Leibniz Institute on Aging – Fritz Lipmann Institute

THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

Media Release
February 4, 2026

Storing defective energy: How the aging brain remains efficient

An international research team led the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in Jena, Germany, and the University of Tennessee Health Science Center, Memphis, USA, has uncovered new insights into healthy brain aging. Researchers found that aging leads to the accumulation of defective energy molecules in the brains of aged mice, like humans, and identified the responsible genetic sequence. Importantly, no evidence was found that this accumulation would impair brain function, highlighting that age-related brain changes are not necessarily harmful.

Jena/Memphis. In a recent study published in *Cell Systems*, an international research team led by Dr. Dennis de Bakker from the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in Jena and Prof. Robert W. Williams from the University of Tennessee Health Science Center, Memphis, USA, studied how astrocytes, specialized supporting cells in the brain, undergo changes during aging. These cells surround the nerve cells, supply them with nutrients, regulate their environment, and play a key role in the brain's energy metabolism.

Astrocytes also act as an energy reserve, as they can store energy in the form of glycogen, a rapidly available supply of sugar that can be quickly released when needed, for example when nerve cells are particularly active. Typically, glycogen is a molecule with several added molecular chains, also called branches, which is important for its function. With increasing age, however, under-branched glycogen becomes more common, which are harder to break down and are instead stored in clumps called polyglucosan bodies (PGBs). These unusual structures can occur throughout the brain but are enriched in the hippocampus, a region of the brain that is especially important for learning and memory.

Aging brain cells undergo changes in energy storage

The researchers were able to show that in old mice, under-branched glycogen accumulates particularly strongly in the astrocytes of the hippocampus. However, this does not occur evenly, but rather in unusually clumped structures called PGBs. These occur with varying frequency depending on the genetic background of the mice.

“We saw that some animals formed particularly large numbers of these glycogen aggregates as they aged, while others had almost none,” explains Dr. de Bakker, research group leader at the FLI. ‘Genetic differences are enough to multiply this effect many times over.’

Storage of dysfunctional glycogen is modulated by a locus on chromosome 1

Comparing numerous genetically defined mouse lines, the researchers found a clear result: a specific section of the genome has a significant influence on how energy storage in astrocytes changes with age. The gene locus acts like a switch that determines the degree of PGB burden. It's interesting to note that it's not the nerve cells themselves that are affected, but only

their supporting environment. Astrocytes are essential for brain metabolism, and changes in them have often been interpreted as a warning signal.

“For a long time, it was assumed that such accumulations in the brain were a sign of beginning functional loss or disease,” explains Prof. Williams, co-leader of the study. “However, our research results show that this is not necessarily the case.”

No measurable consequences for memory and cognitive function

Perhaps the most surprising result of the study is that even highly pronounced glycogen aggregates had no measurable impact on the cognitive function of the animals, agree co-first authors Alicia Gómez-Pascual and Dow M. Glikman. In a series of behavioral tests on memory, learning ability, and spatial orientation, mice with many aggregates achieved results comparable to those of animals without PGBs. This suggests that the observed cellular changes may be part of a normal, genetically controlled aging process and are not necessarily pathological.

“Aging means change, but not every change in old age is automatically dangerous”, explains Dr. de Bakker. “Our data show that the brain is surprisingly robust and resilient to certain biochemical changes.”

Relevance for aging and dementia research

“This study is an impressive demonstration of how experimental data can gain value over time through sustained collaboration. The original data were generated nearly 30 years ago by Prof. Mathias Jucker, now a leading Alzheimer’s disease researcher at the University of Tübingen, during his time at the U.S. National Institute on Aging. Dr. Rupert Overall at Humboldt University of Berlin revitalized the investigation into this data by assembling a team of early-career scientists, who were able to identify key candidate genes that contribute to differences in the number of polyglucosan aggregates within hippocampal astrocytes. The challenge now is to translate these findings into therapeutics, addressing both normal age-related cognitive decline and the far more debilitating diseases that erode memory and function,” summarizes Prof. Williams.

The study helps to reclassify age-related changes in the brain, because in aging and dementia research, it is important to distinguish precisely whether these changes contribute to disease or are merely side effects of the normal aging process.

“In the long term, our new findings could help to avoid misinterpretations of age-related changes and focus more on those mechanisms that impair brain function. With this basic understanding, which changes are harmless, and which are not, it should be possible to search more specifically for the truly problematic processes,” says the research team.

