# BRAIN INTRACRANIAL VOL 9

Hand in the middle of microchip light projection.© Paper Boat Creative/Getty Images

## Scientists discover how to use your body to process data in wearable devices

A scientist in Japan has demonstrated how the human body could be used like a computer to process data and solve complex problems.

This breakthrough is possible because human tissue has properties useful for a kind of data processing called "reservoir computing," the author of the study Yo Kobayashi, associate professor in the University of Osaka's Department of Mechanical Science & Bioengineering, wrote in a new study published March 20 in the journal IEEE Access.

In reservoir computing, inputs are fed into a system with a large number of "nodes" or "dimensions" (the reservoir) and then interpreted to isolate important data or predict future results. While in many cases the reservoir is digital, it's possible to use other physical systems.

To demonstrate the possibility of using human tissue to process data, the researcher asked participants to bend their wrists at a variety of angles.

He then used ultrasound to image the resulting deformation in the muscles. From that data, he built a computer model of a physical reservoir that could successfully emulate nonlinear dynamical systems in benchmark testing.

It achieves this by using the deformation field within the muscle to represent the state of the reservoir. The nonlinearity — the fact that the input doesn't affect nodes in the reservoir in a straight line — enables input signals to be mapped onto a high-dimensional state space, which facilitates complex calculations. In this case, the input is the signal pattern of the wrist joint angle.

"One potential application area of this technology is wearable devices," Kobayashi said in a statement. "In the future, it may be possible to use our own tissue as a convenient computational resource. Since soft tissue is present throughout the body, a wearable device could delegate calculations to the tissue, enhancing performance."

He also suggested that the process could be applied to medical and life support devices, as well as other human-machine interaction technology, relying on human tissue for additional processing resources.

# Computing in a bucket of water

One common way to illustrate how reservoir computing works is the "bucket of water" method. In this scenario, a series of water tanks arranged in a grid or other formation comprise the reservoir, with pipes of various sizes linking them nonlinearly. This means that water doesn't flow in a straight line from one tank to another. Instead, adding water or perturbations to the system can change the level of water tanks throughout, or that water could exit a tank at one point but then be reintroduced later as the result of a single input.

Inputs are reflected throughout the system in the form of water levels fluctuating in the various tanks, and dynamically changing over time. The state of the reservoir is captured over time by measuring the level of water in each tank, and then a trainable computer layer reads and interprets the results.

The reservoir is responsible for "distorting" or "blending" the input signal in many different nonlinear ways, generating a diverse set of temporal features. The reservoir doesn't explicitly "solve" nonlinear equations in a traditional numerical sense. Instead, it learns to mimic the input-output behavior of the system governed by those equations. Nonlinearities within the reservoir allow it to capture and represent nonlinear relationships present in the input data and the underlying system dynamics.

Human tissue can function as a reservoir because it shares some qualities with a water-based reservoir. For one, it has nonlinear qualities, specifically stress-strain nonlinearity, which means that the relationship between stress applied to tissue and the resulting strain isn't a straight line. It's also viscoelastic, meaning that it has both elastic (like a rubber band) and viscous (like a thick fluid) qualities when deformed — in other words, it has a physical "memory" of its past deformation and can thus store information.

Beyond the aforementioned applications, reservoir computing has shown promise in predicting chaotic systems like the weather. It's also been proposed as a way to predict other systems that vary over time, things like stock prices or air quality. By interpreting previous data through the system, it may be possible to predict future outcomes.

As Kobayashi pointed out, his work is just a first step — while reasserting its potential in the future.

"This study only performed benchmark tests; hence, it is imperative to determine the applicability of the actual computational process in future scenarios. However, these findings pave the way for the successful exploitation of human tissue dynamics in a wide range of computational tasks and applications."

APRIL 24, 2025

# What happens in the brain when your mind blanks

by Cell Press

Credit: Pixabay/CC0 Public Domain

Mind blanking is a common experience with a wide variety of definitions ranging from feeling "drowsy" to "a complete absence of conscious awareness." In an opinion article published in *Trends in Cognitive Sciences*, a team of neuroscientists and philosophers compiles what we know about mind blanking, including insights from their own work observing people's brain activity.

"During wakefulness, our thoughts transition between different contents. However, there are moments that are seemingly devoid of reportable content, referred to as mind blanking," writes the research team, which was formed as a result of collaboration at the 25th Annual Meeting of the Association for the Scientific Study of Consciousness in Amsterdam in 2022.

"It remains unclear what these blanks represent, highlighting the definitional and phenomenological ambiguities surrounding mind blanking."

In the past, mind blanking has only been studied using research and experiments developed to study mind wandering—a similar internal experience in which our thoughts "flow seamlessly like a stream."

The researchers argue that mind blanking is a distinct experience that involves feeling sleepier, more sluggish, and making more errors, and should be inspired by mind wandering research, but considered independently.

"We sought to better understand mind blanking by parsing through 80 relevant research articles—including some of our own in which we recorded participants' brain activity when they were reporting that they were 'thinking of nothing,'" explains author Athena Demertzi of GIGA Research at University of Liège, Belgium.

Takeaways from their research include:

- Mind blank frequency varies greatly between different people, but a person experiences the phenomenon about 5%–20% of the time on average.

- Common experiences defined as "mind blanking" include lapses of attention, memory issues, and a cessation of inner speech, among others.

- Mind blanks tend to happen toward the end of long, sustained attention tasks like exams and after sleep deprivation or intense physical exercise, but are also a typical waking state.

- Children with attention deficit hyperactivity disorder (ADHD) report mind blanking more frequently than neurotypical people.

- Mind blanking is part of the clinical description of generalized anxiety disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). It is also relevant to several other clinical conditions, including strokes, seizures, traumatic brain injuries, and Kleine–Levin syndrome—which causes people to sleep up to 20 hours per day.

- Experiments observing brain activity during rest using technologies including fMRI and electroencephalography show that there are specific neural signatures in the frontal, temporal, and visual networks of the brain before a mind blank.

- During mind blanks after sustained attention tasks, people's heart rates and pupil sizes decreased and their brains showed lower signal complexity—a state typically observed in unconscious people. During the blank, they observed disruptions in sensory processing and slow, sleep-like EEG waves. The authors describe these states in which parts of a person's brain appear asleep as "local sleep episodes."

- An increase in neural activity in posterior cortical brain regions can also lead to mind blanking, as is the case when high-speed thinking leads to slower cognitive function.

- When people were prompted to actively "empty their minds," researchers observed deactivations in the inferior frontal gyrus, Broca's area, supplementary motor cortex, and hippocampus.

The researchers speculate that the common factor between different forms of blanking may be related to changes in arousal levels, leading to a malfunction of key cognitive mechanisms such as memory, language, or attention.

Given that blanking experiences vary so greatly—both in terms of people's subjective experiences and their neural activity—the researchers propose a framework that describes mind blanking as a dynamic group of physiologically driven experiences mediated by arousal states, or a person's state of physiological "vigilance." As they describe it, this means that when the brain is in a high- or low-arousal state, a mind blank is more likely to occur.

"The experience of a 'blank mind' is as intimate and direct as that of bearing thoughts," says author Jennifer Windt of Monash University in Australia.

"Our aim here is to start a conversation and see how mind blanking relates to other seemingly similar experiences, such as meditation," adds author Antoine Lutz of the Lyon Neuroscience Research Center in France.

The team hopes that acknowledging mind blanking as a distinct mental state in future research will help build toward a deeper understanding of mind blanking.

"We believe that the investigation of mind blanking is insightful, important, and timely," says lead author Thomas Andrillon of the University of Liège.

"Insightful because it challenges the common conception that wakefulness involves a constant stream of thoughts. Important because mind blanking highlights the interindividual differences in subjective experience. Collectively, we stress that ongoing experiences come in shades with varying degrees of awareness and richness of content."

**More information:** Where is my mind? A neurocognitive investigation of mind blanking, *Trends in Cognitive Sciences* (2025). DOI: 10.1016/j.tics.2025.02.002
**Journal information:** Trends in Cognitive Sciences
Provided by Cell Press

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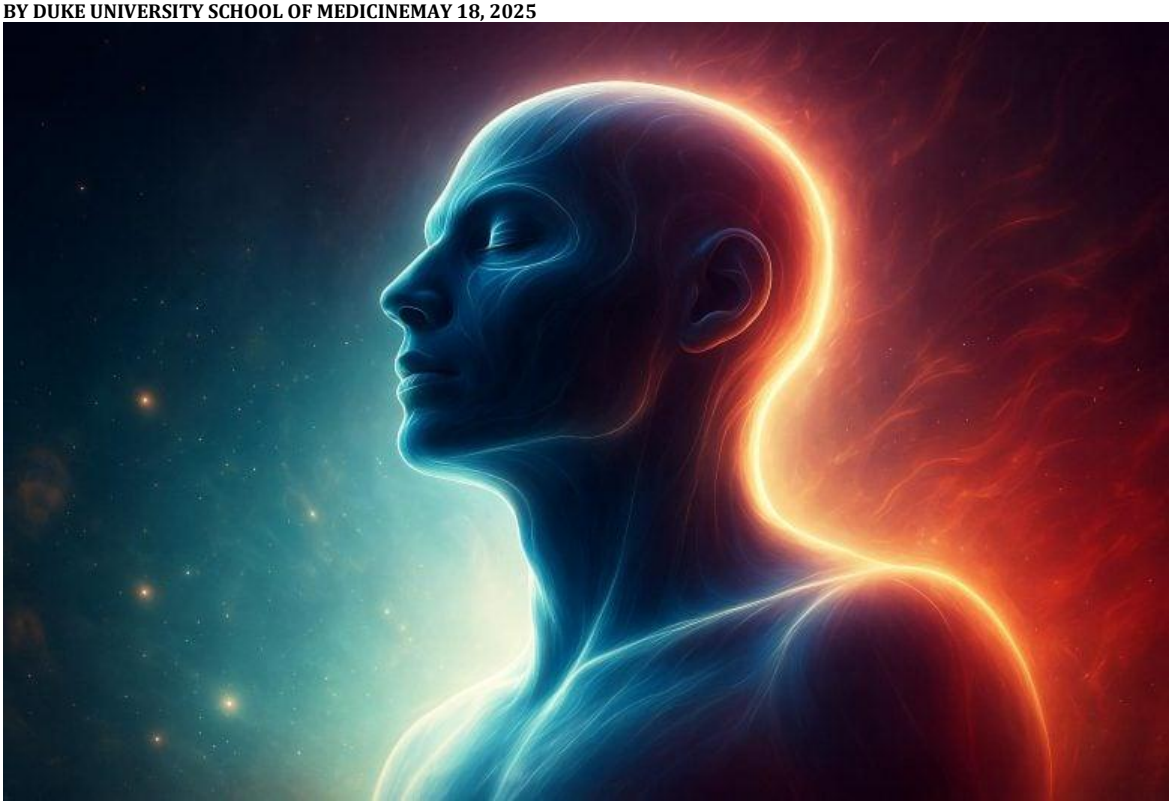
# 4 Tiny DNA Tweaks That Supercharged the Human Brain

**BY DUKE UNIVERSITY SCHOOL OF MEDICINEMAY 18, 2025**



Just four DNA differences in one small region of the genome may help explain why humans have bigger, more complex brains than chimps. These tweaks drive neuron growth—but may also raise the risk of neurological disease. Credit: SciTechDaily.com

## How Four Small DNA Changes Helped Shape the Human Brain

*A tiny sliver of our genome may hold the key to what makes us human. Duke scientists have zeroed in on "Human Accelerated Regions," mysterious stretches of DNA that don't code for proteins but play a crucial role in brain development.*

### Unlocking the Genetic Secrets That Set Humans Apart

While humans share 98.8% of their DNA with chimpanzees, it's the tiny remaining difference that holds the key to what sets us apart. Now, scientists at Duke University are uncovering how small genetic changes help shape the human brain in powerful ways. Their findings were recently published in *Nature*.

Led by Dr. Debby Silver, a professor of molecular genetics and microbiology, and senior research associate Dr. Jing Liu, the team zeroed in on mysterious stretches of DNA known as Human Accelerated Regions, or HARs. These parts of our genome don't code for proteins, but they're located near genes that play crucial roles in brain development.

## Small Genetic Tweaks, Big Brain Effects

There are about 3,000 HARs scattered throughout the human genome. The researchers focused on just one of them and discovered that it plays a surprising role in how brain cells are formed. Specifically, they found that this tiny DNA region can influence how neural progenitor cells—early-stage cells that later become neurons—multiply and develop.

This is important because the human cerebral cortex, the outer layer of the brain responsible for higher thinking, is both larger and more intricately folded than in other primates. That extra space allows for more neurons, which support complex brain functions like abstract thinking, emotional control, language, and creativity.

Cross section of an embryonic mouse brain. Progenitors are green, mitotic cells are red, and neurons are purple. Credit: Duke University

## Mouse Models Reveal the Power of HARs

Using a genetically engineered mouse model with this human HAR, they observed that these mice had slightly larger cerebral cortexes and more neurons than the control mice. These changes trace back to activity in the Wnt signaling pathway – a key regulator of progenitor cell proliferation and neuronal differentiation.

They also edited human stem cells to include the chimpanzee version of the HAR, which differs by just four nucleotides, and saw less neural progenitor proliferation. But if they put the human nucleotide sequence into chimpanzee stem cells, neural progenitor proliferation increased.

## The Price of Cognitive Evolution

"We're exposing one of the mysteries," Silver said, "of how these small differences in our DNA can contribute to known anatomical differences."

There is a downside, though, to having bigger brains. "Over the course of evolution," Silver said, "we've acquired changes that have helped to collectively contribute to making us human, but with those changes, there also becomes an increased propensity for disease."

Liu and colleagues observed there are gene variants associated with autism in this HAR sequence. "This reinforces the importance of studying this locus in particular," said Silver. "These comparative approaches can tell us about the molecular mechanisms that make us human and can tell us about molecular features that may make us more prone to diseases."

## One Tiny Region, Four Changes, Big Insights

This is just one piece of the puzzle. "We're studying just four changes in one transcriptional enhancer, Silver said, "so the changes we are seeing are subtle." The more pieces of the puzzle you can fit together, the broader picture you can get on exactly what makes us human.

Reference: "A human-specific enhancer fine-tunes radial glia potency and corticogenesis" by Jing Liu, Federica Mosti, Hanzhi T. Zhao, Davoneshia Lollis, Jesus E. Sotelo-Fonseca, Carla F. Escobar-Tomlienovich, Camila M. Musso, Yiwei Mao, Abdull J. Massri, Hannah M. Doll, Nicole D. Moss, Andre M. M. Sousa, Gregory A. Wray, Ewoud R. E. Schmidt and Debra L. Silver, 14 May 2025, *Nature*.
DOI: 10.1038/s41586-025-09002-1

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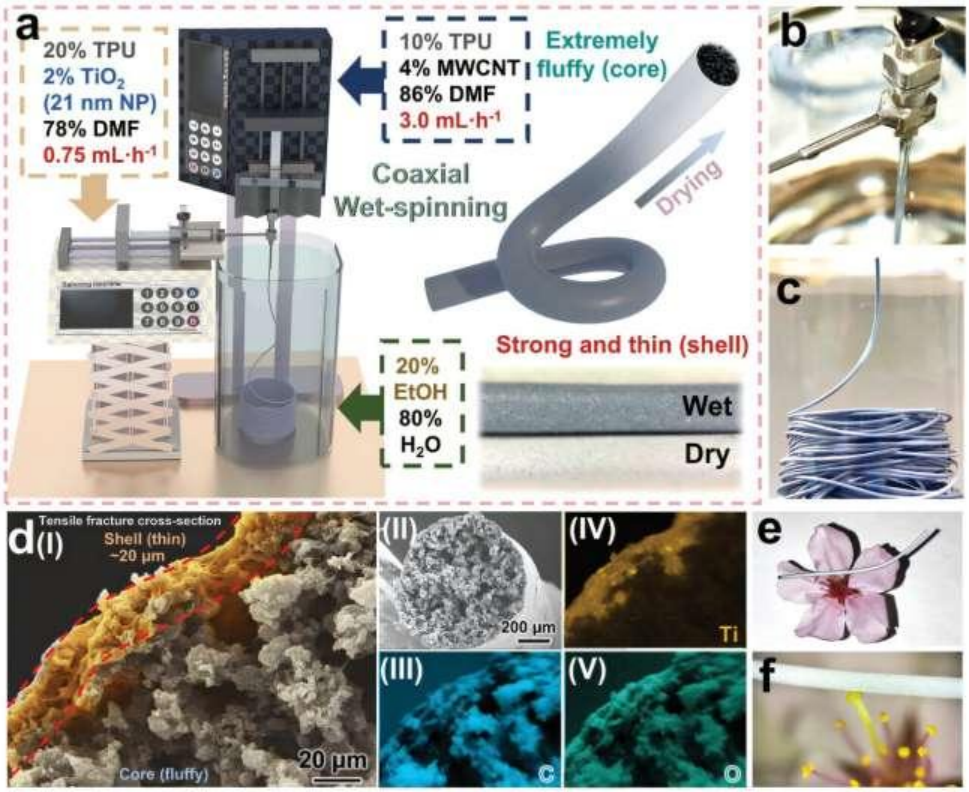
APRIL 28, 2025

# DNA-inspired flexible fiber design enhances sensors for wearables

by Shinshu University




Preparation of TT/MT fluffy core-shell fibers: a) Schematic diagram of wet-spinning and the proportion of slurry. b) Photo of the needle for wet-spinning. c) Photo of fibers during the wet-spinning process. d) Cross-sectional SEM image of TT/MT fluffy fibers and EDS map of the external structure of TT/MT fluffy fibers. e,f) Display of the lightweight TT/MT fibers. Credit: *Advanced Science* (2025). DOI: 10.1002/advs.202416564

A fiber sensor inspired by the shape of DNA, developed by researchers at Shinshu University, introduces a new design for more durable, flexible fiber sensors in wearables. Traditional fiber sensors have electrodes at both ends, which often fail under repeated movement when placed on body joints.

The proposed double-helical design, however, places both electrodes on one end, allowing the sensor to endure repeated stretching and movement, effectively addressing a key limitation of conventional wearable sensors.

Flexible fiber sensors are widely used in smart wearables, as their compact size and lightweight feel make them suitable for everyday use. However, current designs, commonly placed at joints, face limited application due to mechanical challenges. Traditional fiber sensors with electrodes at both ends are vulnerable when applied to joints like fingers or knees, where repeated movement pulls on connecting wires, causing them to break loose or produce measurement inaccuracies.

To solve this issue, a team of researchers from Shinshu University, Japan, has developed a new type of flexible sensor with a double-helical structure that mimics the shape of DNA. This new design places both electrodes on one end of the fiber, reducing strain during movement and significantly improving durability. Their findings were published online on February 4, 2025 in the journal *Advanced Science*.

"Effective electrode design is critical to the performance and lifespan of wearable sensors. But in one-dimensional fiber sensors, this has long been a challenge. Our design addresses this issue directly," says Associate Professor Chunhong Zhu, the lead author of the study from the Institute for Fiber Engineering and Science.

The researchers drew inspiration from the stability of DNA's double helix, which is maintained by hydrogen bonds between complementary base pairs. In a similar fashion, they twisted two specially designed coaxial fibers together to create a tightly bound, stable structure.

Each fiber is produced using a method called coaxial wet-spinning, with an insulating outer layer and a fluffy, conductive inner core. The core contains multi-walled carbon nanotubes (MWCNTs), while the outer layer includes thermoplastic polyurethane (TPU) and titanium dioxide ($TiO_2$) nanoparticles, which make the fibers fluffier and stronger.

After heat treatment, the two fibers naturally form a double helix with built-in positive and negative terminals on the same end, eliminating the need for complex wiring at both ends—a common problem in traditional designs. "The TT/MT dual-helical fiber has two electrodes at one end and a free end with no electrodes, greatly simplifying the wiring of flexible sensors," says Mr. Ziwei Chen, co-author of the study.

The resulting TT/MT dual-helical fiber sensor is remarkably slender, measuring less than 1 mm in diameter, making it easy to seamlessly integrate into wearable textiles. In addition, it proved to be highly durable, enduring repeated stretching and bending. In laboratory tests, it withstood over 1,000 stretching cycles and extended more than 300% beyond its original length without breaking.

With both electrodes located on the same side, the sensor can be used across joints with the side containing the electrodes attached to areas with limited movement, such as the back of the hand, cheeks, or knees, without risking wire damage. This opens up applications for tracking finger gestures, facial expressions, and gait movements, and even detecting breathing patterns during sleep.

Researchers have developed a flexible fiber sensor with a double-helical structure that places both electrodes on one end. This design improves durability, allowing the sensor to endure repeated stretching and bending, and makes it easier to integrate into wearable devices, especially for use on body joints. Credit: Associate Professor Chunhong Zhu from Shinshu University

In one test, the researchers placed the sensor inside a glove and used a machine-learning model to help it learn how to recognize finger movements. The glove was able to identify six common hand gestures with 98.8% accuracy. In another test, the sensor detected how long each finger pull lasted and used that to send Morse code wirelessly, showcasing its potential as a tool for assisting people with disabilities.



