much. "There are very good rules for how many hours a day you should work out, and how many days a week, and what kinds of rest periods you should take--but that's all with respect to the rest of your body," says Greenough. "As for the brain, it's just not known, and we need studies like that."

Finally, there's the question that's been dogging Chuck Hillman since he first picked up a hockey stick: why, if jocks on average have more capable brains than the rest of the public, do they have an undeserved reputation for being dumb? Why does a term like "scholar-athlete," which would have made so much sense to the ancient Greeks, get snickered at today? The reason, says Hillman, is found not in science but in common sense: our schools have failed young athletes by cutting them too much slack. "A lot of it comes from schools' giving them an easy road," he says. "Kids get this wholly inaccurate label because they're good at sports, and then their schools falsify classes for them and don't prepare them to graduate." Having a big, gorgeous, healthy brain isn't enough, of course; it also has to be full. "You can optimize your brain to learn," says Ratey, "but then you have to be in an environment where you can do that--and you have to want it." In that case, it's the "scholar," not the "athlete," that counts. ^