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Phys Ed

How Exercise Can Calm Anxiety

By GRETCHEN REYNOLDS
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In an eye-opening demonstration of nature's ingenuity, researchers at Princeton University recently discovered that exercise creates vibrant new brain cells — and then shuts them down when they shouldn't be in action.

For some time, scientists studying exercise have been puzzled by physical activity's two seemingly incompatible effects on the brain. On the one hand, exercise is known to prompt the creation of new and very excitable brain cells. At the same time, exercise can induce an overall pattern of calm in certain parts of the brain.

Most of us probably don't realize that neurons are born with certain predispositions. Some, often the younger ones, are by nature easily excited. They fire with almost any provocation, which is laudable if you wish to speed thinking and memory formation.

But that feature is less desirable during times of everyday stress. If a stressor does not involve a life-or-death decision and require immediate physical action, then having lots of excitable neurons firing all at once can be counterproductive, inducing anxiety.

Studies in animals have shown that physical exercise creates excitable neurons in abundance, especially in the hippocampus, a portion of the brain known to be involved in thinking and emotional responses.

But exercise also has been found to reduce anxiety in both people and animals.

How can an activity simultaneously create ideal neurological conditions for anxiety and leave practitioners with a deep-rooted calm, the Princeton researchers wondered?

So they gathered adult mice, injected them with a substance that marks newborn cells in the brain, and for six weeks, allowed half of them to run at will on little wheels, while the others sat quietly in their cages.

Afterward, the scientists determined each group's baseline nervousness. Given access to cages with open, well-lighted areas, as well as shadowy corners, the running mice were more willing to cautiously explore and spend time in open areas, an indication that they were more confident and less anxious than the sedentary animals.

The researchers also checked the brains of some of the runners and the sedentary mice to determine how many and what varieties of new neurons they contained.

As expected, the runners' brains teemed with many new, excitable neurons. The sedentary mice's brains also contained similar, volatile newborn cells, but not in such profusion.

The runners' brains, however, also had a notable number of new neurons specifically designed to release the neurotransmitter GABA, which inhibits brain activity, keeping other neurons from firing easily. In effect, these are nanny neurons, designed to shush and quiet activity in the brain.

In the runners' brains, there were large new populations of these cells in a portion of the hippocampus, the ventral region, associated with the processing of emotions. (The rest of the hippocampus, the dorsal region, is more involved with thinking and memory.)

What role these nanny neurons were playing in the animals' brains and subsequent behavior was not altogether clear.

So the scientists next gently placed the remaining mice in ice-cold water for five minutes. Mice do not enjoy cold water. They find immersion stressful and anxiety-inducing, although it is not life-threatening.

Then the scientists checked these animals' brains. They were looking for markers, known as immediate early genes, that indicate a neuron has recently fired.

They found them, in profusion. In both the physically fit and the sedentary mice, large numbers of the excitable cells had fired in response to the cold bath. Emotionally, the animals had become fired up by the stress.

But with the runners, it didn't last long. Their brains, unlike those of the sedentary animals, showed evidence that the shushing neurons also had been activated in large numbers, releasing GABA, calming the excitable neurons' activity and presumably keeping unnecessary anxiety at bay.

In effect, the runners' brains had responded to the relatively minor stress of a cold bath with a quick rush of worry and a concomitant, overarching calm.

What all of this suggests, says Elizabeth Gould, director of the Gould Lab at Princeton, who wrote the paper with her graduate student Timothy Schoenfeld, now at the National Institute of Mental Health, and others, "is that the hippocampus of runners is vastly different from that of sedentary animals. Not only are there more excitatory neurons and more excitatory synapses, but the inhibitory neurons are more likely to become activated, presumably to dampen the excitatory neurons, in response to stress." The findings were published in The Journal of Neuroscience.

It's important to note, she adds, that this study examined long-term training responses. The runners' wheels had been locked for 24 hours before their cold bath, so they would gain no acute calming effect from exercise. Instead, the difference in stress response between the runners and the sedentary animals reflected fundamental remodeling of their brains.

Of course, as we all know, mice are not men or women. But, Dr. Gould says, other studies "show that physical exercise reduces anxiety in humans," suggesting that similar remodeling takes place in the brains of people who work out.