The design also shows promise for use in Bluetooth-connected wearables, enabling real-time remote monitoring for rehabilitation and sports training, according to the researchers. The team envisions these sensors being embedded in clothing for high-risk activities like mountaineering, where they could send emergency alerts in case of accidents, falls, or health issues such as hypoxia.

With this innovative design, the researchers hope to inspire the development of the next generation of intelligent fibers that are not only durable and sensitive but also easy to integrate into daily wear.

"Our design strategy, exemplified by the TT/MT dual-helical fiber highlighted in our study, also provides a versatile approach that can inspire the development of various intelligent fibers tailored for different applications," says Dr. Zhu.

**More information:** Ziwei Chen et al, Structure and Wiring Optimized TT/MT Double-Helical Fiber Sensors: Fabrication and Applications in Human Motion Monitoring and Gesture Recognition, *Advanced Science* (2025). DOI: 10.1002/advs.202416564
**Journal information:** Advanced Science

APRIL 28, 2025

# Sleep's dual role: How it consolidates memories while preparing the brain for new learning

by University of Toyama

Through behavioral experiments in mice coupled with advanced neuronal imaging, researchers found how sleep helps consolidate past experiences in engram cells and prepare engram-to-be cells to store future experiences. Credit: Kaoru Inokuchi from the University of Toyama, Japan

Memory formation, storage, and retrieval are fundamental processes that define who we are and how we interact with the world. At the cellular level, these processes rely on specialized neurons called engram cells—neuronal populations that physically encode our experiences and allow us to recall them later. Over the past few decades, scientists have made significant progress in identifying these neuronal ensembles and understanding some aspects of memory allocation.

Although sleep is widely known to be essential for memory processing and consolidation, many of its underlying mechanisms and functions are unclear. Traditional views have largely focused on sleep as a backward-looking process that serves to strengthen past experiences, but could it simultaneously help prepare the brain for new learning?

In a recent effort to tackle this question, a research team from Japan, led by Distinguished Professor Kaoru Inokuchi from the University of Toyama, uncovered a dual role for sleep in memory processing. Their paper, which will be published in *Nature Communications* on April 28, 2025, explores how the brain simultaneously preserves past memories while preparing for future ones during sleep periods.

The study was co-authored by Specially Appointed Assistant Professor Khaled Ghandour, also from the University of Toyama; Dr. Tatsuya Haga from the National Institute of Information and Communications Technology; Dr. Noriaki Ohkawa from Dokkyo Medical University; and Professor Tomoki Fukai from OIST.

The researchers employed an advanced imaging system that combines live calcium imaging with engram cell labeling, allowing them to track neuronal activity in mice before, during, and after learning experiences. This approach gave them unprecedented insights into how specific populations of neurons behave across different cognitive states, including during sleep periods before and after learning events.

Distinguished Professor Kaoru Inokuchi and Specially Appointed Assistant Professor Khaled Ghandour explain the rationale, goals, and main findings of this research, which focuses on the importance of sleep to both consolidate past memories and prime the brain for future memories. Credit: Kaoru Inokuchi from the University of Toyama, Japan
Their findings revealed that two parallel processes occur during post-learning sleep. First, engram cells that encoded an initial learning experience showed reactivation patterns—confirming the well-established consolidation process. Remarkably, they also identified a separate population of neurons, which they termed "engram-to-be cells," that became increasingly synchronized during post-learning sleep. These cells were later shown to encode a new, different learning experience.

"Engram-to-be cells exhibited increased coactivity with existing engram cells during sleep, suggesting that this interaction helps shape new memory networks," explains Prof. Inokuchi.

To understand the mechanisms behind this phenomenon, the team developed a neural network model simulating hippocampal activity. The model suggested that synaptic depression and scaling, which are mechanisms that adjust connection strengths between neurons during sleep, are essential for the emergence of engram-to-be cells. When these processes were disabled in the model, the preparation of neurons for future learning was significantly impaired.

The study also revealed interesting dynamics between existing engram cells and engram-to-be cells, showing increased co-activation during post-learning sleep. This hints at some form of information transfer or coordination between neural networks representing past and future memories.

These findings have significant implications for our understanding of learning and memory. They suggest that the quality of sleep between learning sessions may determine not only how well we remember what we've already learned, but also how effectively we can learn new information. This could influence approaches to education, cognitive enhancement, and the treatment of memory disorders.

Additionally, the research opens new avenues for exploring how sleep disturbances might impact not just memory consolidation but also the brain's preparedness for future learning challenges. "We believe that manipulating brain activity during sleep or sleep patterns may uncover methods to enhance memory by unlocking the brain's latent potential," says Prof. Inokuchi.

Overall, this study underscores the critical role of sleep in maintaining cognitive function and overall well-being. "We want people to understand that sleep is not just about rest—it plays a crucial role in how the brain processes information," Prof. Inokuchi concludes, "With that in mind, we hope everyone will begin to value sleep more and use it as a way to improve their overall quality of life."

**More information:** Parallel processing of past and future memories through reactivation and synaptic plasticity mechanisms during sleep, *Nature Communications* (2025). DOI: 10.1038/s41467-025-58860-w
**Journal information:** Nature Communications

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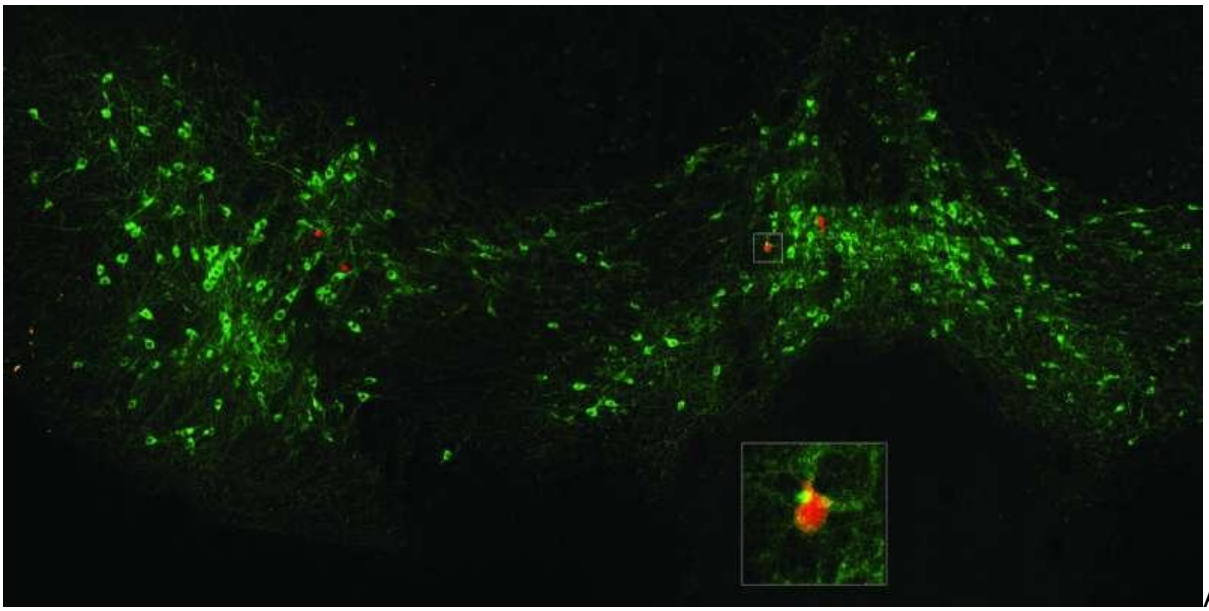
APRIL 28, 2025

# Dopamine signals when a fear can be forgotten, study shows

by Massachusetts Institute of Technology



An edited version of a figure from the research shows the ventral tegmental area, highlighting dopamine-associated neurons in green and one that connects to the posterior amygdala (magnified in inset) in red. Credit: Tonegawa Lab/MIT Picower Institute

Dangers come but dangers also go and when they do, the brain has an "all-clear" signal that teaches it to extinguish its fear.

A new study in mice by MIT neuroscientists shows that the signal is the release of dopamine along a specific interregional brain circuit. The research therefore pinpoints a potentially critical mechanism of mental health, restoring calm when it works, but prolonging anxiety or even post-traumatic stress disorder when it doesn't.

"Dopamine is essential to initiate fear extinction," said Michele Pignatelli di Spinazzola, co-author of the new study from the lab of senior author Susumu Tonegawa, Picower Professor of biology and neuroscience at the RIKEN-MIT Laboratory for Neural Circuit Genetics in The Picower Institute for Learning and Memory and an HHMI Investigator.

In 2020, Tonegawa's lab showed that learning to be afraid, and then learning when that's no longer necessary, results from a competition between populations of cells in the brain's amygdala region. When a mouse learns that a place is "dangerous" (because it gets a little foot shock there), the fear memory is encoded by neurons in the anterior of the basolateral amygdala (aBLA) that express the gene Rspo2.

When the mouse then learns that a place is no longer associated with danger (because they wait there and the zap doesn't recur), neurons in the posterior basolateral amygdala (pBLA) that express the gene Ppp1r1b encode a new fear extinction memory that overcomes the original dread.

Notably, those same neurons encode feelings of reward, helping to explain why it feels so good when we realize that an expected danger has dwindled.

In the new study, the lab, led by former members Xiangyu Zhang and Katelyn Flick, sought to determine what prompts these amygdala neurons to encode these memories. The rigorous set of experiments the team reports in the *Proceedings of the National Academy of Sciences* show that dopamine is sent to the different amygdala populations from distinct groups of neurons in the ventral tegmental area (VTA).

"Our study uncovers a precise mechanism by which dopamine helps the brain unlearn fear," said Zhang, who also led the 2020 study and is now Senior Associate at Orbimed, a health care investment firm.

"We found that dopamine activates specific amygdala neurons tied to reward, which in turn drive fear extinction. We now see that unlearning fear isn't just about suppressing it—it's a positive learning process powered by the brain's reward machinery. This opens up new avenues for understanding and potentially treating fear-related disorders like PTSD."

# Forgetting fear

The VTA was the lab's prime suspect to be the source of the signal because the region is well known for encoding surprising experiences and instructing the brain, with dopamine, to learn from them. The first set of experiments in the paper used multiple methods for tracing neural circuits to see whether and how cells in the VTA and the amygdala connect.

They found a clear pattern: Rspo2 neurons were targeted by dopaminergic neurons in the anterior and left and right sides of the VTA. Ppp1r1b neurons received dopaminergic input from neurons in the center and posterior sections of the VTA. The density of connections was greater on the Ppp1r1b neurons than for the Rspo2 ones.

The circuit tracing showed that dopamine is available to amygdala neurons that encode fear and its extinction, but do those neurons care about dopamine? The team showed that indeed they express "D1" receptors for the neuromodulator. Commensurate with the degree of dopamine connectivity, Ppp1r1b cells had more receptors than Rspo2 neurons.

Dopamine does a lot of things, so the next question was whether its activity in the amygdala actually correlated with fear encoding and extinction. Using a method to track and visualize it in the brain, the team watched dopamine in the amygdala as mice underwent a three-day experiment.

On day one, they went to an enclosure where they experienced three little zaps on the feet. On day two, they went back to the enclosure for 45 minutes where they didn't experience any new shocks –at first the mice froze in fear but then relaxed after about 15 minutes. On day three, they returned again to test whether they had indeed extinguished the fear they showed at the beginning of day two.

The dopamine activity tracking revealed that during the shocks on day one, Rspo2 neurons had the larger response to dopamine, but in the early moments of day two, when the anticipated shocks didn't come and the mice eased up on freezing in fear, the Ppp1r1b neurons showed the stronger dopamine activity. More strikingly, the mice that learned to extinguish their fear most strongly also showed the greatest dopamine signal at those neurons.

## Causal connections

The final sets of experiments sought to show that dopamine is not just available and associated with fear encoding and extinction, but also actually causes them. In one set, they turned to optogenetics, a technology that enables scientists to activate or quiet neurons with different colors of light.

Sure enough, when they quieted VTA dopaminergic inputs in the pBLA, doing so impaired fear extinction. When they activated those inputs, it accelerated fear extinction. The researchers were surprised that when they activated VTA dopaminergic inputs into the aBLA they could reinstate fear even without any new foot shocks, impairing fear extinction.

The other way they confirmed a causal role for dopamine in fear encoding and extinction was to manipulate the amygdala neurons' dopamine receptors. In Ppp1r1b neurons, overexpressing dopamine receptors impaired fear recall and promoted extinction, whereas knocking the receptors down impaired fear extinction. Meanwhile, in the Rspo2 cells, knocking down receptors reduced the freezing behavior.

"We showed that fear extinction requires VTA dopaminergic activity in the pBLA Ppp1r1b neurons by using optogenetic inhibition of VTA terminals and cell-type-specific knockdown of D1 receptors in these neurons," the authors wrote.

The scientists are careful in the study to note that while they've identified the "teaching signal" for fear extinction learning, the broader phenomenon of fear extinction occurs brainwide, rather than in just this single circuit.

But the circuit seems to be a key node to consider as drug developers and psychiatrists work to combat anxiety and PTSD, Pignatelli di Spinazzola said.

"Fear learning and fear extinction provide a strong framework to study generalized anxiety and PTSD," he said. "Our study investigates the underlying mechanisms suggesting multiple targets for a translational approach such as pBLA and use of dopaminergic modulation."

Marianna Rizzo is also a co-author of the study.

**More information:** Tonegawa, Susumu, Dopamine induces fear extinction by activating the reward-responding amygdala neurons, *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2501331122. doi.org/10.1073/pnas.2501331122
**Journal information:** Proceedings of the National Academy of Sciences
Provided by Massachusetts Institute of Technology

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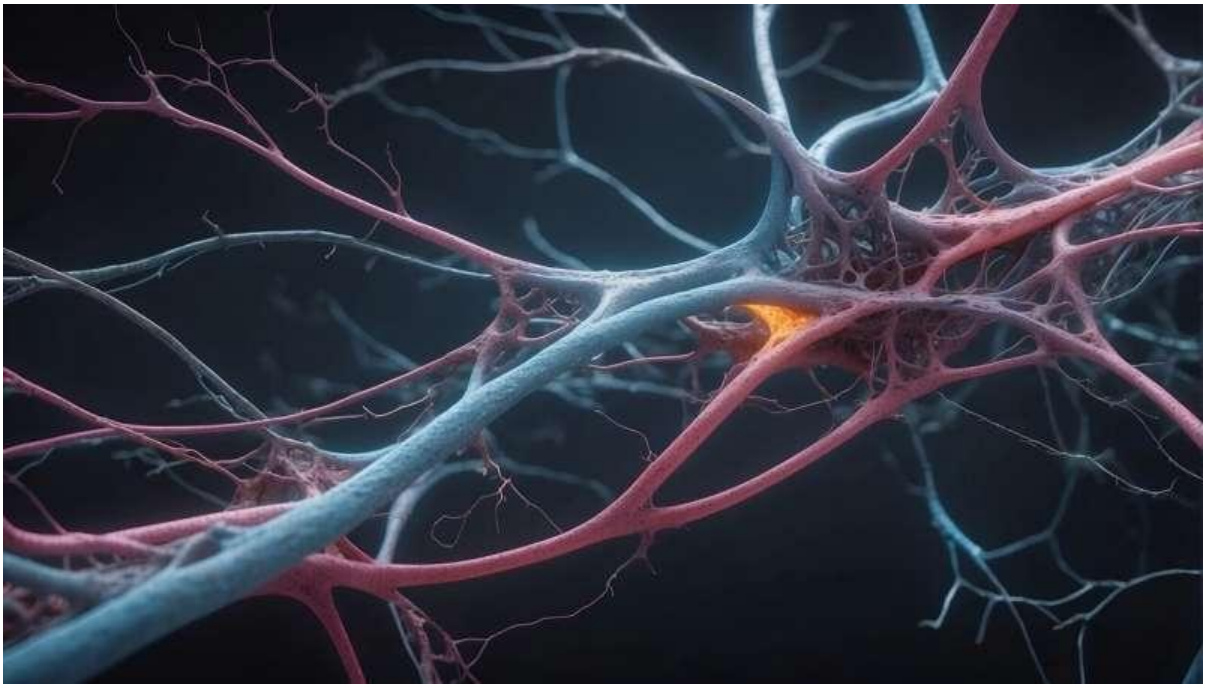
MAY 1, 2025

# How researchers discovered specific brain cells that enable intelligent behavior

by Mohamady El-Gaby , The Conversation



Credit: Pixabay/CC0 Public Domain

For decades, neuroscientists have developed mathematical frameworks to explain how brain activity drives behavior in predictable, repetitive scenarios, such as while playing a game. These algorithms have not only described brain cell activity with remarkable precision but also helped develop artificial intelligence with superhuman achievements in specific tasks, such as playing Atari or Go.

Yet these frameworks fall short of capturing the essence of human and animal behavior: our extraordinary ability to generalize, infer and adapt. Our study, published in *Nature* late last year, provides insights into how brain cells in mice enable this more complex, intelligent behavior.

Unlike machines, humans and animals can flexibly navigate new challenges. Every day, we solve new problems by generalizing from our knowledge or drawing from our experiences. We cook new recipes, meet new people, take a new path—and we can imagine the aftermath of entirely novel choices.

It was in the mid-20th century that psychologist Edward Tolman described the concept of "cognitive maps". These are internal, mental representations of the world that organize our experiences and allow us to predict what we'll see next.

Starting in the 1970s, researchers identified a beautiful system of specialized cells in the hippocampus (the brain's memory center) and entorhinal cortex (an area that deals with memory, navigation, and time perception) in rodents that form a literal map of our environments.

These include "place cells," which fire at specific locations, and "grid cells" that create a spatial framework. Together, these and a host of other neurons encode distances, goals and locations, forming a precise mental map of the physical world and where we are within it.

Now our attention has turned to other areas of cognition beyond finding our way around generalization, inference, imagination, social cognition and memory. The same areas of the brain that help us navigate in space are also involved in these functions.

## Cells for generalizing?

We wanted to know if there are cells that organize the knowledge of our behavior, rather than the outside world, and how they work. Specifically, what are the algorithms that underlie the activity of brain cells as we generalize from past experience? How do we rustle up that new pasta dish?

We did find such cells. There are neurons that tell us "where we are" in a sequence of behavior (we haven't named the cells).

To uncover the brain cells, networks and algorithms that perform these roles, we studied mice, training the animals to complete a task. The task had a sequence of actions with a

repeating structure. Mice moved through four locations, or "goals," containing a water reward (A, B, C and D) in loops.

When we moved the location of the goals, the mice were able to infer what came next in the sequence—even when they had never experienced that exact scenario before.

When mice reached goal D in a new location for the first time, they immediately knew to return to goal A. This wasn't memory, because they'd never encountered it. Instead, it shows that the mice understood the general structure of the task and tracked their position within it.

The mice had electrodes implanted into their brains, which allowed us to capture neural activity during the task. We found that specific cells in the cortex (the outermost layer of the brain) collectively mapped the animal's goal progress. For example, one cell could fire when the animal was 70% of the way to its goal, regardless of where the goal was or how far away.

Some cells tracked progress towards immediate subgoals—like chopping vegetables in our cooking analogy—while others mapped progress towards the overall goal, such as finishing the meal.

Together, these goal progress cells created a system that gave us our location in a behavioral space rather than in a physical space. Crucially, the system is flexible and can be updated if the task changes. This encoding allows the brain to predict the upcoming sequence of actions without relying on simple associative memories.

## Common experiences

Why should the brain bother to learn general structural representations of tasks? Why not create a new representation for each one? For generalization to be worthwhile, the tasks we complete must contain regularities that can be exploited—and they do.

The behavior we compose to achieve our goals is replete with repetition. Generalization allows knowledge to extend beyond individual instances. Throughout life, we encounter a highly structured distribution of tasks. Each day we solve new problems by generalizing from past experiences.

A previous encounter with making bolognese can inform a new ragu recipe, because the same general steps apply to both (such as starting with frying onions and adding fresh herbs at the end). We propose that the goal-progress cells in the cortex serve as the building blocks—internal frameworks that organize abstract relationships between events, actions and outcomes. While we've only shown this in mice, it is plausible that the same thing happens in the human brain.