Media Release
February 4, 2026

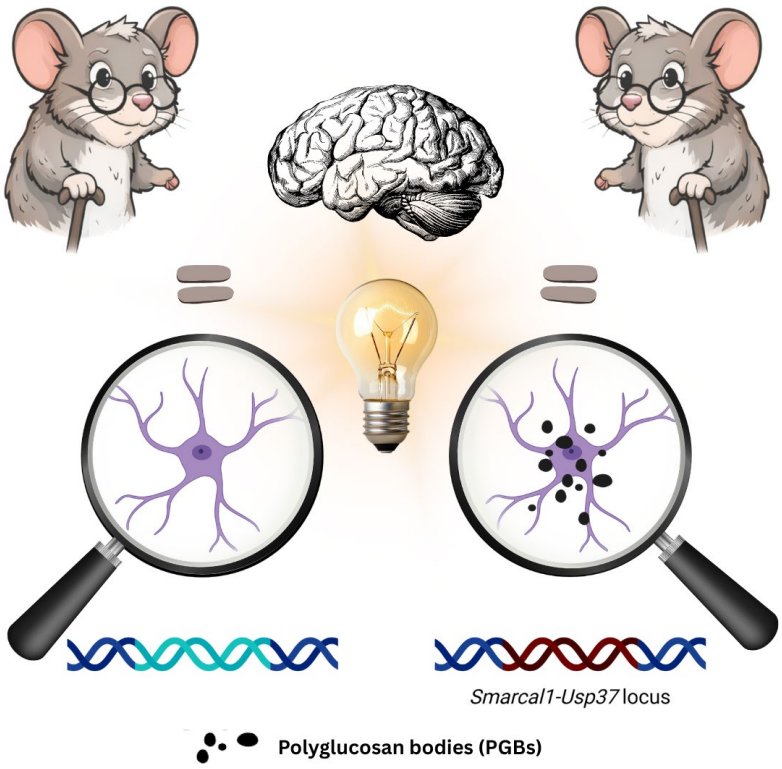
Publication

The *Smarcal1-Usp37* locus modulates glycogen aggregation in astrocytes of the aged hippocampus. Alicia Gómez-Pascual*, Dow M. Glikman*, Hui Xin Ng*, James E. Tomkins*, Lu Lu, Ying Xu, David G. Ashbrook, Catherine Kaczorowski, Gerd Kempermann, John Killmar, Khyobeni Mozhui, Oliver Ohlenschläger, Rudolf Aebersold, Donald K. Ingram, Evan G. Williams, Mathias Jucker, Rupert W. Overall, Robert W. Williams#, Dennis E.M. de Bakker#. Cell Systems 2026, 101488, doi.org/10.1016/j.cels.2025.101488.

https://www.sciencedirect.com/science/article/pii/S2405471225003217

* Equal contribution / # Co-corresponding authors

Picture



In the aging brains of mice, glycogen accumulates in the astrocytes (support cells) of the hippocampus. These accumulations occur with varying frequency and are genetically controlled, but do not affect learning and memory performance. They are a result of the normal aging process. (Image: FLI / Kerstin Wagner; generated with ChatGPT)

Media Release
February 4, 2026

Contact

Dr. Kerstin Wagner
Press & Public Relations
Phone: 03641-656378, Email: presse@leibniz-fli.de

Background

The Leibniz Institute on Aging - Fritz Lipmann Institute (FLI) in Jena is a federal and state government-funded research institute and member of the Leibniz Association (Leibniz-Gemeinschaft). FLI conducts internationally recognized, high-impact research on the biology of aging at the molecular, cellular, and systems levels. Scientists from around 40 countries investigate the mechanisms of aging to uncover its root causes and pave the way for strategies that promote healthy aging. Further information: www.leibniz-fli.de.

The **Leibniz Association** connects 96 independent research institutions that range in focus from natural, engineering, and environmental sciences to economics, spatial, and social sciences and the humanities. Leibniz Institutes address issues of social, economic, and ecological relevance.

They conduct basic and applied research, including in the interdisciplinary Leibniz Research Alliances, maintain scientific infrastructure, and provide research-based services. The Leibniz Association identifies focus areas for knowledge transfer, particularly with the Leibniz research museums. It advises and informs policymakers, science, industry, and the general public.

Leibniz institutions collaborate intensively with universities – including in the form of Leibniz ScienceCampi – as well as with industry and other partners at home and abroad. They are subject to a transparent, independent evaluation procedure. Because of their importance for the country as a whole, the Leibniz Association Institutes are funded jointly by Germany's central and regional governments. The Leibniz Institutes employ around 21,400 people, including 12,170 researchers. The financial volume amounts to 2 billion euros. For more information: www.leibniz-gemeinschaft.de/en/.

The **University of Tennessee Health Science Center (UTHSC)** is the State of Tennessee's flagship university for the health sciences with campuses in Memphis, Knoxville, Chattanooga, and Nashville. The Department of Genetics, Genomics and Informatics on the Memphis campus is a major center for system genetics and the home of GeneNetwork.org—the oldest web service in biomedical research (Jan 1994) that was used extensively in project. Further information: www.uthsc.edu/