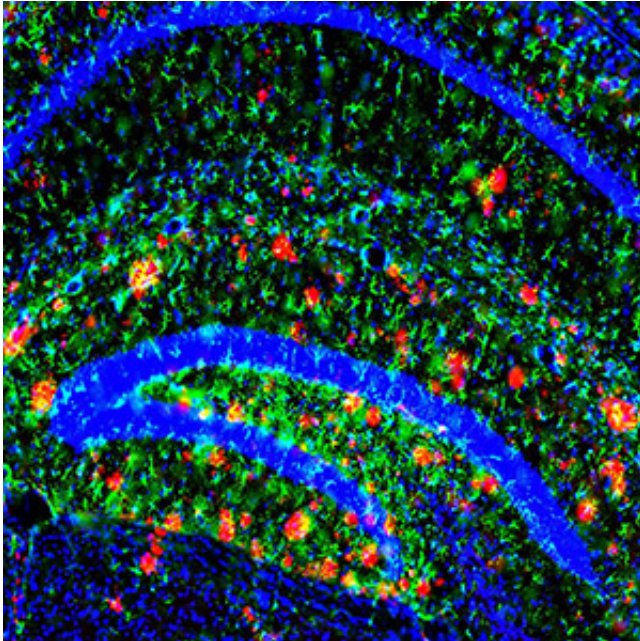


Brain's ability to dispose of key Alzheimer's protein drops dramatically with age

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Credit: Washington University School of Medicine in St. Louis

The greatest risk factor for Alzheimer's disease is advancing age. After 65, the risk doubles every five years, and 40 percent or more of people 85 and older are estimated to be living with the devastating condition.

Researchers at Washington University School of Medicine in St. Louis have identified some of the key changes in the aging [brain](#) that lead to the increased risk. The changes center on amyloid beta 42, a main ingredient of Alzheimer's [brain plaques](#). The protein, a natural byproduct of [brain activity](#), normally is cleared from the brain before it can clump together into plaques. Scientists long have suspected it is a primary driver of the disease.

"We found that people in their 30s typically take about four hours to clear half the amyloid beta 42

from the brain," said senior author Randall J. Bateman, MD, the Charles F. and Joanne Knight Distinguished Professor of Neurology. "In this new study, we show that at over 80 years old, it takes more than 10 hours."

The slowdown in clearance results in rising levels of amyloid beta 42 in the brain. Higher levels of the protein increase the chances that it will clump together to form Alzheimer's plaques.

The results appear online in the *Annals of Neurology*.

For the study, the researchers tested 100 volunteers ages 60 to 87. Half had clinical signs of Alzheimer's disease, such as memory problems. Plaques had begun to form in the brains of 62 participants.

The subjects were given detailed mental and physical evaluations, including brain scans to check for the presence of plaques. The researchers also studied participants' cerebrospinal fluids using a technology developed by Bateman and co-author David Holtzman, MD, the Andrew B. and Gretchen P. Jones Professor and head of the Department of Neurology at Washington University. The technology—known as stable isotope-linked kinetics (SILK)—allowed the researchers to monitor the body's production and clearance of amyloid beta 42 and other proteins.

In patients with evidence of plaques, the researchers observed that amyloid beta 42 appears to be more likely to drop out of the fluid that bathes the brain and clump together into plaques. Reduced clearance rates of amyloid beta 42, such as those seen in older participants, were associated with clinical symptoms of Alzheimer's disease, such as memory loss, dementia and personality changes.

Scientists believe the brain disposes of amyloid

beta in four ways: by moving it into the spine, pushing it across the blood-brain barrier, breaking it down or absorbing it with other proteins, or depositing it into plaques.

"Through additional studies like this, we're hoping to identify which of the first three channels for [amyloid beta](#) disposal are slowing down as the brain ages," Bateman said. "That may help us in our efforts to develop new treatments."

More information: Patterson, B. W., Elbert, D. L., Mawuenyega, K. G., Kasten, T., Ovod, V., Ma, S., ... Bateman, R. J. (2015). Age and amyloid effects on human central nervous system amyloid-beta kinetics. *Ann Neurol.*, n/a–n/a. [DOI: 10.1002/ana.24454](#)

Provided by Washington University School of Medicine in St. Louis

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