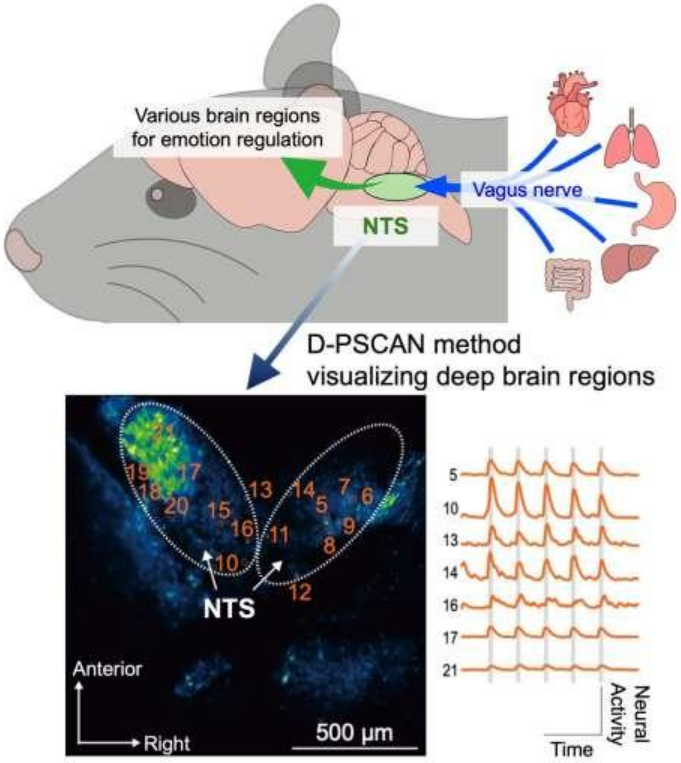
By documenting these cellular networks and the algorithms that underlie them, we are building new bridges between human and animal neuroscience, and between biological and artificial intelligence—and pasta.

**Journal information:** Nature

MAY 2, 2025

# Decoding the brainstem: A new window into brain–body–mind interactions

by National Institutes of Natural Sciences




Double-prism-based brainstem imaging under cerebellar architecture and neural circuits. Credit: Masakazu Agetsuma

The communication between the brain and bodily organs is fundamental to emotion regulation and overall mental health. The nucleus tractus solitarii (NTS) in the brainstem is a critical hub structure mediating this interaction via the vagus nerve. Despite its

importance, the NTS's deep location has historically posed challenges for observation in living animals.

In a study published in *Cell Reports Methods*, researchers at the National Institute for Physiological Sciences have developed a live NTS imaging method (named "D-PSCAN," or Double-Prism-based brainStem imaging under Cerebellar Architecture and Neural circuits). This novel deep-brain imaging technique enables high-resolution, minimally invasive visualization of the NTS neural activity in living mice.

The D-PSCAN method is based on the double microprism assembly carefully and systematically implanted between the cerebellum and brainstem, preserving cerebellar function while providing a broad and detailed view of the NTS.

"One major challenge in studying the NTS is its deep location beneath the cerebellum, which has made observation in living animals difficult," explains lead author Masakazu Agetsuma.

"Previously, some approaches involved removing the cerebellum to access the NTS, but this posed a major limitation: the cerebellum, major motor coordination center, has also been recognized as important for emotional regulation. Therefore, a method to observe the NTS while preserving cerebellar function has been needed."

## Detailed activity of the NTS can now be observed

The research team evaluated the D-PSCAN method by investigating the NTS's response to the electrical stimulation of the vagus nerve, which conveys signals from internal organs to the NTS.

They observed the specific thresholds of vagus nerve stimulation (VNS) intensity required to elicit neural responses in the NTS. They also observed that varying stimulation parameters causes distinct patterns of neural activation, including sensitization or, conversely, inhibitory effects.

Vagus nerve stimulation (VNS) has been clinically used for drug-resistant epilepsy and is currently under investigation as a treatment for depression and other psychiatric and neurological disorders. Therefore, these results highlight the potential of the D-PSCAN method for gaining valuable insights into optimizing VNS parameters for therapeutic applications.

To further investigate NTS function under more physiological conditions than electrical stimulation, the research team applied the D-PSCAN method to examine its response to the gut hormone cholecystokinin, which is naturally released after feeding. As a result, they successfully detected NTS neural activity evoked by cholecystokinin.

"The brain-body interaction plays a critical role in emotion regulation, and gaining a deeper understanding of this function is expected to contribute both to the treatment of

neuropsychiatric disorders and to the advancement of mental health and well-being," says Agetsuma.

"The D-PSCAN can offer a new approach to elucidate brain–body–mind interactions, and represents a valuable research tool for basic neuroscience to clinical applications."

The implications of this research extend beyond the study of emotion regulation. The NTS receives input from various organs, including the heart and gut, and is involved in diverse functions such as appetite regulation, energy metabolism, and gut microbiota.

The in vivo NTS imaging technique developed in this study, D-PSCAN, is expected to be widely applied across these research areas.

**More information:** Masakazu Agetsuma et al, Minimally invasive, wide-field two-photon imaging of the brainstem at cellular resolution, *Cell Reports Methods* (2025). DOI: 10.1016/j.crmeth.2025.101010
**Journal information:** Cell Reports Methods
Provided by National Institutes of Natural Sciences

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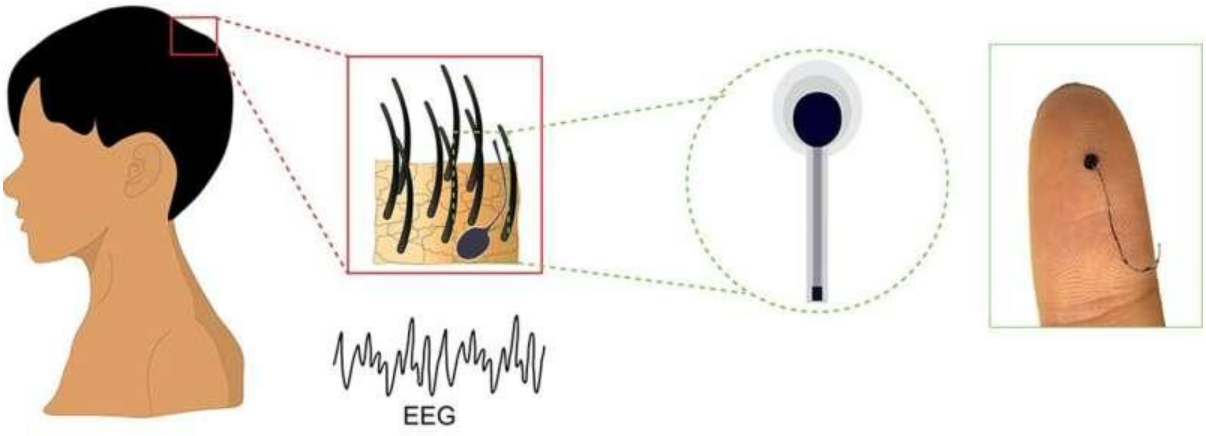
MAY 2, 2025

# The future of brain activity monitoring may look like a strand of hair

by Christine Yu , Pennsylvania State University




The lightweight and flexible electrode, which looks like a strand of hair, attaches directly to

the scalp and delivers stable, high-quality recordings of the brain's signals. Credit: Zhou Lab / Penn State. Creative Commons

The future of electroencephalography (EEG) monitoring may soon look like a strand of hair. In place of the traditional metal electrodes, a web of wires and sticky adhesives, a team of researchers from Penn State created a hairlike device for long-term, non-invasive monitoring of the brain's electrical activity. The lightweight and flexible electrode attaches directly to the scalp and delivers stable, high-quality recordings of the brain's signals.

EEG is critical for diagnosing and assessing neurological conditions like epilepsy and brain injuries. In some cases, clinicians need to monitor brain waves for longer periods of time, for example, to evaluate seizures, sleep disorders and conditions that affect the blood vessels and blood flow in the brain.

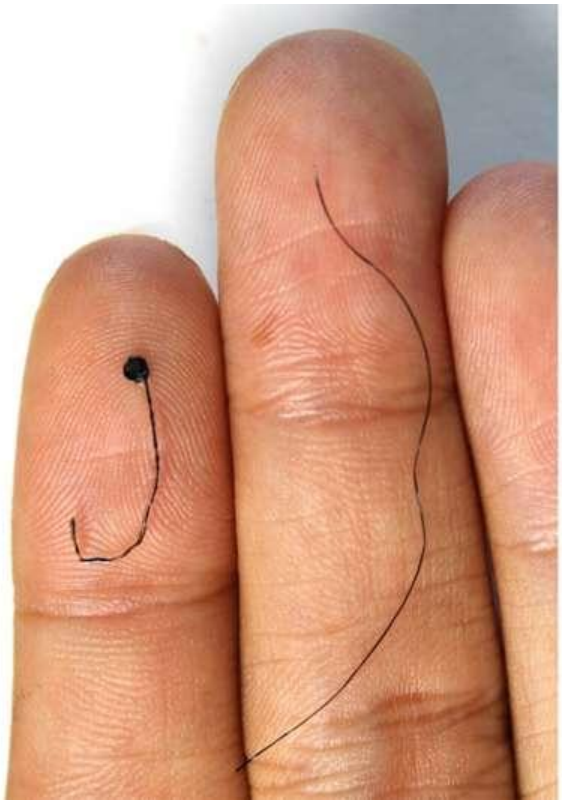
The researchers described the new electrodes, which were shown to maintain stable performance for over 24 hours of continuous wear, in a study published in the journal npj Biomedical Innovations. This technology holds promise for use in consumer health and wellness products, in addition to clinical health care applications, according to the researchers.

"This electrode allows for more consistent and reliable monitoring of EEG signals and can be worn without being noticeable, which enhances both functionality and patient comfort," said Tao Zhou, Wormley Family Early Career Professor of engineering science and mechanics and senior author on the paper.

EEG monitoring is a widely used method to measure the brain's electrical activity, Zhou explained. Small metal electrodes are placed on the scalp and pick up the faint electrical impulses generated by cells in the brain. The electrodes are attached to wires that are then connected to a machine that displays the brain's activity as patterns that look like waves.

The traditional EEG monitoring process, however, can be a cumbersome—and sometimes messy—affair. Its limitations make it difficult to use for continuous, long-term monitoring.

To get a good recording of the brain's activity, the electrodes need to conform to the scalp. Any gaps between the electrode and the skin or dense hair can diminish the quality of the recorded signal. Researchers and clinicians must apply gels to the scalp to maintain good surface-to-surface contact between the electrodes and skin and signal quality. For some people, though, the gels can cause skin irritation.



Comparison of the hairlike electrode, on left, and a human hair. Credit: Zhou Lab / Penn State. Creative Commons

It's a time-consuming process that must be repeated when the gels dry out, especially for someone needs to be monitored continuously or over the course of multiple sessions. The application and re-application process is imprecise, too, and can result in different amounts of gel used on the electrodes.

"This will change the impedance—or interface—between the electrodes and the scalp and it can affect the brain signal that's recorded," Zhou said. "We also don't always apply the electrodes in the exact same position either because we're human. But if you change the position, even a little bit, the brain signals you're monitoring can be different."

The conventional EEG electrodes are rigid, too, and can shift when someone moves their head, even slightly, which can compromise the data uniformity.

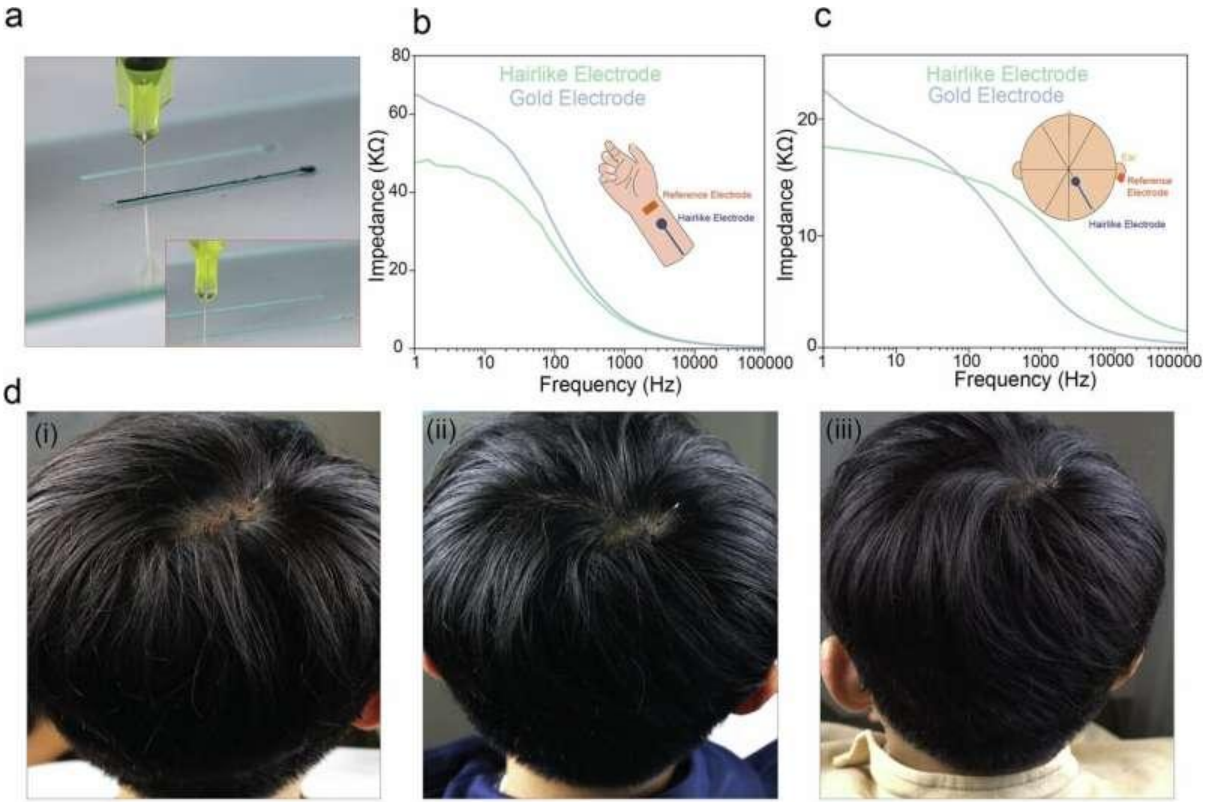
To address these limitations, the research team designed a small monitoring device that looks like a strand of hair and is made from 3D-printed hydrogel material. One end is the electrode. It looks like a small dot and captures the brain's electrical signals from the scalp. There's a long, thin wire-like component that extends from the electrode, which connects to the monitoring system.

The device also uses a 3D-printable bioadhesive ink that allows the electrode to stick directly onto the scalp without the need for any gloopy gels or other skin preparation. This minimizes the gap between the electrode and scalp, improving the signal quality. The lightweight, flexible and stretchable nature of the device also means that the device stays

put—even when combing hair and donning and removing a baseball cap—and can be worn for longer periods of time, making it suitable for chronic monitoring.

The team found that the new device performed comparably to gold electrodes, the current standard electrodes used for EEG. However, the hairlike electrode maintained better contact between the electrode and skin and performed reliably for over 24 hours of continuous wear without any degradation in signal quality. Because the electrodes don't have to be removed and replaced like traditional EEG monitoring systems, they eliminate the risk of inconsistent data, even across different monitoring sessions.

"You don't have to worry if the position of the electrode has changed or if the impedance has changed because the electrodes haven't moved," Zhou said.




Printing of hairlike electrodes and characterization of their stability, electrical and mechanical properties. Credit: *npj Biomedical Innovations* (2025). DOI: 10.1038/s44385-025-00009-x

Unlike the traditional metal electrodes, the new electrodes mimic human hair and are inconspicuous on the head. Since the device is 3D-printed, Zhou explained that they can print the electrode in different colors to match a person's hair, too.

"This makes it discreet, and people may be more comfortable wearing this, especially if they require continuous EEG monitoring and need to wear the electrodes for an extended period of time," Zhou said.

Currently, the EEG is still wired; patients need to be connected to a machine while their brain activity is recorded. In the future, the researchers hope to make the system wireless so that people can move around more freely during recording sessions.

Other Penn State authors on the paper include lead authors Salahuddin Ahmed and Marzia Momin, both doctoral students in the Department of Engineering Science and Mechanics. Jiashu Ren, doctoral student in the Department of Engineering Science and Mechanics; Hyunjin Lee, doctoral student in the Department of Biomedical Engineering; Li-Pang Huang, research assistant; and Basma AlMahmood, undergraduate student in the Department of Physics also contributed to the paper.

Other authors include Chi-Ching Kuo, Archana Pandiyan and Loganathan Veeramuthu from the Department of Molecular Science and Engineering, National Taipei University of Technology.

**More information:** Salahuddin Ahmed et al, Stick-and-play bioadhesive hairlike electrodes for chronic EEG recording on human, *npj Biomedical Innovations* (2025). DOI: 10.1038/s44385-025-00009-x
Provided by Pennsylvania State University

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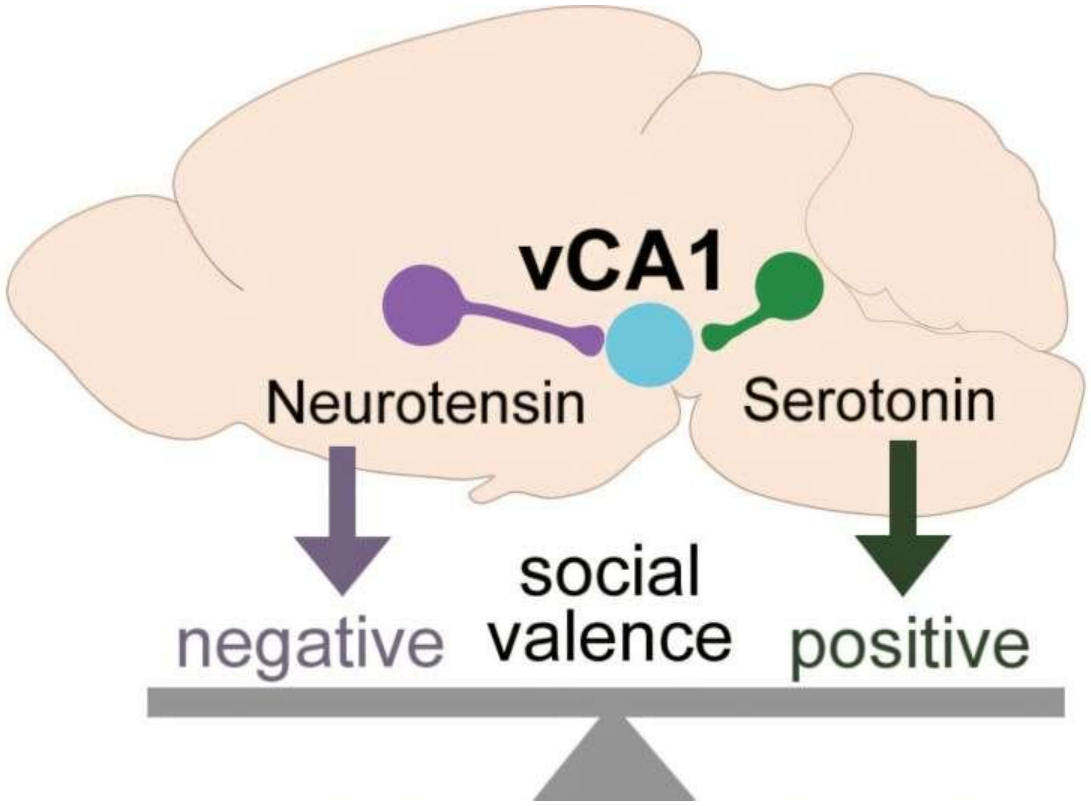
APRIL 30, 2025

# Mechanism by which the brain weighs positive vs. negative social experiences revealed

by The Mount Sinai Hospital




Schematic summary of the paper. Credit: Xiaoting Wu, Ph.D.

Mount Sinai researchers have identified for the first time the neural mechanisms in the brain that regulate both positive and negative impressions of a social encounter, as well as how an imbalance between the two could lead to common neuropsychiatric disorders like autism spectrum disorder (ASD) and schizophrenia.

The study, published in *Nature*, also describes how activating a serotonin receptor in the brain of a mouse model of ASD restored positive emotional value (also known as "valence"), with encouraging implications for the development of future therapies.

"The ability to recognize and distinguish unpleasant from pleasant interactions is essential for humans to navigate their social environment," says Xiaoting Wu, Ph.D., Assistant

Professor of Neuroscience at the Icahn School of Medicine at Mount Sinai, and senior author of the study.

"Until now, it has been unclear how the brain assigns positivity or negativity—'valence'—to social experiences, and how that information can be flexibly updated in a constantly changing environment."

At the center of this complex neural circuitry is the hippocampus, located deep in the temporal lobe of the brain and responsible for forming new memories, learning, and emotions.

The Mount Sinai researchers described how two neuromodulators—serotonin and neurotensin, which influence processes such as mood, arousal, and neural plasticity—are released into the hippocampal subregion known as ventral CA1, where they control opposing social valence assignment. Both neurotransmitters impact distinct populations of ventral CA1 neurons through their respective receptors, serotonin 1B and neurotensin 1.

While deficits in social valence are known to be prevalent in many neuropsychiatric disorders, their underlying neural mechanisms and pathophysiology have remained elusive.

"Through our work we've provided the first foundational insights into the neural basis of social valence," notes Dr. Wu.

"We have demonstrated that the neuromodulators serotonin and neurotensin signal opposing valence, revealing a fundamental principle of brain function in the form of a neuromodulatory switch that allows behavioral adaptation based on social history."

