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How Fat May Hurt the Brain, and How Exercise May Help

By Gretchen Reynolds

Obesity may have harmful effects on the brain, and exercise may counteract many of those negative effects, according to sophisticated new neurological experiments with mice, even when the animals do not lose much weight. While it's impossible to know if human brains respond in precisely the same way to fat and physical activity, the findings offer one more reason to get out and exercise.

It's been known for some time that obesity can alter cognition in animals. Past experiments with lab rodents, for instance, have shown that obese animals display poor memory and learning skills compared to their normal-weight peers. They don't recognize familiar objects or recall the location of the exit in mazes that they've negotiated multiple times.

But scientists hadn't understood how excess weight affects the brain. Fat cells, they knew, manufacture and release substances into the bloodstream that flow to other parts of the body, including the heart and muscles. There, these substances jump-start biochemical processes that produce severe inflammation and other conditions that can lead to poor health.

Many thought the brain, though, should be insulated from those harmful effects. It contains no fat cells and sits behind the protective blood-brain barrier that usually blocks the entry of undesirable molecules.

However, recent disquieting studies in animals indicate that obesity weakens that barrier, leaving it leaky and permeable. In obese animals, substances released by fat cells can ooze past the barrier and into the brain.

The consequences of that seepage became the subject of new neurological experiments conducted by researchers at Georgia Regents University in Augusta and published last month in The Journal of Neuroscience. For the studies, the scientists gathered mice bred to overeat and grow obese, which,

after a few weeks of sitting quietly in their cages and eating at will, the animals had obligingly accomplished. As they grew rotund and accumulated more fat cells, the researchers found, their blood showed increasingly hefty doses of a substance called interleukin 1 that is created by fat cells and known to cause inflammation.

In these mice, as interleukin 1 migrated to the head, it passed the blood-brain barrier and entered areas such as the hippocampus, a part of the brain critical for learning and memory. There, it essentially gummed up the works, the researchers found when they examined tissue from the animals' brains, which had high levels of interleukin 1 together with widespread markers of inflammation. While inflammation can represent a healthy response to invading molecules, it hurts cells if it persists.

The researchers also noted extremely low levels in these mice brains of a biochemical associated with healthy synapse function. Synapses are the structures that connect one neuron to another and shunt messages between them. Healthy synapses respond to demands on the brain by slowing or speeding messages, keeping the brain's nervous-system traffic manageable. But low levels of the marker of synapse health suggested to the researchers that in these obese animals' inflamed brains, synapses were no longer functioning properly and messages between neurons likely jerked, hiccuped or stalled.

That possibility was borne out by subsequent tests on the memory and thinking of some of the remaining obese mice. They performed miserably.

But whether excessive fat cells alone were the underlying cause of the changes in the animals' brains was not clear. Other physiological factors "could have been contributing," said Alexis Stranahan, a professor at the Medical College of Georgia at Georgia Regents, who oversaw the study. So, to isolate the impact of the fat, the researchers simply removed most of it, surgically excising the large bands of fat that each mouse bore around its middle.

After recovery, these slenderized mice showed almost no interleukin 1 in their bloodstreams and, Algernon-like, soon were acing cognitive tests that had stumped them before surgery.

Conversely, when the scientists implanted the preserved fat pads into previously lean mice — and haven't we all had nightmares about something like that happening to us in our sleep? — the animals almost immediately grew dimmer, performing far worse than previously on cognitive tests,

although nothing else in their lives had changed.

The results convincingly implicated fat cells as the primary cause of the mice's cognitive decline.

But while provocative, the findings had little practical value for people, the scientists realized, since even the most extensive liposuction procedure in humans would remove far less fat than had been excised from the obese mice.

So the scientists turned, as a less-invasive alternative, to exercise. Gathering more of the obesity-prone mice, they allowed all of them to grow heavy, but then started half on a daily 45-minute program of treadmill running, with encouragement provided by small puffs of air if they began to flag. The other mice remained sedentary.

After 12 weeks, the running mice still weighed about the same as the unexercised animals. But they had lost significant amounts of fat from around their middles, while adding lean muscle. More telling, they did much better on cognitive tests than the sedentary mice and, when the researchers examined tissue from their hippocampi, showed little evidence of inflammation and robust levels of the chemical marker of synaptic health. The results suggested that, as the scientists write in the study, "treadmill training normalized hippocampal function," even in animals born to be fat and that remained heavy.

Of course, these studies were conducted in mice, not people, whose brains may respond very differently. But the possibility that humans, too, may respond in similar ways is tantalizing, Dr. Stranahan said, and the takeaway from her study worth repeating. "Get out and move," she said, even — and especially — if you carry extra weight. Talk with your doctor about a safe and tolerable exercise program, and then try to stick with that routine so that extra pounds won't weigh too heavily on your mind.