"I think it's not a huge stretch," she concludes, "to suggest that the hippocampi of active people might be less susceptible to certain undesirable aspects of stress than those of sedentary people."

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Phys Ed: Why Exercise Makes You Less Anxious

By GRETCHEN REYNOLDS

Joubert/Photo Researchers, Inc A neuron in the brain.

Researchers at Princeton University recently made a remarkable discovery about the brains of rats that exercise. Some of their neurons respond differently to stress than the neurons of slothful rats. Scientists have known for some time that exercise stimulates the creation of new brain cells (neurons) but not how, precisely, these neurons might be functionally different from other brain cells.

In the experiment, preliminary results of which were presented last month at the annual meeting of the Society for Neuroscience in Chicago, scientists allowed one group of rats to run. Another set of rodents was not allowed to exercise. Then all of the rats swam in cold water, which they don't like to do. Afterward, the scientists examined the animals' brains. They found that the stress of the swimming activated neurons in all of the brains. (The researchers could tell which neurons were activated because the cells expressed specific genes in response to the stress.) But the youngest brain cells in the running rats, the cells that the scientists assumed were created by running, were less likely to express the genes. They generally remained quiet. The "cells born from running," the researchers concluded, appeared to have been "specifically buffered from exposure to a stressful experience." The rats had created, through running, a brain that seemed biochemically, molecularly, calm.

For years, both in popular imagination and in scientific circles, it has been a given that exercise enhances mood. But how exercise, a physiological activity, might directly affect mood and anxiety — psychological states — was unclear. Now, thanks in no small part to improved research techniques and a growing understanding of the biochemistry and the genetics of thought itself, scientists are beginning to tease out how exercise remodels the brain, making it more resistant to stress. In work undertaken at the University of Colorado, Boulder, for instance, scientists have examined the role of serotonin, a

neurotransmitter often considered to be the "happy" brain chemical. That simplistic view of serotonin has been undermined by other researchers, and the University of Colorado work further dilutes the idea. In those experiments, rats taught to feel helpless and anxious, by being exposed to a laboratory stressor, showed increased serotonin activity in their brains. But rats that had run for several weeks before being stressed showed less serotonin activity and were less anxious and helpless despite the stress.

Other researchers have looked at how exercise alters the activity of dopamine, another neurotransmitter in the brain, while still others have concentrated on the antioxidant powers of moderate exercise. Anxiety in rodents and people has been linked with excessive oxidative stress, which can lead to cell death, including in the brain. Moderate exercise, though, appears to dampen the effects of oxidative stress. In an experiment led by researchers at the University of Houston and reported at the Society for Neuroscience meeting, rats whose oxidative-stress levels had been artificially increased with injections of certain chemicals were extremely anxious when faced with unfamiliar terrain during laboratory testing. But rats that had exercised, even if they had received the oxidizing chemical, were relatively nonchalant under stress. When placed in the unfamiliar space, they didn't run for dark corners and hide, like the unexercised rats. They insouciantly explored.

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"It looks more and more like the positive stress of exercise prepares cells and structures and pathways within the brain so that they're more equipped to handle stress in other forms," says Michael Hopkins, a graduate student affiliated with the Neurobiology of Learning and Memory Laboratory at Dartmouth, who has been studying how exercise differently affects thinking and emotion. "It's pretty amazing, really, that you can get this translation from the realm of purely physical stresses to the realm of psychological stressors."

The stress-reducing changes wrought by exercise on the brain don't happen overnight, however, as virtually every researcher agrees. In the

University of Colorado experiments, for instance, rats that ran for only three weeks did not show much reduction in stress-induced anxiety, but those that ran for at least six weeks did. "Something happened between three and six weeks," says Benjamin Greenwood, a research associate in the Department of Integrative Physiology at the University of Colorado, who helped conduct the experiments. Dr. Greenwood added that it was "not clear how that translates" into an exercise prescription for humans. We may require more weeks of working out, or maybe less. And no one has yet studied how intense the exercise needs to be. But the lesson, Dr. Greenwood says, is "don't quit." Keep running or cycling or swimming. (Animal experiments have focused exclusively on aerobic, endurance-type activities.) You may not feel a magical reduction of stress after your first jog, if you haven't been exercising. But the molecular biochemical changes will begin, Dr. Greenwood says. And eventually, he says, they become "profound."