Specifically, the team developed a novel social cognitive paradigm that involved exposing mice to negative and positive social encounters. In the negative social encounter, the test mouse was exposed to a mean/aggressive mouse; in the positive encounter, the mouse was exposed to a potential mate.

In both assays, the mice had negative or neutral/positive or neutral interaction and then got to choose which mouse they would like to spend more time with. Without prior experience, the mice did not have a preference, but with experience, they associated a mouse with a positive or negative valence and then learned to avoid the "bad" mouse or approach the "good" mouse.

Just as importantly, the team uncovered specific drug targets for positive and negative valence, knowledge that could potentially factor into future treatments. Specifically, serotonin acting on the serotonin 1B receptor generates a positive impression of a social encounter, while neurotensin acting on the neurotensin 1 receptor creates a negative impression.

Imbalanced emotional processing of those two social experiences is known to be a debilitating symptom of ASD. Consequently, by activating the serotonin 1B receptor,

researchers were able to restore a positive impression associated with rewarding social experiences.

"We identified a specific neuromodulator receptor which we then targeted to rescue social cognitive deficits in a mouse model of ASD," Dr. Wu explains.

"On a broader scale, our work provides critical insights into complex social behaviors while revealing potential therapeutic targets that can be leveraged to improve social cognitive deficits in common neuropsychiatric disorders."

**More information:** Xiaoting Wu, Serotonin and neurotensin inputs in the vCA1 dictate opposing social valence, *Nature* (2025). DOI: 10.1038/s41586-025-08809-2. www.nature.com/articles/s41586-025-08809-2
**Journal information:** Nature
Provided by The Mount Sinai Hospital

# The Molecular Bond That Helps Secure Your Memories

*How do memories last a lifetime when the molecules that form them turn over within days, weeks or months? An interaction between two proteins points to a molecular basis for memory.*

Carlos Arrojo for *Quanta Magazine*

## Introduction *May 7, 2025*

When Todd Sacktor() was about to turn 3, his 4-year-old sister died of leukemia. “An empty bedroom next to mine. A swing set with two seats instead of one,” he said, recalling the lingering traces of her presence in the house. “There was this missing person — never spoken of — for which I had only one memory.” That memory, faint but enduring, was set in the downstairs den of their home. A young Sacktor asked his sister to read him a book, and she brushed him off: “Go ask your mother.” Sacktor glumly trudged up the stairs to the kitchen.

It’s remarkable that, more than 60 years later, Sacktor remembers this fleeting childhood moment at all. The astonishing nature of memory is that every recollection is a physical trace, imprinted into brain tissue by the molecular machinery of neurons. How the essence of a lived moment is encoded and later retrieved remains one of the central unanswered questions in neuroscience.

Sacktor became a neuroscientist in pursuit of an answer. At the State University of New York Downstate in Brooklyn, he studies the molecules involved in maintaining the neuronal connections underlying memory. The question that has always held his attention was first articulated in 1984() by the famed biologist Francis Crick: How can memories persist for years, even decades, when the body's molecules degrade and are replaced in a matter of days, weeks or, at most, months?

In 2024, working alongside a team that included his longtime collaborator André Fenton(), a neuroscientist at New York University, Sacktor offered a potential explanation in a paper published in *Science Advances*. The researchers discovered that a persistent bond between two proteins() is associated with the strengthening of synapses, which are the connections between neurons. Synaptic strengthening is thought to be fundamental to memory formation. As these proteins degrade, new ones take their place in a connected molecular swap that maintains the bond's integrity and, therefore, the memory.

In 1984, Francis Crick described a biological conundrum: Memories last years, while most molecules degrade in days or weeks. "How then is memory stored in the brain so that its trace is relatively immune to molecular turnover?" he wrote in *Nature*.

National Library of Medicine/Science Source

The researchers present "a very convincing case" that "the interaction between these two molecules is needed for memory storage," said Karl Peter Giese(), a neurobiologist at King's College London who was not involved with the work. The findings offer a compelling response to Crick's dilemma, reconciling the discordant timescales to explain how ephemeral molecules maintain memories that last a lifetime.

## Molecular Memory

Early in his career, Sacktor made a discovery that would shape the rest of his life. After studying under the molecular memory pioneer James Schwartz at Columbia University, he opened his own lab at SUNY Downstate to search for a molecule that might help explain how long-term memories persist.

The molecule he was looking for would be in the brain's synapses. In 1949, the psychologist Donald Hebb proposed that repeatedly activating neurons strengthens the connections between them, or, as the neurobiologist Carla Shatz later put it: "Cells that fire together, wire together." In the decades

since, many studies have suggested that the stronger the connection between neurons that hold memories, the better the memories persist.

In the early 1990s, in a dish in his lab, Sacktor stimulated a slice of a rat's hippocampus — a small region of the brain linked to memories of events and places, such as the interaction Sacktor had with his sister in the den — to activate neural pathways in a way that mimicked memory encoding and storage. Then he searched for any molecular changes that had taken place. Every time he repeated the experiment, he saw elevated levels of a certain protein within the synapses. "By the fourth time, I was like, this is it," he said.

It was protein kinase M zeta, or PKMζ for short. As the rats' hippocampal tissue was stimulated, synaptic connections strengthened and levels of PKMζ increased(). By the time he published his findings in 1993, he was convinced that PKMζ was crucial for memory.

Over the next two decades, he would go on to build a body of work showing that PKMζ's presence helps maintain memories long after their initial formation. When Sacktor blocked the molecule's activity an hour after a memory was formed, he saw that synaptic strengthening was reversed. This discovery suggested that PKMζ was "necessary and sufficient()" to preserve a memory over time, he wrote in *Nature Neuroscience* in 2002. In contrast, hundreds of other localized molecules impacted synaptic strengthening only if disrupted within a few minutes of a memory's formation. It appeared to be a singular molecular key to long-term memory.

To test his hypothesis in live animals, he teamed up with Fenton, who worked at SUNY Downstate at the time and had experience training lab animals and running behavioral experiments. In 2006, the duo published their first paper showing that blocking PKMζ could erase rats' memories() a day or a month after they had formed. This suggested that the persistent activity of PKMζ is required to maintain a memory.

Individually, PKMζ and KIBRA don't last a lifetime — but by binding to each other, they help ensure your memories might.

The paper was a bombshell. Sacktor and Fenton's star protein PKMζ gained widespread attention, and labs around the world found that blocking it could erase various types of memories, including those related to fear and taste. PKMζ seemed like a sweeping explanation for how memories form and are maintained at the molecular level. But then their hypothesis lost momentum. Other researchers genetically engineered mice to lack PKMζ, and in 2013, two independent() studies() showed that these mice could still form memories. This cast doubt on the protein's role and brought much of the ongoing research to a halt.

Sacktor and Fenton were undeterred. “We knew we had to figure it out,” Sacktor said. In 2016, they published a rebuttal(), demonstrating that in the absence of PKMζ, mice recruit a backup mechanism, involving another molecule, to strengthen synapses.

The existence of a compensatory molecule wasn’t a surprise. “The biological system is not such that you lose one molecule and everything goes. That’s very rare,” Giese said. But identifying this compensatory molecule prompted a new question: How did it know where to go to replace PKMζ? It would take Sacktor and Fenton nearly another decade to find out.

## The Maintenance Bond

A classic test of a molecule’s importance is to block it and see what breaks. Determined to pin down PKMζ’s role once and for all, Sacktor and Fenton set out to design a way to disrupt it more precisely than ever before. They developed a new molecule to inhibit the activity of PKMζ. It “worked beautifully,” Sacktor said. But it wasn’t clear how.

One day in 2020, Matteo Bernabo, a graduate student from a collaborating lab at McGill University, was presenting findings related to the PKMζ inhibitor when a clue emerged from the audience. “I suggested that it worked by blocking the PKMζ’s interaction with KIBRA,” recalled Wayne Sossin(), a neuroscientist at McGill.
KIBRA is a scaffolding protein. Like an anchor, it holds other proteins in place inside a synapse. In the brain, it is abundant in regions associated with learning and memory. “It’s not a protein that a lot of people work on,” Sossin said, but there is considerable “independent evidence that KIBRA has something to do with memory” — and even that it is associated with PKMζ(). Most research has focused on KIBRA’s role in cancer. “In the nervous system,” he said, “there are only three or four of us [studying it].” Sacktor and Fenton joined them.

André Fenton and his team found that an interaction between two proteins is key to keeping memory intact over time.
Lisa Robinson

To find out if KIBRA and PKMζ work together in response to synaptic activity, the researchers used a technique that makes interacting proteins glow. When they applied electrical pulses to hippocampal slices, glowing dots of evidence appeared: Following bursts of synaptic activity that produced long-term

synaptic strengthening, a multitude of KIBRA-PKMζ complexes formed, and they were persistent.

Then the team tested the bond during real memory formation by giving mice a drug to disrupt the formation of these complexes. They saw that the mice's synaptic strength and task memory were lost — and that once the drug wore off, the erased memory did not return, but the mice could acquire and remember new memories once again.

But are the KIBRA-PKMζ complexes needed to maintain memory over the long term? To find out, the researchers disrupted the complex four weeks after a memory was formed. Doing so did indeed wipe out the memory. This suggested that the interaction between KIBRA and PKMζ is crucial not only for forming memories, but also for keeping them intact over time.

"It's the persistent association between two proteins that maintains the memory, rather than a protein that lasts by itself for the lifetime of the memory," said Panayiotis Tsokas, a neuroscientist working with Sacktor and lead author on the new *Science Advances* paper.

The KIBRA and PKMζ proteins stabilize each other by forming a bond. That way, when a protein degrades and needs to be replaced, the other remains in place. The bond itself and its location at the specific synapses that were activated during learning are preserved, allowing a new partner to slot itself in, perpetuating the alliance over time. Individually, PKMζ and KIBRA don't last a lifetime — but by binding to each other, they help ensure your memories might.

The discovery helps addresses the conundrum first identified by Crick, namely how memories persist despite the relatively short lifetimes of all biological molecules. "There had to be a very, very interesting answer, an elegant answer, for how this could come about," Fenton said. "And that elegant answer is the KIBRA-PKMζ interacting story."

This work also answers a question that researchers had put on the shelf. Sacktor's earlier study showed that increasing levels of PKMζ strengthened synapses and memories. But how did the molecule know where to go within

the neuron? "We figured, well, one day, maybe we'll understand that," Sacktor said. Now, the researchers think that KIBRA acts as a synaptic tag that guides PKMζ. If true, this would help explain how only the specific synapses involved in a particular physical memory trace are strengthened, when a neuron may have thousands of synapses that connect it to various other cells.

"These experiments very nicely show that KIBRA is necessary for maintaining the activity of PKMζ at the synapse," said David Glanzman(), a neurobiologist at the University of California, Los Angeles, who was not involved in the study. However, he cautioned that this doesn't necessarily translate to maintaining memory because synaptic strengthening is not the only model for how memory works.

Glanzman's own past research on sea slugs at first appeared to show that disrupting a molecule analogous to PKMζ erases memory. "Originally, I said it was erased," Glanzman said, "but later experiments showed we could bring the memory back." These findings prompted him to reconsider whether memory is truly stored as changes in the strength of synaptic connections. Glanzman, who has worked for 40 years under the synaptic model, is a recent proponent of an alternative view called the molecular-encoding model, which posits that molecules inside a neuron store memories.

While he has no doubt that synaptic strengthening follows memory formation, and that PKMζ plays a major role in this process, he remains unsure if the molecule also stores the memory itself. Still, Glanzman emphasized that this study addresses some of the challenges of the synaptic model, such as molecular turnover and synapse targeting, by "providing evidence that KIBRA and PKMζ form a complex that is synapse-specific and persists longer than either individual molecule."

Although Sacktor and Fenton believe that this protein pair is fundamental to memory, they know that there may be other factors yet to be discovered that help memories persist. Just as PKMζ led them to KIBRA, the complex might lead them further still.

# Specific brain cells enable intelligent behaviour

**NEUROSCIENCE**
ByInvited Researcher May 14, 2025 0 comments Print
*Author:* ***Mohamady El-Gaby****, Postdoctoral Neuroscientist, University of Oxford*For decades, neuroscientists have developed mathematical frameworks to explain how brain activity drives behaviour in predictable, repetitive scenarios, such as while playing a game. These algorithms have not only described brain cell activity with remarkable precision but also helped develop artificial intelligence with superhuman achievements in specific tasks, such as playing Atari or Go.

Yet these frameworks fall short of capturing the essence of human and animal behaviour: our extraordinary ability to generalise, infer and adapt. Our study, published in Nature late last year, provides insights into how brain cells in mice enable this more complex, intelligent behaviour.

Unlike machines, humans and animals can flexibly navigate new challenges. Every day, we solve new problems by generalising from our knowledge or drawing from our experiences. We cook new recipes, meet new people, take a new path – and we can imagine the aftermath of entirely novel choices.

It was in the mid-20th century that psychologist Edward Tolman described the concept of “cognitive maps”. These are internal, mental representations of the world that organise our experiences and allow us to predict what we’ll see next.

Starting in the 1970s, researchers identified a beautiful system of specialised cells in the hippocampus (the brain’s memory centre) and entorhinal cortex (an area that deals with memory, navigation, and time perception) in rodents that form a literal map of our environments.

These include “place cells”, which fire at specific locations, and “grid cells” that create a spatial framework. Together, these and a host of other neurons encode distances, goals and locations, forming a precise mental map of the physical world and where we are within it.

And now our attention has turned to other areas of cognition beyond finding our way around generalisation, inference, imagination, social cognition and memory. The same areas of the brain that help us navigate in space are also involved in these functions.

## Cells for generalising?

We wanted to know if there are cells that organise the knowledge of our behaviour, rather than the outside world, and how they work. Specifically, what are the algorithms that underlie the activity of brain cells as we generalise from past experience? How do we rustle up that new pasta dish?

And we did find such cells. There are neurons that tell us “where we are” in a sequence of behaviour (we haven’t named the cells).

To uncover the brain cells, networks and algorithms that perform these roles, we studied mice, training the animals to complete a task. The task had a sequence of actions with a repeating structure. Mice moved through four locations, or “goals”, containing a water reward (A, B, C and D) in loops.

When we moved the location of the goals, the mice were able to infer what came next in the sequence – even when they had never experienced that exact scenario before.

When mice reached goal D in a new location for the first time, they immediately knew to return to goal A. This wasn’t memory, because they’d never encountered it. Instead, it shows that the mice understood the general structure of the task and tracked their position within it.

The mice had electrodes implanted into the brain, which allowed us to capture neural activity during the task. We found that specific cells in the cortex (the outermost layer of the brain) collectively mapped the animal’s goal progress. For example, one cell could fire when the animal was 70% of the way to its goal, regardless of where the goal was or how far away.

Some cells tracked progress towards immediate subgoals – like chopping vegetables in our cooking analogy – while others mapped progress towards the overall goal, such as finishing the meal.

Together, these goal progress cells created a system that gave our location in behavioural space rather than a physical space. Crucially, the system is flexible and can be updated if the task changes. This encoding allows the brain to predict the upcoming sequence of actions without relying on simple associative memories.

## Common experiences

Why should the brain bother to learn general structural representations of tasks? Why not create a new representation for each one? For generalisation to be worthwhile, the tasks we complete must contain regularities that can be exploited — and they do.

The behaviour we compose to reach our goals is replete with repetition. Generalisation allows knowledge to extend beyond individual instances. Throughout life, we encounter a highly structured distribution of tasks. And each day we solve new problems by generalising from past experiences.

A previous encounter with making bolognese can inform a new ragu recipe, because the same general steps apply to both (such as starting with frying onions and adding fresh herbs at the end). We propose that the goal-progress cells in the cortex serve as the building blocks – internal frameworks that organise abstract relationships between events, actions and outcomes. While we've only shown this in mice, it is plausible that the same thing happens in the human brain.

By documenting these cellular networks and the algorithms that underlie them, we are building new bridges between human and animal neuroscience, and between biological and artificial intelligence. And pasta.

MAY 5, 2025

# Exploring how people face moral dilemmas

by Society for Neuroscience

Credit: Pixabay/CC0 Public Domain

People typically evaluate the preferences of both themselves and others before making decisions in moral dilemmas. Researchers have theorized how people face moral dilemmas, but experimental data is lacking.

In a *JNeurosci* paper, JuYoung Kim and Hackjin Kim at Korea University provide what they claim is the first experimental data to address the question of how people face moral dilemmas.

The researchers assessed study participants' awareness of their own bodily signals and how closely they aligned with unknown group moral preferences in different scenarios. Awareness of internal states was measured using self-reports and self-evaluations of heartbeats. Group consensus was measured by the number of participants selecting the same ethical option across various scenarios.

The researchers found a link between internal bodily awareness and making decisions that aligned with the group consensus. This link was mediated by brain activity states during rest that featured activity in brain regions associated with self-referential processing and internal attention.

Thus, according to the authors, this newfound link between internal state sensitivity and moral alignment may influence the moral intuitions a person develops as they learn the moral expectations of others.

**More information:** Neural Processes Linking Interoception to Moral Preferences Aligned with Group Consensus, *JNeurosci* (2025). DOI: 10.1523/JNEUROSCI.1114-24.2025
**Journal information:** Journal of Neuroscience

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MAY 7, 2025

# How the brain detects surprises, and why it could matter for mental health

by Friedrich Miescher Institute for Biomedical Research

FMI researchers adapted a mouse experiment for humans using EEG and VR, finding similar

brain responses to visual mismatches during movement. Credit: Friedrich Miescher Institute for Biomedical Research

What happens in the brain when our senses don't match our expectations—for example, when we take a step, but there's no sound or the sound is delayed or distorted? A new study led by FMI neuroscientists sheds light on how the brain detects and processes these moments of sensory surprise. The findings could not only deepen our understanding of how the brain interprets the world, but might also open new avenues for diagnosing and tracking psychiatric conditions.

Our brains are constantly predicting what we should see and hear based on our own movements and previous experiences. When reality doesn't match these predictions, certain neurons respond with a distinctive signal—a so-called prediction error.

Previous research from the Keller group at the FMI had shown that when mice run through a virtual tunnel and the visual flow is suddenly paused, their brains produce a strong prediction error signal, but it was unclear whether this was unique to vision.

Magdalena Solyga, a postdoc with Keller, set out to find out. In her experiments, Solyga designed a setup where mice ran through a dark corridor, with the loudness of a sound increasing in proportion to their running speed. Occasionally, the sound was muted—creating a mismatch between what the mouse expected to hear and what it actually heard. Neurons in the auditory cortex responded strongly, indicating that prediction error signaling is not limited to vision but may be a general function of sensory brain areas.

Next, Solyga introduced mismatches in both sight and sound at the same time. In this version of the experiment, both the visual flow and the sound were tied to the mouse's running speed—and both were occasionally paused together. The result was a surprisingly strong brain response, larger than the sum of the individual visual or auditory mismatches. Some neurons responded only to this combined mismatch, suggesting the brain integrates different types of sensory errors in a complex, non-linear way, Solyga says.

Building on results in mice, the team adapted their experiment for humans using EEG recordings and virtual reality headsets. In early tests, human participants walked while navigating a virtual environment. When the visual scene froze unexpectedly while the participant's body kept moving, the researchers observed a clear brain response indicating a visual mismatch, similar to the one seen in mice. The team is now beginning to test combined mismatches in people as well.

One of the long-term goals of this research is to develop reliable brain-based biomarkers for psychiatric conditions. If people with psychosis show abnormal or absent mismatch responses, these brain signals could potentially be used to aid diagnosis or track the effects of treatment—offering a more objective measure than current self-reported symptoms.

However, translating this research into clinical practice will take time. Recording brain signals during movement is technically challenging, as movement introduces noise into

EEG data. So far, the team has tested 17 healthy adults and is aiming to recruit up to 50 participants to ensure robust results. Factors such as hairstyle and movement artifacts can affect signal quality, making it essential to gather data from a large group to be able to draw generalizable conclusions about how the brain works, Solyga says.

The study also raises new scientific questions. "We have no idea how the potentiation of brain response to prediction errors is happening: is it through direct communication between two sensory areas, or is there a region in the brain that gets information about all the mismatches happening?," she says. "There are so many exciting directions to explore."

The study is published in the journal *eLife*.

