Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/rare-seasonal-brain-shrinkage-shrews-driven-water-loss-not-cell-death

Rare seasonal brain shrinkage in shrews is driven by water loss, not cell death

Knowing how shrews loose brain volume over winter is the first step to understanding how they reverse this loss and regrow healthy brains in summer.

To the point:

- **Water behind Dehnel's phenomenon:** study found that common shrews shrink their brains in winter not by losing cells, but by losing water
- **Brain scans:** team used MRI scanning, the same technology used in hospitals, to peer inside the brains of live shrews across seasons
- **What humans can learn:** brain shrinkage in humans is typically a sign of disease, like Alzheimer's. But shrews can shrink their brain *without* compromising function or causing damage. Shrews could become a model system for exploring potential pathways for medical treatment of human brain disease

Common shrews are one of only a handful of mammals known to flexibly shrink and regrow their brains. This rare seasonal cycle, known as Dehnel's phenomenon, has puzzled scientists for decades. How can a brain lose volume and regrow months later without sustaining permanent damage?

A study using non-invasive MRI has scanned the brains of shrews undergoing shrinkage, identifying a key molecule involved in the phenomenon: water.

"Our shrews lost nine percent of their brains during shrinkage, but the cells did not die," says first author Dr. Cecilia Baldoni, a postdoctoral researcher from the Max Planck Institute of Animal Behavior in Germany. "The cells lost water."

Normally, brain cells that lose water become damaged and ultimately die, but in shrews, the opposite happened. "The cells remained alive and even increased in number," says Baldoni.

This finding solves a mystery—and opens up potential pathways for the treatment of human brain disease. "We see that brain shrinkage in shrews matches closely what happens in patients suffering from Alzheimer's, Parkinson's, and other brain diseases," says Associate Prof. John Nieland, an expert in human brain disease at Aalborg University, Denmark.

The study also shows that a specific protein known for regulating water—aquaporin 4—was likely involved in moving water out of the brain cells of shrews. "We see this same protein present in higher quantities in the diseased brains of humans, too," says Nieland.

That the shrunken brains of shrews share characteristics with diseased human brains makes the case that these miniature mammals, with their ability to reverse brain loss, could also offer clues for medical treatments. "The next step is to learn how shrews regrow their brains so that we might find ways to teach human brains to do the same," Nieland adds.

Peering inside a shrinking brain

Dehnel's phenomenon, or reversible brain shrinkage, is rare among animals. Up until now, it is known only in European moles, stoats and weasels, and some species of shrews. Among these, common shrews are the most studied. When undergoing Dehnel's, their brains become smaller from summer to late winter, then regrow in spring.

Scientists call this reversible resizing "brain plasticity," and it is thought to help shrews conserve energy when food is scarce. "These tiny mammals, which are no bigger than your thumb, have to eat every few hours, whether it's in summer when there's lots to eat or in winter when there's very little," says Dina Dechmann, a group leader at the Max Planck Institute of Animal Behavior who has studied Dehnel's phenomenon for over 13 years.

The researchers used high-resolution MRI to scan the brains of wild common shrews caught in Germany in summer and then recaptured in winter. The medical imaging technique allowed the scientists to non-invasively see inside the brains of living animals over seasons.

“In this way, we could track how the brains of individuals changed as they experienced shrinkage from summer to winter,” says senior author Prof. Dominik von Elverfeldt from the Faculty of Medicine at the University of Freiburg, Germany, who led the imaging. They also compared these scans to microscopic examination of brain tissue in summer and winter to determine the number of cells at each stage.

How shrews pull off Dehnel’s

Overall, the brains of shrews in the study lost around nine percent volume in winter, which the team observed to be due to the movement of water out of brain cells. But when the team zoomed in on different brain regions, they noticed that not all areas shrank equally. This uneven effect could explain Dehnel’s phenomenon’s great ecological paradox: how do animals survive with smaller brains?

“Shrews still need to find food, escape predators, and go about their daily lives all winter, which they manage to do with a smaller brain,” says Baldoni. By human standards, says Nieland, “it’s astonishing what these shrews accomplish with brain loss of almost ten percent. We commonly see Alzheimer’s patients suffering from the same percentage brain reduction, and the loss of function in these patients is tremendous.”

The study’s neuroimaging results point to a potential answer. Most brain regions shrank in winter and exhibited consistent shifts in water balance characterized by less water inside the cells and more water surrounding them. However, the neocortex and cerebellum deviated from this general pattern, keeping a more stable balance of water inside and outside their cells.

“These regions are responsible for cognitive skills such as memory as well as motor control,” says Baldoni. “The shrews seem to be adjusting their brains for winter like we might adjust heating in a house, keeping the essential rooms heated while dropping power in areas where we can afford to reduce operations.”

For the ecologists, the study explains the mechanism behind a rare seasonal strategy and raises new questions. “Now that we understand the physiology better, we are keen to link this to the behavioral consequences of Dehnel’s phenomenon,” says Baldoni. “How does having a smaller brain affect behavior? Can shrews solve the same navigational and coordination challenges in winter as they can in summer?”

Potential path to medical treatment?

For the neurologists, the story of what shrews can offer human medicine has just begun. Many brain diseases—Multiple Sclerosis, Parkinson's disease, Amyotrophic Lateral Sclerosis (ALS), and Alzheimer's disease—involve brain volume decline due to water loss. But for humans, this loss progresses in only one direction.

“So far there is no treatment for any brain disease that can prevent or reverse this loss of brain volume,” says Nieland. “We have now discovered, in shrews, an animal that is getting human-like symptoms of brain disease, but has biological tools not only to stop this process, but to reverse it too.”

The next step for the team is to study the second phase of Dehnel’s—the brain’s regrowth from winter to summer. By doing so, they hope to unlock clues for treatment of brain diseases. Adds Nieland: “The idea that we might have a model animal that can help us learn how to treat diseases that are currently incurable is the most exciting thing I can think of.”

Publication:
Cecilia Baldoni, Marco Reisert, Bethany Smith, Javier Lazaro, Yuanyuan Zeng, William R. Thomas, Moritz Hertel, Liliana M. Dávalos, John Nieland, Dina K.N. Dechmann, Dominik von Elverfeld, Programmed seasonal brain shrinkage in the common shrew via water loss without cell death, Current Biology
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Further information

Carla Avolio
Communications and Media Officer
Phone: +49 (0) 176 77871256

Email: cavolio(at)ab.mpg.de

- Max-Planck-Institute of Animal Behavior