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Problem forgetting may be a natural mechanism gone awry

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Better tie that string around your finger a little tighter. It may turn out the reason some people grow increasingly forgetful as they age is less about how old they are and more about subtle changes in the way the brain files memories and makes room for new ones - differences perhaps better blamed on patterns of cell-to-cell communication than the number of birthday candles decorating the cake.

A researcher with the McKnight Brain Institute of the University of Florida has found that rats become forgetful because a routine part of the memory process falls out of kilter, no matter their ages.

This change seems to be related to the chemicals necessary for brain cells to communicate with each other. The findings, published this month in the online edition of Neurobiology of Learning and Memory, expand the possibility that drugs or therapies could be developed to tune up the brain's memory mechanisms.

"Aging is associated with an increased rate of forgetting," said Thomas Foster, Ph.D., the Evelyn F. McKnight chair for brain research in memory loss at the College of Medicine. "My work indicates that the problem may be a slight shift in a normal forgetting mechanism."

Scientists believe a memory forms when communication increases between brain cells called neurons. During memory formation, signals jump across narrow gaps between cells called synapses, and this output becomes increasingly larger.

But for this activity to efficiently create a memory, it helps if signaling decreases among less-involved neurons. It's like quieting other people in the room so you can have a phone conversation. Scientists call the process of decreasing the signal at less-involved synapses "long-term depression," or LTD.

"This is a normal process that helps with the sculpting of memory," Foster said. "After all, we do not remember everything in perfect detail and we would not want to. This same mechanism probably is used to clear the brain circuits and make them ready to be used the next day. However, this mechanism in excess may lead to rapid forgetting as seen during brain aging."

Foster's lab group used aged and young rats to examine the relationships between LTD, aging and memory. The animals were trained to find a hidden platform to climb out of a pool of water - something they learned quickly with repetition.

When the researchers examined the animals' neurons and used a slow, weak electrical signal to make the synapses less sensitive - an effort to squelch or depress the cellular communication - he found that the samples from younger animals and older animals that had the highest memory scores throughout their lives were more resistant to the interference. However, aged animals with impaired memories displayed what was termed as "robust long-term depression."

Going back to the phone call example, not only did the rest of the room get quieter, the callers did, too. The assumption is if a memory is encoded by making synapses stronger, then memory can be disrupted by something that weakens those connections.

"When we see someone we know or perhaps even ourselves becoming more forgetful, we now know that this is not an inevitable process,"

Foster said. “Further, as we begin to understand the mechanisms of memory, it becomes possible to predict promising targets for therapeutic strategies aimed at postponing or alleviating age-related memory impairment.”

Foster said it will be important to understand whether a change in cellular signaling is necessary to enable new memories to be formed by discarding old ones.

“The basic gist is that information storage requires a balance between mechanisms that make synapses stronger and weaker,” said Mark F. Bear, Ph.D., director of the Picower Institute for Learning and Memory at the Massachusetts Institute of Technology, who was not involved with the research. “In aging and disease, if that balance is disrupted to favor LTD, the unchecked synaptic weakening leads to memory loss. The good news is we are developing a good understanding of these mechanisms, and that will help us find ways to protect memory.”

Source: University of Florida