**More information:** Magdalena Solyga et al, Multimodal mismatch responses in mouse auditory cortex, *eLife* (2025). DOI: 10.7554/eLife.95398.3
**Journal information:** eLife
Provided by Friedrich Miescher Institute for Biomedical Research

MAY 14, 2025

# Neuroscientists reveal insights into how the brain forms habits and why they are so hard to break

by Sainsbury Wellcome Centre

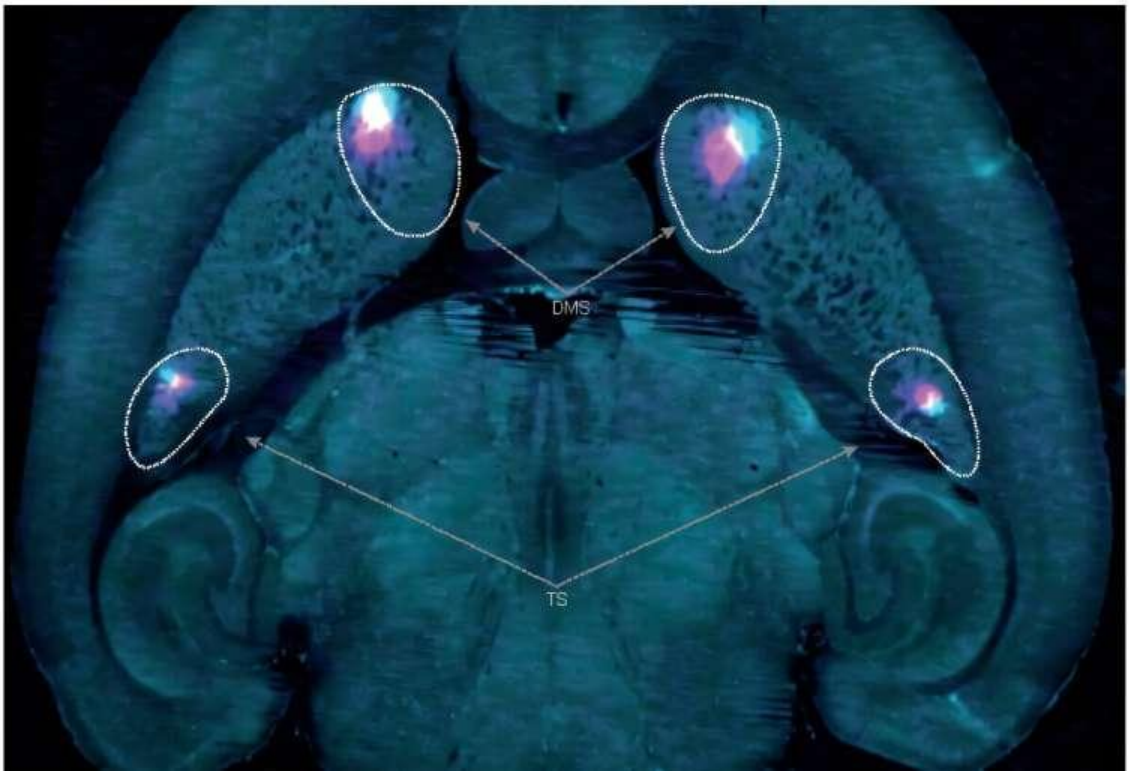



Image shows the two regions of the brain that were inactivated during the task – the dorsomedial striatum (DMS) and the tail of the striatum (TS). Credit: Hernando Martinez Vergara.

Neuroscientists at the Sainsbury Wellcome Center (SWC) at UCL have discovered that the brain uses a dual system for learning through trial and error. This is the first time a second learning system has been identified, which could help explain how habits are formed and provide a scientific basis for new strategies to address conditions related to habitual learning, such as addictions and compulsions.

Published in *Nature*, the study in mice could also have implications for developing therapeutics for Parkinson's. The study is titled "Dopaminergic action prediction errors serve as a value-free teaching signal."

"Essentially, we have found a mechanism that we think is responsible for habits. Once you have developed a preference for a certain action, then you can bypass your value-based system and just rely on your default policy of what you've done in the past. This might then allow you to free up cognitive resources to make value-based decisions about something else," explained Dr. Marcus Stephenson-Jones, Group Leader at SWC and lead author of the study.

The researchers uncovered a dopamine signal in the brain that acts as a different kind of teaching signal to the one previously known.

Dopamine signals in the brain were already understood to form reward prediction errors (RPE), where they signal to the animal whether an actual outcome is better or worse than expected. In this new study, the scientists discovered that, in parallel to RPE, there is an additional dopamine signal, called action prediction error (APE), which updates how often an action is performed.

These two teaching signals give animals two different ways of learning to make a choice, learning to choose either the most valuable option or the most frequent option.

"Imagine going to your local sandwich shop. The first time you go, you might take your time choosing a sandwich and, depending on which you pick, you may or may not like it. But if you go back to the shop on many occasions, you no longer spend time wondering which sandwich to select and instead start picking one you like by default. We think it is the APE dopamine signal in the brain that is allowing you to store this default policy," explained Dr. Stephenson-Jones.

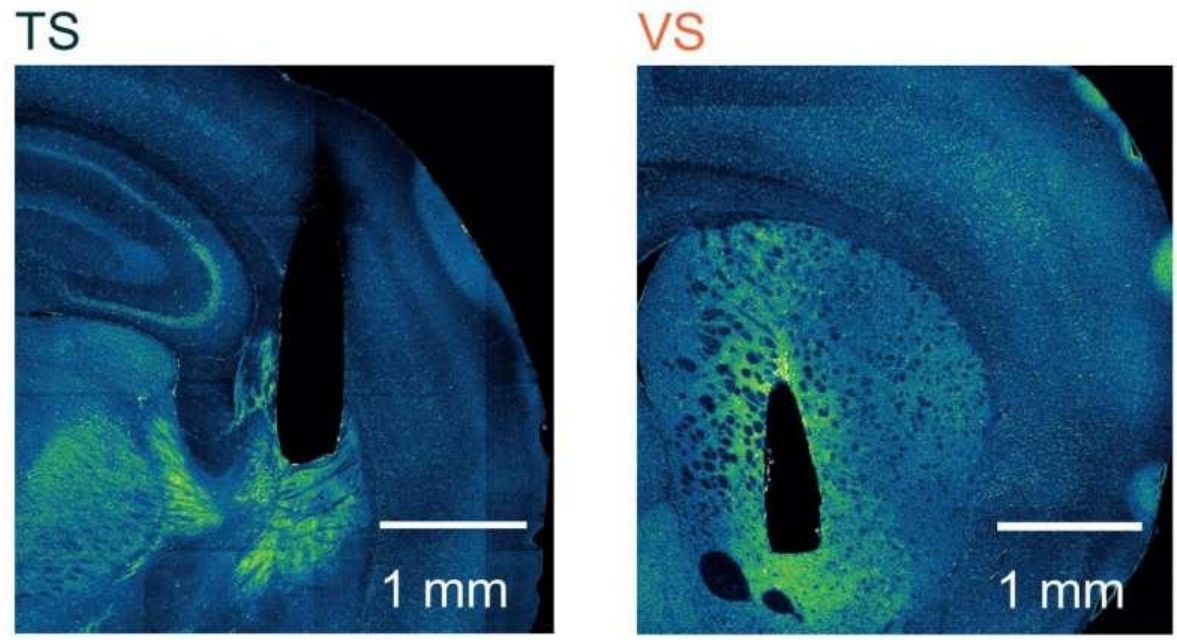
The newly discovered learning system provides a much simpler way of storing information than having to directly compare the value of different options.

This might free up the brain to multi-task. For example, once you have learned to drive, you can also hold a conversation with someone during your journey. While your default system is doing all the repetitive tasks to drive the car, your value-based system can decide what to talk about.

Previous research discovered the dopamine neurons needed for learning reside in three areas of the midbrain: the ventral tegmental area, substantia nigra pars compacta, and substantia nigra pars lateralis. While some studies showed that these neurons were involved in coding for reward, earlier research found that half of these neurons code for movement, but the reason remained a mystery.

RPE neurons project to all areas of the striatum apart from one, called the tail of the striatum. Whereas the movement-specific neurons project to all areas apart from the nucleus accumbens. This means that the nucleus accumbens exclusively signals reward, and the tail of the striatum exclusively signals movement.

By investigating the tail of the striatum, the team were able to isolate the movement neurons and discover their function. To test this, the researchers used an auditory discrimination task in mice, which was originally developed by scientists at Cold Spring Harbor Laboratory.




Fluorescent images showing the locations in the brain that the scientists recorded from – the tail of the striatum (TS) and ventral striatum (VS). Credit: Francesca Greenstreet.
Co-first authors, Dr. Francesca Greenstreet, Dr. Hernando Martinez Vergara and Dr. Yvonne Johansson, used a genetically encoded dopamine sensor, which showed that dopamine release in this area was not related to reward, but it was related to movement.

"When we lesioned the tail of the striatum, we found a very characteristic pattern," explained Dr. Stephenson-Jones.

"We observed that lesioned mice and control mice initially learn in the same way, but once they get to about 60–70% performance, i.e. when they develop a preference (for example, for a high tone go left, for a low tone, go right), then the control mice rapidly learn and develop expert performance, whereas the lesioned mice only continue to learn in a linear fashion.

"This is because the lesioned mice can only use RPE, whereas the control mice have two learning systems, RPE and APE, which contribute to the choice."

To further understand this, the team silenced the tail of striatum in expert mice and found that this had a catastrophic effect on their performance in the task. This showed that while in early learning animals form a preference using the value-based system based on RPE, in late learning they switch to exclusively use APE in the tail of the striatum to store these stable associations and drive their choice.

The team also used extensive computational modeling, led by Dr. Claudia Clopath, to understand how the two systems, RPE and APE, learn together.

These findings hint at why it is so hard to break bad habits and why replacing an action with something else may be the best strategy. If you replace an action consistently enough, such as chewing on nicotine gum instead of smoking, the APE system may be able to take over and form a new habit on top of the other one.

"Now that we know this second learning system exists in the brain, we have a scientific basis for developing new strategies to break bad habits. Up until now, most research on addictions and compulsions has focused on the nucleus accumbens. Our research has opened up a new place to look in the brain for potential therapeutic targets," commented Dr. Stephenson-Jones.

This research also has potential implications for Parkinson's, which is known to be caused by the death of midbrain dopamine neurons, specifically in substantia nigra pars compacta. The type of cells that have been shown to die are movement-related dopamine neurons, which may be responsible for coding APE.

This may explain why people with Parkinson's experience deficits in doing habitual behaviors such as walking, however, they do not experience deficits in more flexible behaviors such as ice skating.

"Suddenly, we now have a theory for paradoxical movement in Parkinson's. The movement-related neurons that die are the ones that drive habitual behavior. And so, movement that uses the habitual system is compromised, but movement that uses your value-based flexible system is fine. This gives us a new place to look in the brain and a new way of thinking about Parkinson's," concludes Dr. Stephenson-Jones.

The research team is now testing whether APE is really needed for habits. They are also exploring what exactly is being learned in each system and how the two work together.

**More information:** Dopaminergic action prediction errors serve as a value-free teaching signal, *Nature* (2025). DOI: 10.1038/s41586-025-09008-9. www.nature.com/articles/s41586-025-09008-9
**Journal information:** Nature
Provided by Sainsbury Wellcome Centre

MAY 14, 2025

# How the brain allows us to infer emotions

by RIKEN

Xiaowei Gu and Joshua Johansen at the RIKEN Center for Brain Science in Japan have discovered key circuitry in the rat brain that allows the learning of inferred emotions. The study reveals how the frontal part of the brain coordinates with the amygdala—a brain region important for simple forms of emotional learning—to make this higher-order emotional ability possible.

Published in *Nature*, this study is the first to show how the brain codes human-like internal models of emotion.

What are inferred emotions? Consider a child who often watches a wasp fly in and out of its nest in the woods near her house. One day, the child is stung by the wasp for the first time, a frightening experience that changes her emotional response to this creature but also to the nest itself.

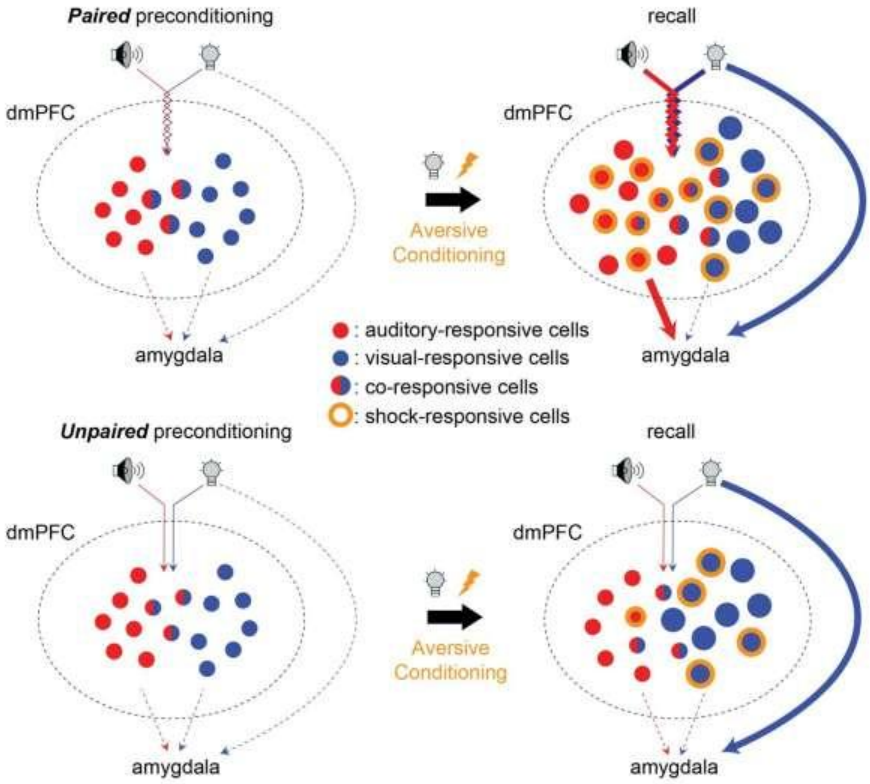
Afterward, seeing the wasp's nest alone makes the child feel anxious and become alert and cautious. In this scenario, the child has built an internal model that links the negative experience with the visual representation of the nest—even though the nest was not there at the time of the fearful event.

Johansen and Gu were interested in understanding the neural mechanisms that allow this type of higher-order emotional processing through inference.

To do so, they created a similar situation in animals; rats learned a neutral association between a noise and an image, then later experienced unpleasantness while seeing the image—a process called aversive conditioning.

The next day, they were tested to see if they could infer from hearing the noise alone that something unpleasant might happen. Under these conditions, rats did indeed freeze when they heard the noise, indicating their fear and showing that they too can learn inferred emotions.

Once they had a successful animal model, the researchers used a combination of calcium imaging and optogenetics to examine changes in neuron activity within a part of the brain called the medial prefrontal cortex (mPFC). As hypothesized, experiments indicated that the mPFC is the basis of emotional inference.




Schematic showing how paired preconditioning affects the amygdala after aversive learning. Aversive learing after paired preconditioning resulted in more neurons that responded to the noise (red dots), responded to both the noise and the image (mixed red and blue dots) and responded to the unpleasant experience (orange ring). Credit: RIKEN
Before undergoing aversive conditioning, neurons in the mPFC responded similarly to both the image and the noise, whether the stimuli had been paired or not. But after aversive learning, calcium imaging showed that the number of noise-responsive and noise/image co-responsive neurons went way up—provided the noise and image had been initially paired together when presented to the animals.

Further testing showed that this phenomenon was possible because the initial sensory pairing "tagged" co-responsive neurons, making them primed to activate during aversive conditioning.

Optogenetically blocking the mPFC during the aversive learning stage prevented rats from being able to make the later inference. In this case, the image and the unpleasant experience, and indirectly, the noise, could not properly become linked in the rats' minds.

Blocking the output from the mPFC to the amygdala during the test phase also prevented rats from responding to the noise with fear. However, in this case it was because they could not properly recall the inferred memory, even though the association had been made the day before.

At the same time, the rats had no problem freezing in response to the image, indicating that only the higher-order ability of inference is rooted in the physical changes that take place in mPFC neurons.

Johansen explains, "Decades of studying aversive learning in rodents have revealed that the amygdala is a critical site for storing simple emotional memories involving directly experienced associations. However, our new findings indicate that the mPFC is a central brain region for higher order human-like emotions, which involve internal models and inference."

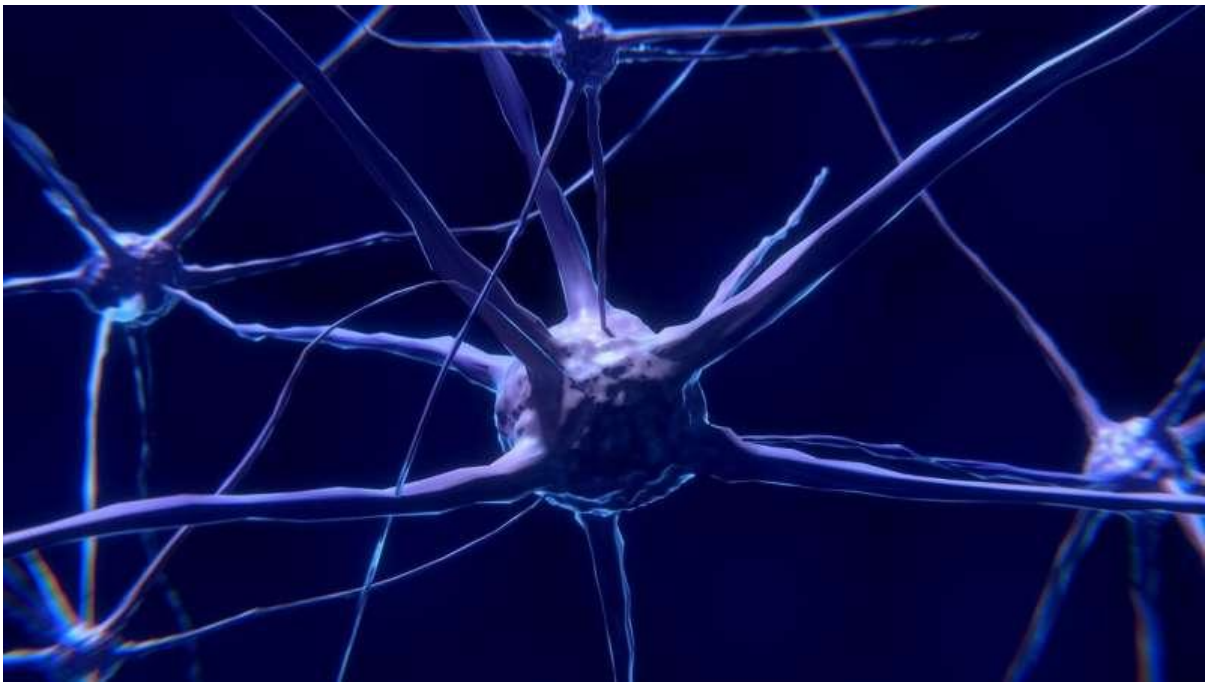
"The value of our study," says Johansen, "is that it opens the door for researchers everywhere to examine the neural mechanisms that mediate higher order emotions, which are more relevant to human psychiatric conditions like anxiety or trauma-related disorders."

**More information:** *Nature* (2025). DOI: 10.1038/s41586-025-09001-2
**Journal information:** Nature
Provided by RIKEN

MAY 14, 2025

# Real-time imaging shows how neuron energy balance changes during stroke-like conditions

by Anne Grimm , Leipzig University



Credit: Pixabay/CC0 Public Domain

A research team at the Carl Ludwig Institute for Physiology at Leipzig University has, for the first time, demonstrated how the energy levels of individual neurons in the brain change during so-called spreading depolarizations—waves of activity that occur in various brain disorders.

The findings provide important foundations for understanding energy metabolism in cases of acute cerebral ischemia, such as that which occurs during a stroke. The study has just been published in the *Proceedings of the National Academy of Sciences*.

Adenosine triphosphate, or ATP, is an essential energy source in neurons. In the new study, researchers at the Carl Ludwig Institute for Physiology used a specially developed mouse model whose brain neurons produce a fluorescent sensor protein. This allowed them to visualize the available amount of energy in individual neurons.

Using high-resolution fluorescence microscopy, the team was able to observe, in real time, how ATP levels in single neurons changed during spreading depolarizations. These waves—in which neurons depolarize one after another, much like a short circuit—are linked to progressive tissue damage after stroke. Until now, it was unclear how ATP, the brain's central energy carrier, behaves in individual neurons during such waves.

"Our study is the first to provide high-resolution insights into how and when neurons lose their energy reserves during an acute mismatch between energy supply and demand, such as in a stroke," says Dr. Karl Schoknecht of the Carl Ludwig Institute for Physiology, lead author of the study.

"Interestingly, the energy reserves are not depleted evenly, but are associated with spreading depolarizations. The model will be used in further projects to test potential therapies aimed at preventing the severe energy loss triggered by these waves," explains the researcher from the Faculty of Medicine.

The findings of the study show that even in "healthy" brain tissue, these waves cause a temporary drop in ATP levels. The effect of spreading depolarizations became particularly pronounced under conditions of energy deprivation—like those that occur during a stroke. In such cases, the waves greatly accelerated the loss of ATP, leading to the exhaustion of the neurons' energy reserves.

However, even after spreading depolarizations, most neurons were still capable of replenishing their ATP stores—provided that glucose and oxygen were resupplied. This means that the collapse of energy metabolism is, in principle, still reversible.

