MedicalXpress

Cognitive decline with age is normal, routine—but not inevitable

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If you forget where you put your car keys and you can't seem to remember things as well as you used to, the problem may well be with the GluN2B subunits in your NMDA receptors.

And don't be surprised if by tomorrow you can't remember the name of those darned subunits.

They help you remember things, but you've been losing them almost since the day you were born, and it's only going to get worse. An old adult may have only half as many of them as a younger person.

Research on these biochemical processes in the Linus Pauling Institute at Oregon State University is making it clear that cognitive decline with age is a natural part of life, and scientists are tracking the problem down to highly specific components of the brain. Separate from some more serious problems like dementia and Alzheimer's disease, virtually everyone loses memory-making and cognitive abilities as they age. The process is well under way by the age of 40 and picks up speed after that.

But of considerable interest: It may not have to be that way.

"These are biological processes, and once we fully understand what is going on, we may be able to slow or prevent it," said Kathy Magnusson, a neuroscientist in the OSU Department of Biomedical Sciences, College of Veterinary Medicine, and professor in the Linus Pauling Institute. "There may be ways to influence it with diet, health habits, continued

mental activity or even drugs."

The processes are complex. In a study just published in the *Journal of Neuroscience*, researchers found that one protein that stabilizes receptors in a young animal – a good thing conducive to learning and memory – can have just the opposite effect if there's too much of it in an older animal.

But complexity aside, progress is being made. In recent research, supported by the National Institutes of Health, OSU scientists used a genetic therapy in laboratory mice, in which a virus helped carry complementary DNA into appropriate cells and restored some GluN2B subunits. Tests showed that it helped mice improve their memory and cognitive ability.

The NMDA receptor has been known of for decades, Magnusson said. It plays a role in memory and learning but isn't active all the time – it takes a fairly strong stimulus of some type to turn it on and allow you to remember something. The routine of getting dressed in the morning is ignored and quickly lost to the fog of time, but the day you had an auto accident earns a permanent etching in your memory.

Within the NMDA receptor are various subunits, and Magnusson said that research keeps pointing back to the GluN2B subunit as one of the most important. Infants and children have lots of them, and as a result are like a sponge in soaking up memories and learning new things. But they gradually dwindle in number with age, and it also appears the ones that are left work less efficiently.

"You can still learn new things and make new memories when you are older, but it's not as easy," Magnusson said. "Fewer messages get through, fewer connections get made, and your brain has to work harder."

Until more specific help is available, she said, some of the best advice for maintaining cognitive function is to keep using your brain. Break old habits, do things different ways. Get physical exercise, maintain a good diet and ensure social interaction. Such activities help keep these "subunits" active and functioning.

Gene therapy such as that already used in mice would probably be a last choice for humans, rather than a first option, Magnusson said. Dietary or drug options would be explored first.

"The one thing that does seem fairly clear is that cognitive decline is not inevitable," she said. "It's biological, we're finding out why it happens, and it appears there are ways we might be able to slow or stop it, perhaps repair the NMDA receptors. If we can determine how to do that without harm, we will."

Provided by Oregon State University