Medical Xpress

# Researchers Discover How Brain Protein Might Control Memory

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Researchers at Johns Hopkins have figured out how one particular protein contributes to long-term memory and helps the brain remember things longer than an hour or two. The findings are reported in two papers in the Nov. 9 issue of *Neuron*.

The protein, called Arc, has been implicated in memory-linked behaviors ranging from song learning in birds to rodents being aware of 3-D space. In people, Arc may be one culprit behind certain long-term memory-based behaviors like drug addiction, the researchers say.

“We think Arc controls how brain cells learn and associate behaviors and remember them over a long period of time,” says Paul F. Worley, M.D., professor of neuroscience and neurology at Hopkins and director of both studies. “For example, the person who quits smoking can wean himself from cravings at home, at work or outside. But if you put him in a bar with a drink in his hand, his brain remembers that former association and suddenly the craving returns. These types of long-term associations are memories wired in your brain.”

Years ago, Worley and his colleagues, studying laboratory rats, found that their brains made lots of Arc protein while the animals were awake and active. In fact, it has been long known that stimulating individual nerve cells - by an act as simple as exploring new environs, for example - causes the cells to make more Arc protein almost immediately. “Arc is an instant and reliable readout for active cells in the brain,” says Worley. But although scientists knew that active cells were making copious amounts of Arc, no one knew exactly what Arc was doing in those cells until now.

To figure out what Arc was doing, the Hopkins team looked for what other proteins Arc “plays” with. Using Arc protein as bait, they went on a molecular fishing expedition in a pond filled with other proteins normally found in the brain and hooked two known to be involved in transporting materials into and out of cells.

“Moving things in and out of cells is critical for normal brain cell function. We were extremely excited that Arc might somehow be involved in this transport because it links transport to memory formation,” says Worley. “This brings us one step closer to understanding how the brain saves memories.”

According to Worley, memories form when nerve cells connect and “talk” to other nerve cells. It’s thought that the stronger these connections are, the stronger the memory.

Like the childhood game called Telephone, where one person taps her neighbor and whispers a message that is passed on in similar fashion to the next person in line, nerve cells connect and “talk” to each other by relaying messages - usually by passing small chemicals - from cell to cell.

When nerve cells connect with each other in the brain, one cell releases chemicals into the space between it and its neighbor. The neighboring cell has protein receptors on its surface that capture the released chemicals. The cell that captures these chemicals then swallows up the receptor-chemical complexes, removing the receptors from the cell’s surface. The more receptors present, according to Worley, the stronger the connection between the two cells. New receptors constantly replace the swallowed-up ones.

The two proteins that came out of the Arc fishing expedition - known as dynamin and endophilin - previously were known to be critical for this swallowing action. And, it turns out that Arc controls these two proteins and therefore controls how often cells swallow receptors from their surfaces.

When the researchers altered Arc so that it was unable to bind these two proteins, cells were unable to "swallow" and wound up with more receptors than normal on their surfaces. Adding more Arc to cells caused the opposite to happen; the cells hyperactively swallowed up too many receptors, leaving few at the surface.

Unfortunately, it's possible to over-excite a cell to death, says Worley, and if the excitation controls come off, the strength of long-term memory is altered.

So what does Arc's control over brain cell receptors mean for our ability to remember where we put the car keys? "We know that animals lacking Arc live only in the here and now. They learn fine in the short term, but tomorrow they will need to relearn everything," says Worley. And in the case of long-term memories that are better forgotten, such as that cigarette craving while sitting in a bar, a better understanding of how these memories form promises hope that there might be a way in the future to forget them entirely.

Source: Johns Hopkins Medical Institutions