In this study, the team simulated stroke conditions by removing glucose and oxygen from the nutrient solution. At the same time, they recorded spreading depolarizations using electrophysiological methods. The findings contribute to the understanding of brain energy metabolism.

**More information:** Karl Schoknecht et al, Spreading depolarizations exhaust neuronal ATP in a model of cerebral ischemia, *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2415358122
**Journal information:** Proceedings of the National Academy of Sciences
Provided by Leipzig University

MAY 14, 2025

# Brain scans reveal what happens in the mind when insight strikes

by Robin Smith , Duke University

Examples of the hidden picture puzzles in the black/white images on the lower panel; corresponding real-world pictures on the upper panel. Credit: Maxi Becker et al

Have you ever been stuck on a problem, puzzling over something for what felt like ages without getting anywhere, but then suddenly the answer came to you like a bolt from the blue?

We've all experienced that "aha! moment," that sudden clarity or magical epiphany you feel when a new idea or perspective pops into your head as if out of nowhere.

Now, new evidence from brain imaging research shows that these flashes of insight aren't just satisfying—they actually reshape how your brain represents information, and help sear it into memory.

Led by researchers at Duke University and Humboldt and Hamburg Universities in Germany, the work has implications for education, suggesting that fostering "eureka moments" could help make learning last beyond the classroom.

If you have an aha experience when solving something, "you're actually more likely to remember the solution," said first author Maxi Becker, a postdoctoral fellow at Humboldt University in Berlin.

The findings were published May 9 in the journal *Nature Communications*.

## How the study worked

In the study, the researchers used a technique called functional magnetic resonance imaging (fMRI) to record people's brain activity while they tried to solve visual brain teasers. The puzzles required them to "fill in the blanks" of a series of two-tone images with minimal detail, using their perception to complete the picture and identify a real-world object.

Such hidden picture puzzles serve as small-scale proxies for bigger eureka moments. "It's just a little discovery that you are making, but it produces the same type of characteristics that exist in more important insight events," said senior author Roberto Cabeza, a professor of psychology and neuroscience at Duke.

For each puzzle the participants thought they solved, the researchers asked whether the solution just popped into their awareness in a flash of sudden insight, or whether they worked it out in a more deliberate and methodical way, and how certain they were of their answer.

The results were striking.

Participants tended to recall solutions that came to them in a flash of insight far better than ones they arrived at without this sense of epiphany. Furthermore, the more conviction a person felt about their insight at the time, the more likely they were to remember it five days later when the researchers asked them again.

"If you have an 'aha! moment' while learning something, it almost doubles your memory," said Cabeza, who has been studying memory for 30 years. "There are few memory effects that are as powerful as this."

A number of changes in the brain may cause people to have better memory for "aha! moments," the researchers found.

## A boost for memory

They discovered that flashes of insight trigger a burst of activity in the brain's hippocampus, a cashew-shaped structure buried deep in the temporal lobe that plays a major role in learning and memory. The more powerful the insight, the greater the boost.

They also found that the activation patterns across the participants' neurons changed once they spotted the hidden object and saw the image in a new light—particularly in certain parts of the brain's ventral occipito-temporal cortex, the region responsible for recognizing visual patterns. The stronger the epiphany, the greater the change in those areas.

"During these moments of insight, the brain reorganizes how it sees the image," said Becker, who did the work in the Cabeza lab.

Lastly, stronger "aha!" experiences were associated with greater connectivity between these different brain regions. "The different regions communicate with each other more efficiently," Cabeza said.

The current study looked at brain activity at two specific moments in time, before and after the eureka moment when the lightbulb appeared. As a next step, the researchers plan to look more closely at what happens during the few seconds in between that allows people to finally see the answer.

"Insight is key for creativity," Cabeza said. In addition to shedding light on how the brain comes up with creative solutions, the findings also lend support for inquiry-based learning in the classroom.

"Learning environments that encourage insight could boost long-term memory and understanding," the researchers wrote.

**More information:** Maxi Becker et al, Insight predicts subsequent memory via cortical representational change and hippocampal activity, *Nature Communications* (2025). DOI: 10.1038/s41467-025-59355-4
**Journal information:** Nature Communications
Provided by Duke University

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MAY 14, 2025

# Could a mini-stroke leave lasting fatigue?

by American Academy of Neurology

A transient ischemic attack, also known as a mini-stroke, is typically defined as a temporary blockage of blood flow to the brain that causes symptoms that go away within a day, but a new study finds that people who have this type of stroke may also have prolonged fatigue lasting up to one year.

The study, published online in *Neurology*, does not prove that mini-strokes cause lasting fatigue; it only shows an association.

"People with a transient ischemic attack can have symptoms such as face drooping, arm weakness or slurred speech and these resolve within a day," said study author Boris Modrau, MD, Ph.D., of Aalborg University Hospital in Denmark.

"However, some have reported continued challenges including reduced quality of life, thinking problems, depression, anxiety and fatigue. Our study found that for some people, fatigue was a common symptom that lasted up to one year after the transient ischemic attack."

The study involved 354 people with an average age of 70 who had a mini-stroke. They were followed for a year.

Participants completed questionnaires about their level of fatigue within the first two weeks of the mini-stroke and again at three, six, and 12 months later.

One questionnaire looked at five different types of fatigue, including overall tiredness, physical tiredness, reduced activity, reduced motivation and mental fatigue. Scores ranged from four to 20 with higher scores indicating more fatigue. Participants had an average score of 12.3 at the start of the study. At three months, the average score decreased slightly to 11.9, at six months to 11.4 and at twelve months to 11.1.

Researchers looked at how many participants experienced fatigue, as defined as a score of 12 or higher. Of the participants, 61% experienced fatigue two weeks after the mini-stroke and 54% experienced fatigue at each of the three other testing time periods at three, six and 12 months.

Participants also had brain scans. Researchers found that the presence of a blot clot on a scan was equal between people with long-term fatigue and those without it, so this did not explain the reason for the level of fatigue.

Researchers did find that previous anxiety or depression was twice as common in those participants who reported lasting fatigue.

"Long-term fatigue was common in our group of study participants, and we found if people experience fatigue within two weeks after leaving the hospital, it is likely they will continue to have fatigue for up to a year," said Modrau.

"For future studies, people diagnosed with a transient ischemic attack should be followed in the weeks and months that follow to be assessed for lingering fatigue. This could help us better understand who might struggle with fatigue long-term and require further care."

A limitation of the study was that while participants were asked to complete the questionnaires themselves, it is possible some responses may have been completed with assistance from relatives or caretakers and this may have influenced responses, including those around fatigue.

**More information:** *Neurology* (2025). www.neurology.org/doi/10.1212/WNL.0000000000213605
**Journal information:** Neurology
Provided by American Academy of Neurology

MAY 14, 2025

# Speaking more than one language can add layers to stroke recovery

by Michael Merschel, American Heart Association

Credit: CC0 Public Domain

You might not put a lot of thought into what it takes to speak, but speaking keeps your brain busy. In every conversation, multiple regions activate to process sounds, give words meaning and control the muscles that move your mouth.

If someone knows more than one language, the process has even more layers—as do the challenges when such a person has a stroke that limits their ability to speak.

Difficulty speaking clearly or understanding language is called aphasia. Its most common cause is stroke, but aphasia can also result from brain injuries or other diseases. And it can be "devastating," said Dr. Mira Goral, a professor of speech-language-hearing sciences at Lehman College and the Graduate Center of the City University of New York.

An estimated 2 million people in the U.S. live with aphasia, commonly as a result of stroke, according to the American Stroke Association. It's not clear how many people have what is

often called bilingual or multilingual aphasia. But in the U.S. alone, about 20% of the population speaks a language besides English at home, according to the Census Bureau.

And the numbers affected are likely to grow, said Dr. Swathi Kiran, founding director of the Center for Brain Recovery at Boston University. She noted that the U.S. Hispanic population has been projected to reach 71 million by 2030, and the largest increase in stroke prevalence is expected to be among Hispanic males.

The condition, however, doesn't know borders. "Most of the world is either bilingual or multilingual," Kiran said.

Language is just one form of communication, Goral said. It involves vocabulary, grammar, the sound of a spoken word or the form of the written one. It requires understanding of tone and context. And there is no single spot in the brain that handles all those functions. "Each of these linguistic aspects are associated with particular networks in the brain," Goral said, and "many, many layers" combine to form "this amazing thing" that we use to communicate.

In a multilingual person, things get even more interesting.

## Brain regions at work

If a brain is like a computer, Kiran said, a language is like software. And multiple languages are like different programs that run on the same equipment. "It's not that when you're learning one language, a certain part of your brain is involved, and when you speak another language, a different part of your brain is involved. It's actually the same structure."

A stroke affects everyone differently, Goral said, but patterns emerge.

The most common type of stroke is an ischemic stroke, when a vessel supplying blood to the brain is obstructed. And the most common place for that kind of stroke is in the left middle cerebral artery, which supplies blood to parts of the brain involved in speech and language. (In most people, most language is processed in the left half of the brain.)

The exact effect of a stroke depends on which part of the brain is damaged.

"If there's a reduction in the blood flow in the main artery, then a person has something called global aphasia," Kiran said. Many regions of the brain will be affected, and the person will have trouble speaking, understanding, reading and communicating.

Depending on which branch of the artery is blocked, the damage may not be that extensive. If the branch affecting the frontal lobe is affected, the person will have trouble speaking fluently but will understand what's being said to them, Kiran said. But if another artery is affected, people may be able to speak fluently but have trouble understanding what's being said.

## Recovering language

In multilingual people who develop aphasia, Goral said, the most common pattern is to experience the aphasia in all of their languages as opposed to just one. This might be because the same structures and networks of the brain are involved in all languages, and stroke can damage the network that allows a bilingual person to toggle back and forth between languages. This could play into the way people recover their language abilities after a stroke, Kiran said.

After a stroke, people may remember their first language, Kiran said. "Sometimes people remember the second language."

How much someone used a language before their stroke is emerging as a key factor. Recent research, she said, suggests that "if you're using both languages a lot before your stroke, they're both probably going to be equally affected." But if you primarily used a newer language more than the one you originally learned, that one might actually come back more quickly.

Kiran said there has been "a lot of buzz" around research suggesting that being bilingual might help protect against dementia or aid recovery after a stroke. It's a "hotly debated" area, she said, but "the theory is that switching back and forth between these languages requires a certain kind of cognitive control" that strengthens thinking ability.

Many people with post-stroke aphasia can improve their language ability over time, Goral said, especially in the early weeks following a stroke. Coupled with speech language therapy, "people can regain a lot of their linguistic and communication abilities."

But, people likely receive therapy in just one language, Goral said, especially in the U.S., where most speech language therapists speak only English.

Many studies have been conducted to try to find out whether the best results for treating aphasia come from treating someone in their first language or one they learned later, she said. "The evidence suggests that treatment can be beneficial in any language."

Whether treatment in one language also helps recover other languages is less clear, Goral said. "The results are mixed. Sometimes we get good carryover to the non-treated language, but sometimes it doesn't happen." Many factors come into play, she said, such as how well someone spoke the language before the stroke or what the people around them are speaking.

Helping people recover all their languages is important, Goral said.

"Multilingual people value all of their languages and the cultures that are associated with the identity that is associated with each of these languages," she said. "So it's important to assess and treat all of the languages that are relevant to the person who is multilingual.

And so to the extent we can, we should offer services in all of the languages that are relevant to that person."

That includes paying attention to people who mix their languages, which she called "a very common phenomenon of bilingual people." Many of the Spanish-English speakers she works with in New York tend to use both languages in the same conversation, sometimes in the same sentence, and it could be worthwhile to assess and help them in "the same linguistic context that they are used to and are comfortable with."

Unfortunately, Kiran said, not enough non-English-speaking therapists or interpreters are available to provide diagnosis, counseling and treatment in the language patients feel more comfortable with.

## Speech therapy challenges and future directions

The need for experts who can provide speech language therapy to multilingual people is expected to grow as the population ages, researchers say. And providing care in multiple languages is important at even the most basic levels, Kiran said.

"This is a problem we see all the time in Boston," she said, where she sees many speakers of Haitian Creole, Vietnamese and Spanish, "and it's hard to even get across the most basic "How do you access care?" kinds of questions."

Kiran's ongoing research uses machine learning to create a "digital twin" of the brain's language networks. Her team's work, which includes a study published in the journal *Stroke* in January, is "telling us a lot about how people learn languages and lose languages and recover languages" and could guide health care practitioners as they make decisions about therapy.

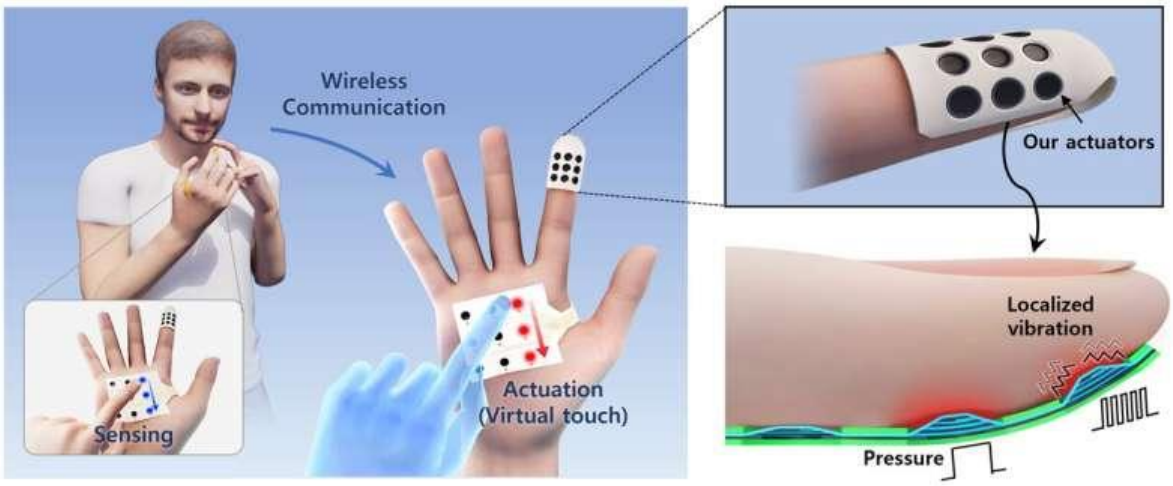
Such research, Kiran said, is "the new frontier for bilingual aphasia."

**More information:** Manuel Jose Marte et al, Machine Learning Predictions of Recovery in Bilingual Poststroke Aphasia: Aligning Insights With Clinical Evidence, *Stroke* (2025). DOI: 10.1161/STROKEAHA.124.047867
**Journal information:** Stroke
Provided by American Heart Association

MAY 8, 2025

# Wearable haptics get thinner: A flexible haptic patch lets you feel the virtual world

by Jung-Hwan Youn




Scenario of bidirectional tactile communication using haptic patch. Credit: Hee-kyung Kwon
As virtual reality (VR) and augmented reality (AR) technologies rapidly evolve, the demand for more immersive, multisensory experiences grows alongside them. Among the key frontiers is tactile feedback—the ability to physically feel the virtual world.

While wearable haptic suits equipped with vibrational motors or fluidic actuators have made strides in enhancing realism, delivering precise, diverse, and natural tactile sensations to the skin remains a major challenge. The limitation has largely stemmed from a lack of compact, lightweight, high-performance tactile actuators.

That's where our research takes a bold step forward. My colleagues and I have developed a new class of thin, flexible tactile actuators designed to deliver rich, nuanced haptic feedback directly to the skin.

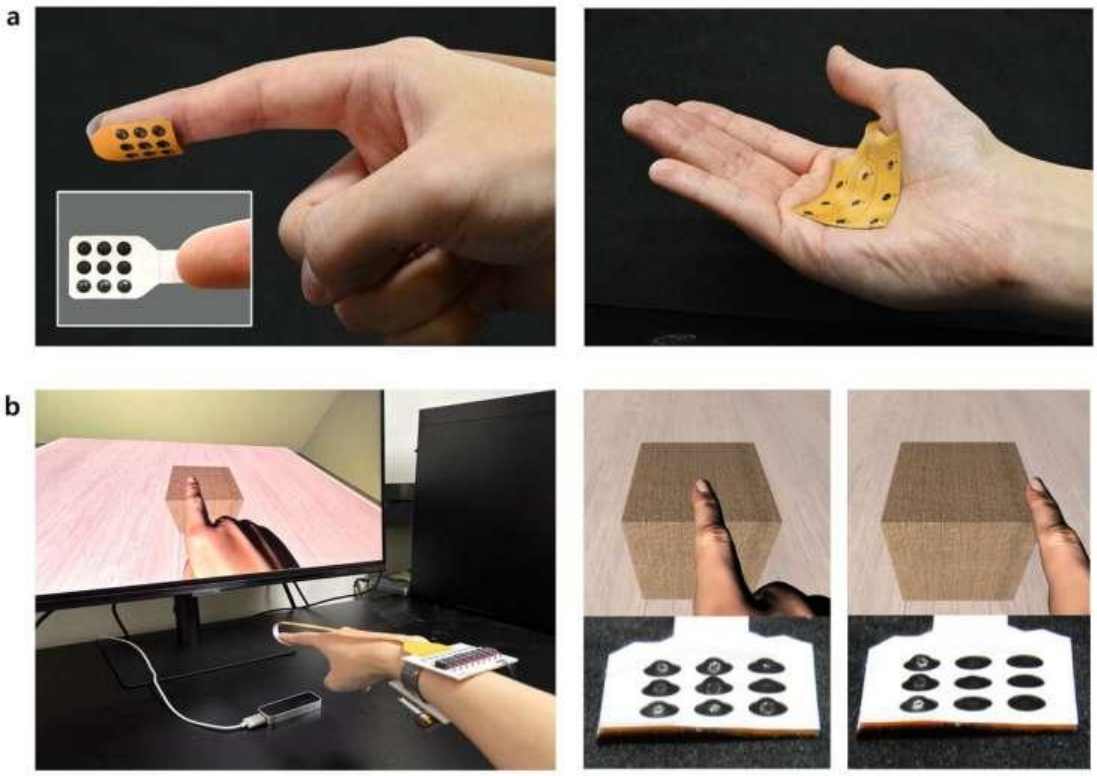
Our work is published in the journal *Science Advances*.


Actuation of our tiny tactile actuators. Credit: Hee-kyung Kwon

# Tiny, powerful tactile actuators

To provide dense and varied tactile sensations, actuators must be both compact and capable of generating a wide range of feedback. Addressing this, we created a novel tactile actuator based on a dielectric elastomer actuator (DEA). DEAs produce significant area expansion when voltage is applied, thanks to the phenomenon known as Maxwell stress. By combining a DEA with a small compressive spring, we successfully converted this area expansion into a linear displacement.

The result is a remarkably small actuator measuring just 6 mm in diameter and 1.1 mm in thickness. Despite its thin, compact design, the actuator can produce tactile sensations ranging from pressure to high-frequency vibrations, all while consuming less than 60 mW of power. Impressively, the actuator is powerful enough to lift a 25 g weight, despite its very light weight of 32 mg.




(a)

Thin flexible haptic patch for fingertip and palm of the hand. (b) VR scenario with synchronized contact geometry of virtual box. Credit: Hee-kyung Kwon

## A flexible, skin-conformal haptic patch

Building upon this actuator, we developed a flexible haptic patch incorporating a dense array of nine actuators within a small fingerpad-sized area. Fabricated on a thin, flexible printed circuit board (PCB), the entire patch weighs only 0.3 g and can comfortably conform to the contours of the skin without hindering natural hand movements. Each actuator is individually controlled, enabling the patch to dynamically render textures, simulate the 3D surfaces of virtual objects, and deliver intricate patterns of tactile feedback.

To complete the system, we integrated a reflective photomicrosensor array, allowing the patch not only to deliver haptic feedback but also to sense touch. This bidirectional capability opens the door for wireless tactile communication in VR environments or between users, where touch sensations can be encoded, transmitted, and recreated in real time.

## Looking ahead

Our work introduces a thin, flexible, and lightweight wearable haptic patch, made possible by this next-generation tactile actuator technology. Beyond VR and AR applications, we believe these actuators hold potential for broader use, including in miniaturized robotics, advanced prosthetics, and medical devices.

By bridging the gap between the digital and physical worlds, this technology marks an exciting step toward making touch a natural part of our digital experiences.

*This story is part of Science X Dialog, where researchers can report findings from their published research articles. Visit this page for information about Science X Dialog and how to participate.*

**More information:** Jung-Hwan Youn et al, Skin-attached haptic patch for versatile and augmented tactile interaction, *Science Advances* (2025). DOI: 10.1126/sciadv.adt4839
**Journal information:** Science Advances

Jung-Hwan is an postdoctroral researcher at the University of Illinois Urbana-Champaign. Before joining, he worked as a post-doc at the Electronics Telecommunication Research Institute (ETRI). He finished his Ph.D. in Korea Advanced Institute of Science and Techonology (KAIST). His research interests include haptics, soft robotics and human-robot interaction.

