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Phys Ed: Your Brain on Exercise

By GRETCHEN REYNOLDS

What goes on inside your brain when you exercise? That question has preoccupied a growing number of scientists in recent years, as well as many of us who exercise. In the late 1990s, Dr. Fred Gage and his colleagues at the Laboratory of Genetics at the Salk Institute in San Diego elegantly proved that human and animal brains produce new brain cells (a process called neurogenesis) and that exercise increases neurogenesis. The brains of mice and rats that were allowed to run on wheels pulsed with vigorous, newly born neurons, and those animals then breezed through mazes and other tests of rodent I.Q., showing that neurogenesis improves thinking.

But how, exactly, exercise affects the staggeringly intricate workings of the brain at a cellular level has remained largely mysterious. A number of new studies, though, includingwork published this month by Mr. Gage and his colleagues, have begun to tease out the specific mechanisms and, in the process, raised new questions about just how exercise remolds the brain.

Some of the most reverberant recent studies were performed at Northwestern University's Feinberg School of Medicine in Chicago. There, scientists have been manipulating the levels of bone-morphogenetic protein or BMP in the brains of laboratory mice. BMP, which is found in tissues throughout the body, affects cellular development in various ways, some of them deleterious. In the brain, BMP has been found to contribute to the control of stem cell divisions. Your brain, you will be pleased to learn, is packed with adult stem cells, which, given the right impetus, divide and differentiate into either additional stem cells or baby neurons. As we age, these stem cells tend to become less responsive. They don't divide as readily and can slump into a kind of cellular sleep. It's BMP that acts as the soporific, says Dr. Jack Kessler, the chairman of neurology at Northwestern and senior author of many of the recent studies. The more active BMP and its various signals are in your brain, the more inactive your stem cells become and the less neurogenesis you undergo. Your brain grows slower, less nimble, older.

But exercise countermands some of the numbing effects of BMP, Dr. Kessler says. In work at his lab, mice given access to running wheels had about 50 percent less BMP-related brain activity within a week. They also showed a notable increase in Noggin, a beautifully named brain protein that acts as a BMP antagonist. The more Noggin in your brain, the less BMP activity exists and the more stem cell divisions and neurogenesis you experience. Mice at Northwestern whose brains were infused directly with large doses of Noggin became, Dr. Kessler says, "little mouse geniuses, if there is such a thing." They aced the mazes and other tests.

Whether exercise directly reduces BMP activity or increases production of Noggin isn't yet known and may not matter. The results speak for themselves. "If ever exercise enthusiasts wanted a rationale for what they're doing, this should be it," Dr. Kessler says. Exercise, he says, through a complex interplay with Noggin and BMP, helps to ensure that neuronal stem cells stay lively and new brain cells are born.

But there are caveats and questions remaining, as the newest experiment from Dr. Gage's lab makes clear. In that study, published in the most recent issue of Cell Stem Cell, BMP signaling was found to be playing a surprising, protective role for the brain's stem cells. For the experiment, stem cells from mouse brains were transferred to petri dishes and infused with large doses of Noggin, hindering BMP activity. Without BMP signals to inhibit them, the stem cells began dividing rapidly, producing hordes of new neurons. But over time, they seemed unable to stop, dividing and dividing again until they effectively wore themselves out. The same reaction occurred within the brains of living (unexercised) mice given large doses of Noggin. Neurogenesis ramped way up, then, after several weeks, sputtered and slowed. The "pool of active stem cells was depleted," a news release accompanying the study reported. An overabundance of Noggin seemed to cause stem cells to wear themselves out, threatening their ability to make additional neurons in the future.

This finding raises the obvious and disturbing question: can you overdose on Noggin by, for instance, running for hours, amping up your production of the protein throughout? The answer, Dr. Gage says, is, almost certainly, no. "Many people have been looking into" that issue, he says. But so far, "there has not been any instance of a negative effect from voluntary running" on the brain health of mice. Instead, he says, it seems that the effects of exercise are constrained and soon plateau, causing enough change in the activity of Noggin and BMP to shake slumbering adult stem cells awake, but not enough to goose them into exhausting themselves.

Still, if there's not yet any discernible ceiling on brain-healthy exercise, there is a floor. You have to do something. Walk, jog, swim, pedal — the exact amount or intensity of the exercise required has not been determined, although it appears that the minimum is blessedly low. In mice, Mr. Gage says, "even a fairly short period" of exercise "and a short distance seems to produce results."