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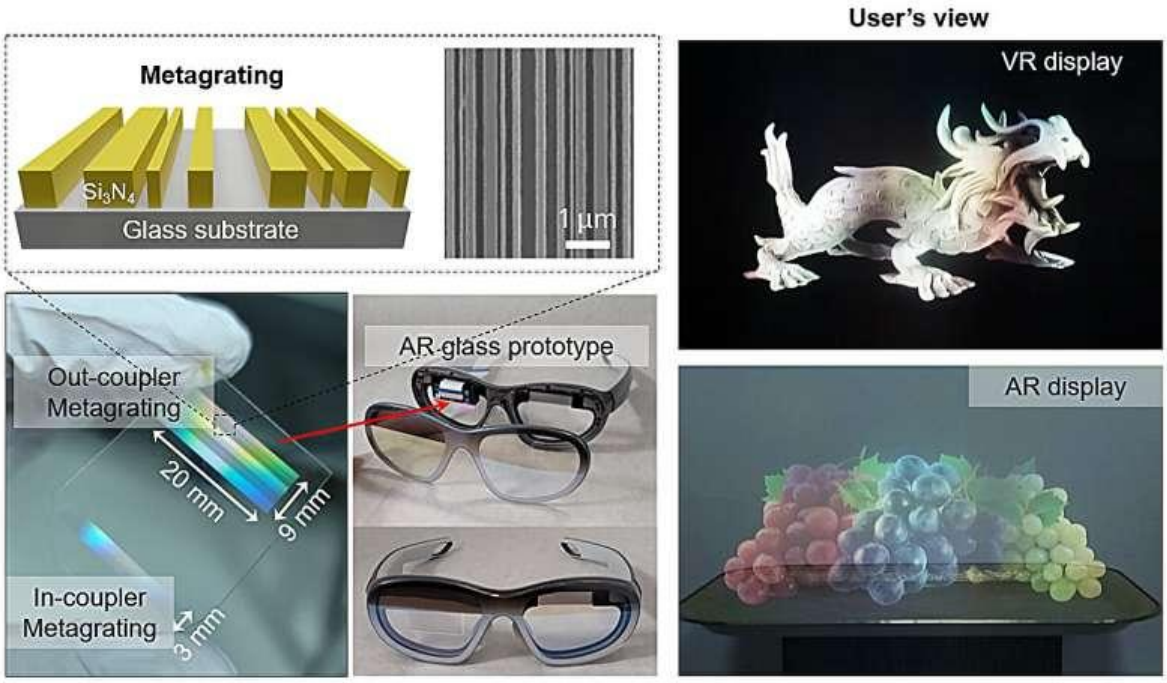
MAY 8, 2025

# One glass, full color: Sub-millimeter waveguide shrinks augmented-reality glasses

by Pohang University of Science and Technology




AR Glass Prototype and Experimental Results Based on Metagrating. Credit: POSTECH

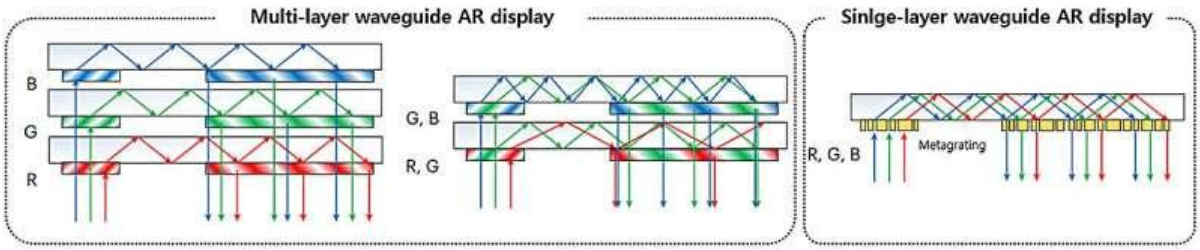
Augmented-reality (AR) technology is rapidly finding its way into everyday life, from education and health care to gaming and entertainment. However, the core AR device remains bulky and heavy, making prolonged wear uncomfortable. A breakthrough from POSTECH now promises to change that.

The study is published in the journal *Nature Nanotechnology*.

One of the main hurdles to the commercialization of AR glasses has been the waveguide. In AR optics, the lens itself also serves as a "highway of light," guiding virtual images directly to the user's eye. Due to chromatic dispersion, conventional designs have required separate waveguide layers for red, green, and blue light—three to six stacked glass sheets—inevitably increasing both weight and thickness.

Professor Junsuk Rho and colleagues at POSTECH have eliminated the need for multiple layers by developing an achromatic metagrating that handles all colors in a single glass layer. The key is an array of nanoscale silicon-nitride ($Si_3N_4$) pillars whose geometry was

finely tuned by a stochastic topology-optimization algorithm to steer light with maximum efficiency.



Architecture of AR waveguide display. Credit: POSTECH

In experiments, the researchers produced vivid full-color images using a 500-μm-thick single-layer waveguide—about one-hundredth the diameter of a human hair. They also secured a comfortable 9-mm eyebox, ensuring images remain sharp even if the viewer's eye shifts slightly.

The new design erases color blur while outperforming multilayer optics in brightness and color uniformity. Once commercialized, this technology could make AR glasses as thin and light as ordinary eyewear, reducing wearer fatigue and trimming manufacturing costs thanks to a simpler process. The era of truly everyday AR is a step closer.

"This work marks a key milestone for next-generation AR displays," said Prof. Rho. "Coupled with scalable, large-area fabrication, it brings commercialization within reach."

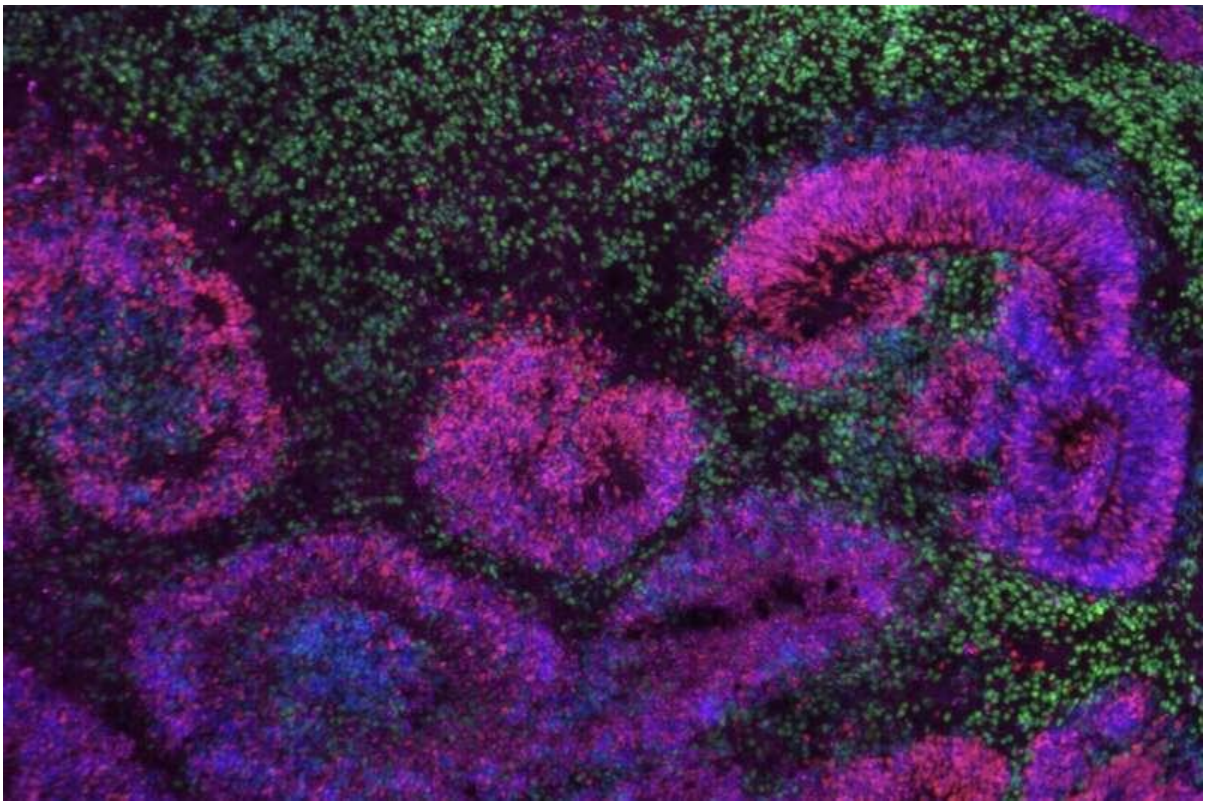
The study, authored by Junsuk Rho (corresponding author, POSTECH), Seokwoo Kim, Joohoon Kim, and Seokil Moon, was carried out by POSTECH's Departments of Mechanical, Chemical and Electrical Engineering and the Graduate School of Interdisciplinary Bioscience & Bioengineering, in collaboration with the Visual Team at Samsung Research.

**More information:** Seokil Moon et al, Single-layer waveguide displays using achromatic metagratings for full-colour augmented reality, *Nature Nanotechnology* (2025). DOI: 10.1038/s41565-025-01887-3
**Journal information:** Nature Nanotechnology
Provided by Pohang University of Science and Technology

MAY 10, 2025

# Study uncovers gene networks driving the development of distinct neuron subtypes in the human cerebral cortex

by Ingrid Fadelli , Medical Xpress



Microscopy image of a cortical organoid, a stem cell-derived model that mimics the developing human brain. The circular rosettes are clusters of neural stem cells giving rise to neurons, shown in green. Credit: Nano et al.

The human brain is known to contain a wide range of cell types, which have different roles and functions. The processes via which cells in the brain, particularly its outermost layer (i.e., the cerebral cortex), gradually become specialized and take on specific roles have been the focus of many past neuroscience studies.

Researchers at the University of California Los Angeles (UCLA) analyzed different datasets collected using single-cell transcriptomics, a technique to study gene expression in individual cells, to map the emergence of different cell types during the brain's development.

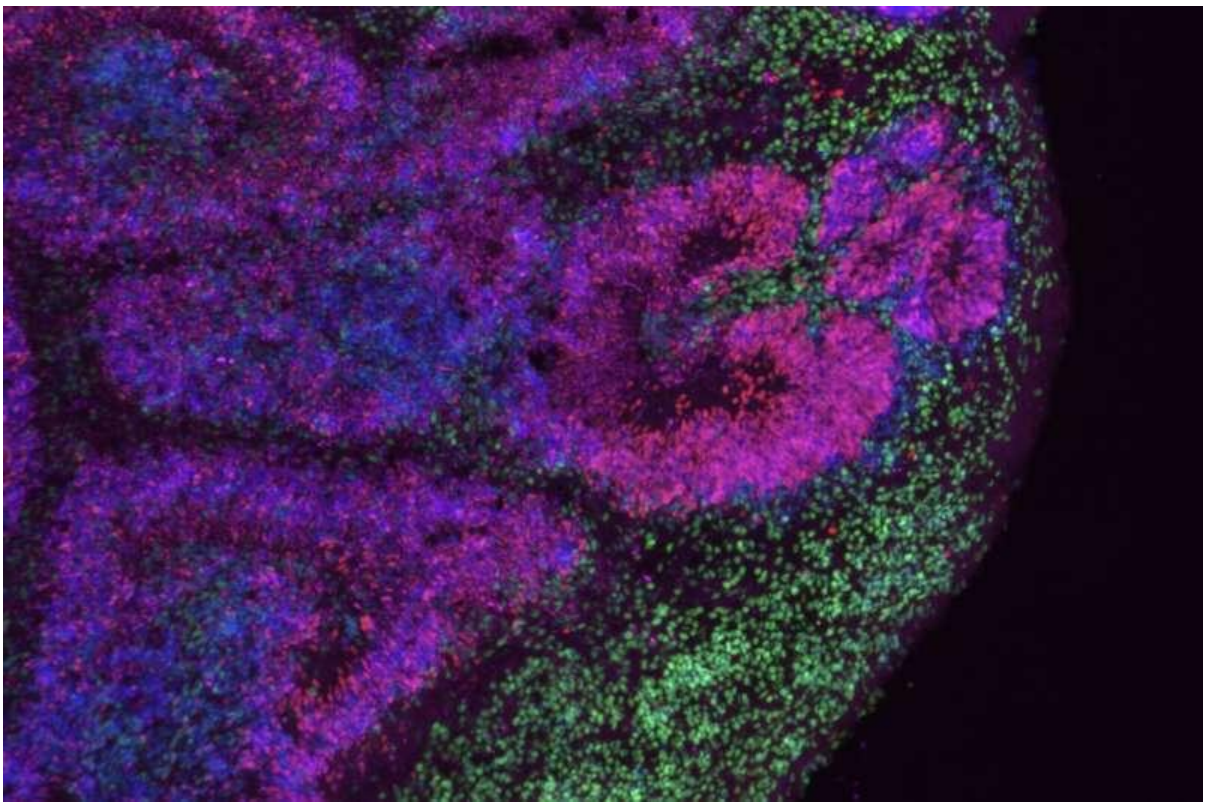
Their findings, published in *Nature Neuroscience*, unveil gene "programs" that drive the specialization of cells in the human cerebral cortex.

"This project initially began as a small bioinformatic side project," Aparna Bhaduri, senior author of the paper, told Medical Xpress.

"We were integrating publicly available datasets to explore gene expression patterns during brain development, but as we progressed, we realized that these gene networks—or modules—provided valuable insights into how distinct cell types emerge in the developing human cortex. Recognizing the potential impact of these findings, we expanded the work into a comprehensive study."

The primary objective of the study by Bhaduri and her colleagues was to uncover co-expression gene networks that contribute to the specification of cell types in the cerebral cortex. Uncovering these genetic modules could in turn shed new light on the overall processes underpinning the healthy and atypical development of the human brain.

"Over the past few years, many different research groups have made molecular profiles of the developing human brain," Patricia R. Nano, first author of the paper, told Medical Xpress. "Given the complexity of the brain, however, each of these profiles understandably cover only certain timepoints of brain development."



Credit: Nano et al.

The team's study began as a small side project aimed at better understanding large datasets collected over the past decades and integrating them into a "meta-atlas" of gene

expression at the single-cell level. After they had created this meta-atlas, however, Bhaduri, Nano and their colleagues realized that they could use it to identify gene modules driving cell specialization.

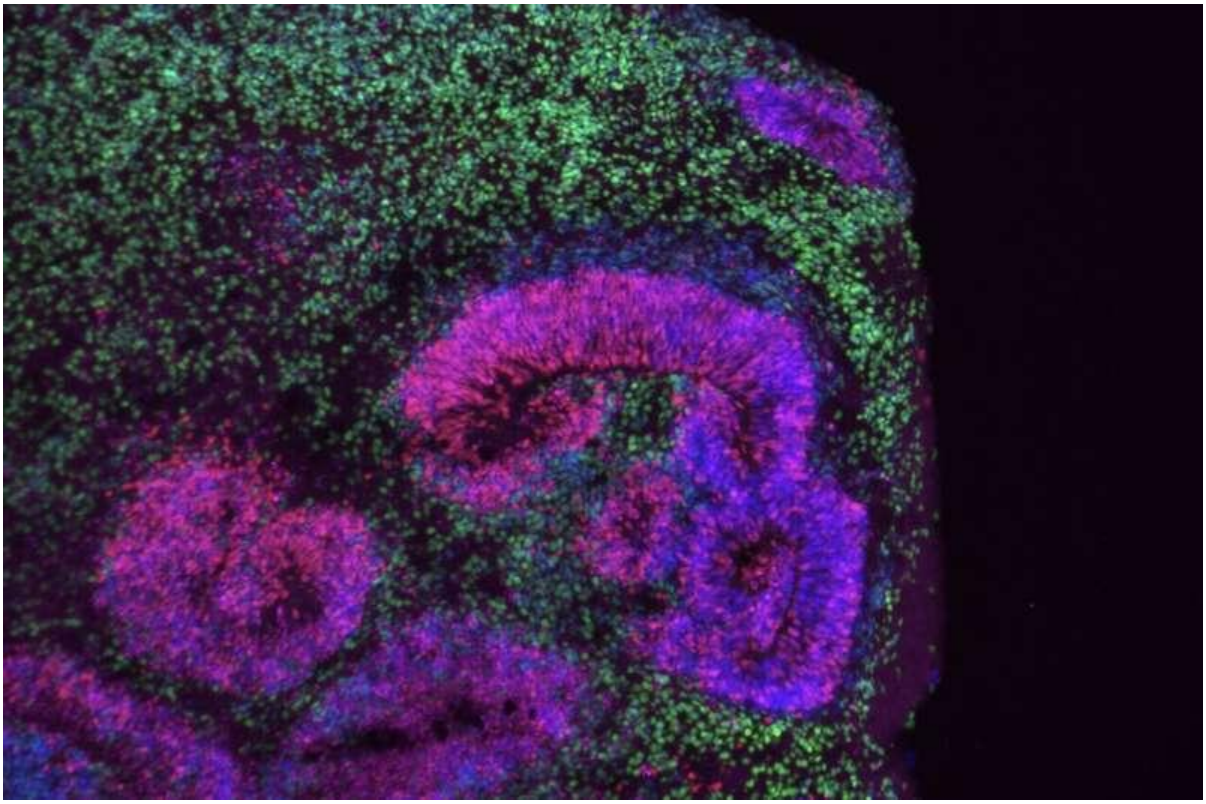
"Once we saw that these modules could represent how different cell types are formed and refined, we knew we had something that could really help others examining the developing human brain," said Nano. "Our work then expanded into a paper set out to not only identify the modules that shape the human brain, but to also test the functions of these modules in models of human brain development."

As a first step in their study, the researchers combined and collectively analyzed data collected in previous research that employed single-cell RNA sequencing techniques. These data essentially describe the gene activity in individual cells during the brain's development.

"By clustering genes that showed similar expression patterns across these diverse datasets, we identified 'gene co-expression networks' or modules, representing groups of genes working together during specific developmental stages," explained Bhaduri.

"To validate our findings, we tested whether these modules were active in actual human brain tissues, confirming their expression patterns using microscopy and staining methods."

After they confirmed that identified gene modules were active in actual human brain tissues, the researchers conducted further experiments using brain organoid models, which are three-dimensional (3D) and miniaturized models of the developing human brain created using stem cells. Using these models, they experimentally verified that these modules contributed to the formation of specific neuron types.



Credit: Nano et al.

"Our study identified and validated specific gene networks that drive the development of distinct neuron subtypes in the human cerebral cortex," said Bhaduri. "For instance, we characterized modules essential for creating deep-layer neurons, revealing previously unknown roles for genes associated with neurodevelopmental disorders."

The study gathered new valuable insight into the genetic processes underpinning the emergence of the human cerebral cortex's complexity during the early stages of development.

In the future, the meta-atlas created by the researchers could also help to better understand the precise genetic and molecular mechanisms behind the development of various developmental disorders, including autism and intellectual disabilities.

"What people have told us to be particularly helpful is the fact that, from datasets made by different labs at different times, we were able to identify gene modules that describe how cell fates arise—providing ways to take maps of the human brain and extract the mechanisms by which it forms," said Nano.

"Similarly to the example Aparna mentioned, our modules can reveal new ways by which disease-risk genes can control specific cell types in the brain."

Bhaduri, Nano and her colleagues hope that the meta-atlas they created will be a valuable resource for other research groups worldwide. For instance, it could help neuroscientists to pin-point gene networks that are disrupted in individuals diagnosed with specific

developmental and neurological disorders, which could in turn be targeted by new therapeutic interventions.

"We are very excited to continue to understand how the human brain comes to be and how these gene programs are important in healthy development and neurological disorders," added Bhaduri.

"For example, we have used a similar meta-atlas approach in glioblastoma, a deadly brain cancer, and are integrating our meta-atlas of human brain development with other measures of stem cell function and decision making.

"We are also interested in further exploring additional neurodevelopmental disorders and comparing modules from this developmental atlas to those developmental trajectories."

**More information:** Patricia R. Nano et al, Integrated analysis of molecular atlases unveils modules driving developmental cell subtype specification in the human cortex, *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01933-2.
**Journal information:** Nature Neuroscience

MAY 12, 2025

# The how and why of the brain's division across hemispheres

by Massachusetts Institute of Technology

Credit: Pixabay/CC0 Public Domain

People have a lot of misconceptions about what the brain's left and right hemispheres do, but one well-known aspect of this division may be even more true than people realize: The brain not only splits up visual spatial perception—processing what's on our left in the right hemisphere and what's on our right in the left hemisphere—it takes cognitive advantage of that.

A new review by MIT neuroscientists explains what the field has learned about this division of labor, the trade-off it involves and how the brain ultimately bridges the divide.

"People hear all these myths about the left brain being more analytical and the right brain being more artistic, or people being right-brained vs. left-brained; 99% of that is nonsense," said paper co-author Earl K. Miller, Picower Professor in The Picower Institute for Learning

and Memory and the Department of Brain and Cognitive Sciences at MIT. "You think with your whole brain."

But when it comes to visual spatial perception, the brain has evolved separate neural resources for the right vs. left sides of gaze even in later stages of cognitive processing, Miller said. Why? To optimize its capacity.

"It's for good reason," said Miller, who co-authored the review in the journal *Neuropsychologia* with Picower Institute research scientist Scott Brincat.

"Perceptual capacity is limited—you can only take in so much at once. If your capacity is fully tied up on the right side of your gaze, you might miss a threat approaching on the left. Splitting resources between both sides helps avoid dangerous perceptual blind spots."

## Separated sight

When Miller was in graduate school, he said, he was taught that the brain neatly divided its visual perception of space between hemispheres until the information reached the prefrontal cortex where it became seamlessly blended. But experiments by Miller and Brincat, as well as many other researchers, have been accumulating evidence to refine that view over the last 20 years.

These studies have shown that even in the prefrontal cortex, neural encoding of information about where an object is, is still biased toward the "contralateral" hemisphere, or the hemisphere opposite of where the object appears in the field of view.

"As a result, the two hemispheres appear to function surprisingly independently, even for high-level cognitive functions like attention and working memory," the authors wrote.

The evidence is apparent in measurements of the brain waves produced by coordinated networks of neurons in each hemisphere. Gamma frequency wave power increases in frontal brain hemispheres when they consider the visual stimuli that appear on the contralateral side.

Meanwhile, studies for decades (including one in 1971) have shown that people and animals can remember more things if their presentation is split between hemispheres rather than presented all on one side. Neuroscientists call this the "bilateral advantage," though it is not perfect. People don't track multiple things, even if split across both sides, as well as they track just one thing on either side.

People also exhibit individualized differences in perceptual capacity across the visual field. Miller has founded the startup company SplitSage to measure these differences with the goal of helping people with visually oriented complex tasks to improve their performance.

Notably, the studies that Brincat and Miller review in the new paper show that the split bias between hemispheres applies only to spatial information—the where something is. Other features like color or shape are processed by both hemispheres.

## Seamless sight

If the brain maintains a separation in its processing of spatial visual perception, even at the stage of allocating attention and juggling objects in working memory, why aren't we confused or surprised when a bird flying from our left passes into the right side of our field of view? We also easily handle cases where our shifting gaze moves an object from one eye's field of view to the other's.

"We experience a seamless world," Miller said.

It turns out that the brain accomplishes the "handoff" from one hemisphere to the other much like two cellular towers do for your phone as you drive around, according to neural activity measurements in studies such as one in 2014 and one that Brincat and Miller led in 2021.

"As a tracked target approaches the visual midline, the hemisphere about to receive the target shows a ramp-up of activity well before the crossing time, as if it is anticipating the target," the authors wrote.

"Further, activity in the sending hemisphere remains high well after the crossing. Thus, for up to a second or more, neural signals reflecting the target are shared across both hemispheres. It is as if both hemispheres are holding the baton."

As with the "bilateral advantage," there is a small performance cost when this transfer happens, studies show.

Deficits in interhemispheric connectivity or synchrony are apparent in neurological and psychiatric diseases including Alzheimer's, anxiety, depression, schizophrenia, obsessive-compulsive disorder and autism spectrum disorders, the authors note. Brincat and Miller's review emphasizes that such disruptions could affect cognition.

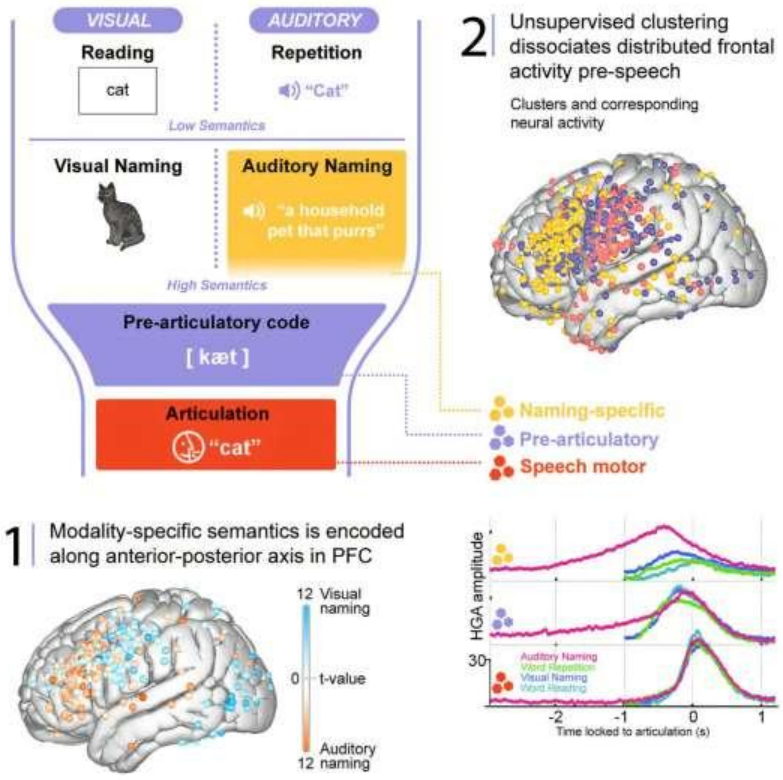
"A foundational understanding of interhemispheric processing, combined with interventions translatable to human patients, offers hope for developing novel network-level treatments," they wrote.

**More information:** Scott L. Brincat et al, Cognitive independence and interactions between cerebral hemispheres, *Neuropsychologia* (2025). DOI: 10.1016/j.neuropsychologia.2025.109153
**Journal information:** Neuropsychologia
Provided by Massachusetts Institute of Technology

MAY 13, 2025

# Mapping the brain's naming network: New insights into how people retrieve words during speech

by NYU Tandon School of Engineering




Credit: *Cell Reports* (2025). DOI: 10.1016/j.celrep.2025.115677

How are we able to recall a word we want to say? This basic ability, called word retrieval, is often compromised in patients with brain damage. Interestingly, many patients who can name words they see, like identifying a pet in the room as a "cat," struggle with retrieving words in everyday discourse.

Scientists have long sought to understand how the brain retrieves words during speech. A new study by researchers at New York University sheds light on this mystery, revealing a left-lateralized network in the dorsolateral prefrontal cortex that plays a crucial role in naming.

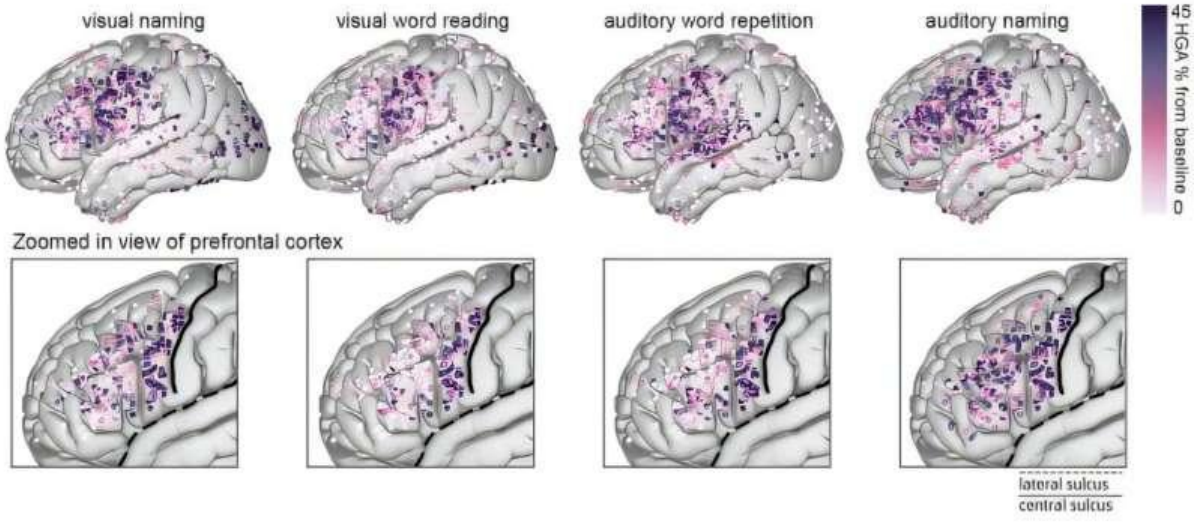
The findings, published in *Cell Reports*, provide new insights into the neural architecture of language, offering potential applications for both neuroscience and clinical interventions.

Word retrieval is a fundamental aspect of human communication, allowing us to link concepts to language. Despite decades of research, the exact neural dynamics underlying this process—particularly in natural auditory contexts—remain poorly understood.

NYU researchers—led by Biomedical Engineering Graduate Student Leyao Yu and Associate Professor of Biomedical Engineering at NYU Tandon and Neurology at NYU Grossman School of Medicine Adeen Flinker—recorded electrocorticographic (ECoG) data from 48 neurosurgical patients to examine the spatial and temporal organization of language processing in the brain.

By using unsupervised clustering techniques, the researchers identified two distinct but overlapping networks responsible for word retrieval. The first, a semantic processing network, was located in the middle and inferior frontal gyri. This network was engaged in integrating meaning and was sensitive to how surprising a word was within a given sentence.

The second, an articulatory planning network, was situated in the inferior frontal and precentral gyri, which played a crucial role in speech production, regardless of whether words were presented visually or auditorily.




Neural dynamics of prefrontal cortex, showing peak activity in the inferior frontal gyrus and middle frontal gyrus prior to speaking, including the strongest activation during auditory naming tasks. Credit: NYU Tandon School of Engineering

## Auditory naming and the prefrontal cortex

The study builds upon decades of work in language neuroscience. Previous research suggested that different regions of the brain were responsible for retrieving words depending on whether they were seen or heard. However, earlier studies relied on methods with limited temporal resolution, leaving many unanswered questions about how these networks interact in real time.

By leveraging the high spatial and temporal resolution of ECoG, the researchers uncovered a striking ventral-dorsal gradient in the prefrontal cortex. They found that while articulatory planning was localized ventrally, semantic processing was uniquely represented in a dorsal region of the inferior frontal gyrus and middle frontal gyrus—a previously underappreciated hub for language processing.

"These findings suggest that a missing piece in our understanding of language processing lies in this dorsal prefrontal region," explains lead author Leyao Yu. "Our study provides the first direct evidence that this area is involved in mapping sounds to meaning in an auditory context."

## Implications for neuroscience and medicine

The study has far-reaching implications, not only for theoretical neuroscience but also for clinical applications. Language deficits, such as anomia—the inability to retrieve words—are common in stroke, brain injury, and neurodegenerative disorders. Understanding the precise neural networks involved in word retrieval could lead to better diagnostics and targeted rehabilitation therapies for patients suffering from these conditions.

Additionally, the study provides a roadmap for future research in brain-computer interfaces (BCIs) and neuroprosthetics. By decoding the neural signals associated with naming, scientists could potentially develop assistive devices for individuals with speech impairments, allowing them to communicate more effectively through direct brain-computer communication.

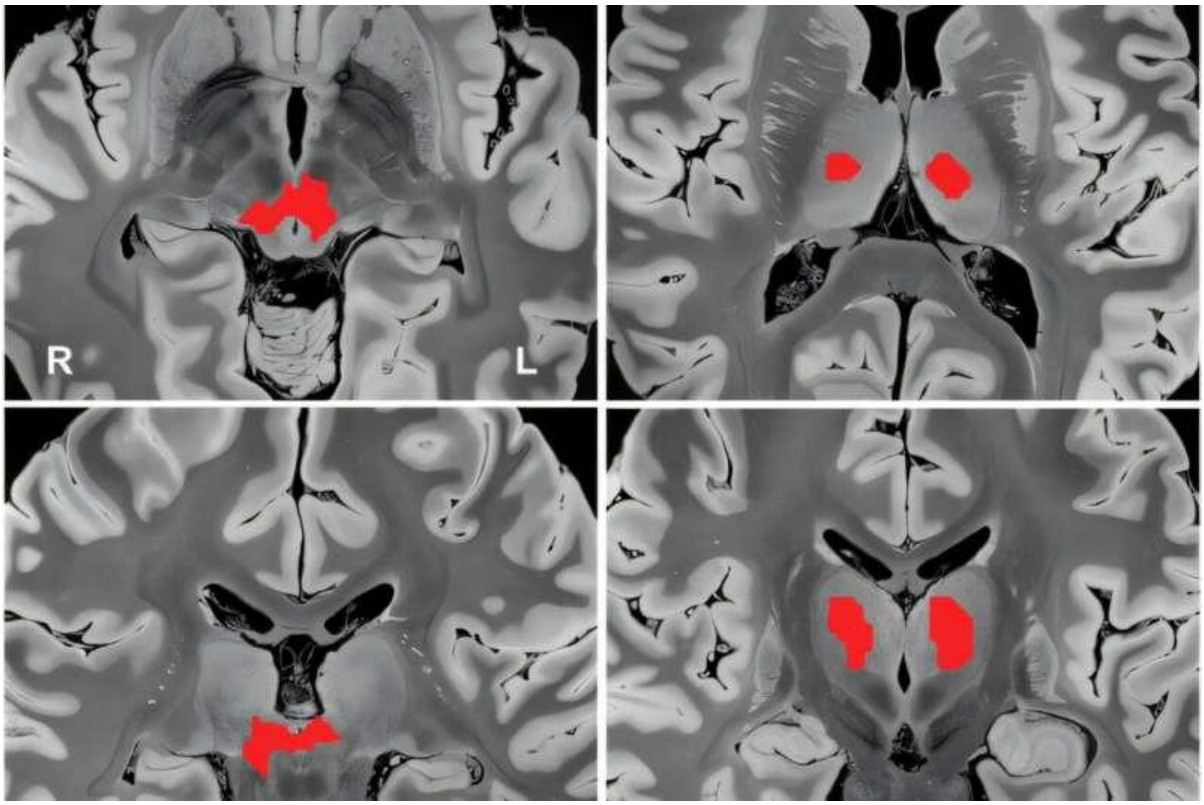
For now, one thing is clear: our ability to name the world around us is not just a simple act of recall, but the result of a sophisticated and finely tuned neural system—one that is now being revealed in greater detail than ever before.

**More information:** Leyao Yu et al, A left-lateralized dorsolateral prefrontal network for naming, *Cell Reports* (2025). DOI: 10.1016/j.celrep.2025.115677
**Journal information:** Cell Reports
Provided by NYU Tandon School of Engineering

MAY 15, 2025

# Deep brain regions link all senses to consciousness, study finds

by Karen Guzman, Yale University




Midbrain and central thalamus show shared subcortical early activations (increases), observed in 11 tasks across four sensory modalities, including, vision, audition, taste, and touch. Credit: *NeuroImage* (2025). DOI: 10.1016/j.neuroimage.2025.121224

A Yale-led study shows that the senses stimulate a region of the brain that controls consciousness—a finding that might inform treatment for disorders related to attention, arousal, and more.

Humans perceive and navigate the world around us with the help of our five senses: sight, hearing, touch, taste and smell. And while scientists have long known that these different senses activate different parts of the brain, a new Yale-led study indicates that multiple senses all stimulate a critical region deep in the brain that controls consciousness.

The study, published in the journal *NeuroImage*, sheds new light on how sensory perception works in the brain and may fuel the development of therapies to treat disorders involving attention, arousal, and consciousness.

In the study, a research team led by Yale's Aya Khalaf focused on the workings of subcortical arousal systems, brain structure networks that play a crucial role in regulating sleep-wake states. Previous studies on patients with disorders of consciousness—such as coma or epilepsy—have confirmed the influence of these systems on states of consciousness.

But prior research has been largely limited to tracking individual senses. For the new study, researchers asked if stimuli from multiple senses share the same subcortical arousal networks. They also looked at how shifts in a subject's attention might affect these networks.

For the study, researchers analyzed fMRI (functional magnetic resonance imaging) datasets collected from 1,561 healthy adult participants as they performed 11 different tasks using four senses: vision, audition, taste, and touch.

They made two important discoveries: that sensory input does make use of shared subcortical systems and, more surprisingly, that all input—regardless of which sense delivered the signal—stimulates activity in two deep brain regions, the midbrain reticular formation and the central thalamus, when a subject is sharply focused on the senses.

The key to stimulating the critical central brain regions, they found, were the sudden shifts in attention demanded by the tasks.

"We were expecting to find activity on shared networks, but when we saw all the senses light up the same central brain regions while a test subject was focusing, it was really astonishing," said Khalaf, a postdoctoral associate in neurology at Yale School of Medicine and lead author of the study.

The discovery highlighted how key these central brain regions are in regulating not only disorders of consciousness, but also conditions that impact attention and focus, such as attention deficit hyperactivity disorder. This finding could lead to better targeted medications and brain stimulation techniques for patients.

"This has also given us insights into how things work normally in the brain," said senior author Hal Blumenfeld, the Mark Loughridge and Michele Williams Professor of Neurology who is also a professor in neuroscience and neurosurgery and director of the Yale Clinical Neuroscience Imaging Center. "It's really a step forward in our understanding of awareness and consciousness."

Looking across senses, this is the first time researchers have seen a result like this, said Khalaf, who is also part of Blumenfeld's lab.

"It tells us how important this brain region is and what it could mean in efforts to restore consciousness," she said.

**More information:** Aya Khalaf et al, Shared subcortical arousal systems across sensory modalities during transient modulation of attention, *NeuroImage* (2025). DOI: 10.1016/j.neuroimage.2025.121224
**Journal information:** NeuroImage
Provided by Yale University

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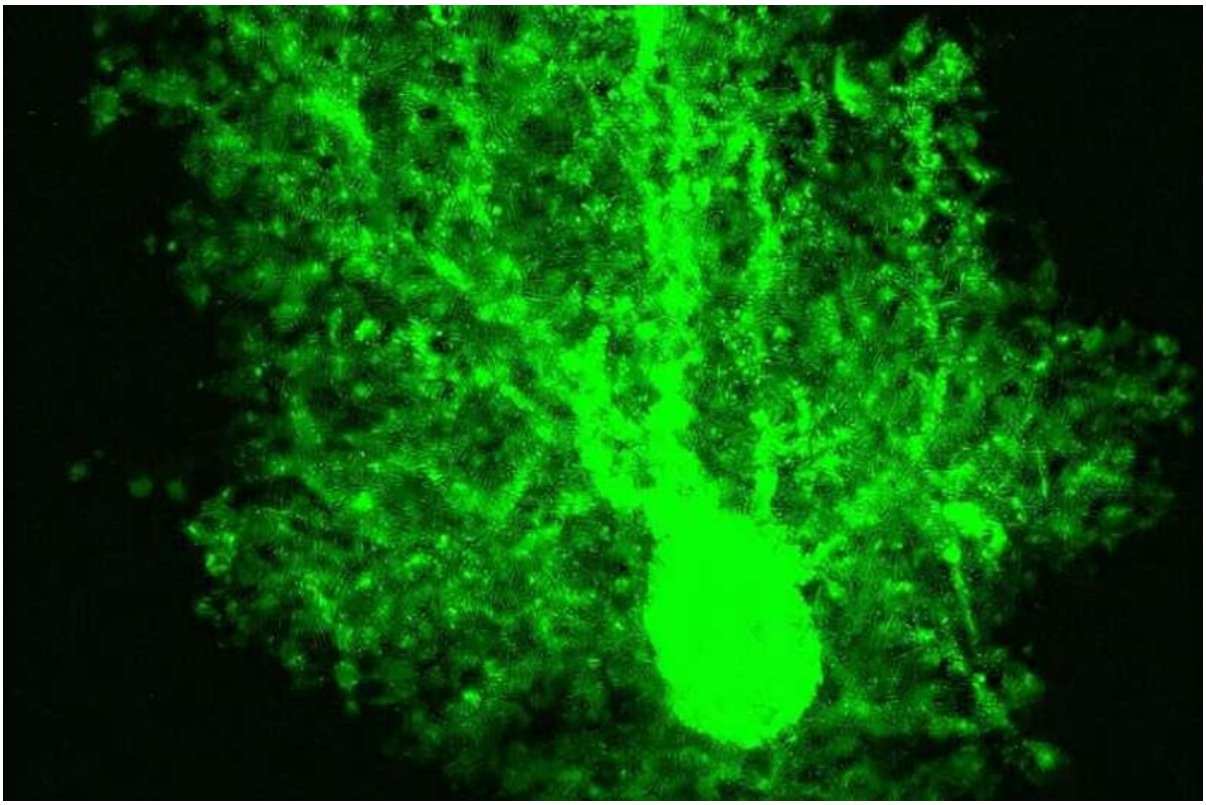
MAY 15, 2025

# An overlooked cell type orchestrates brain rewiring during states of heightened attention by Washington University in St. Louis



Researchers at WashU Medicine have shown in mice that brain cells known as astrocytes are required for a signaling chemical called norepinephrine to modify brain activity, changing the textbook understanding that norepinephrine acts directly on neurons. Above, a mouse astrocyte labeled with a fluorescent green marker. Credit: Yifan Wu

Researchers at Washington University School of Medicine in St. Louis have upended the decades-old dogma of how connections between brain cells are rearranged during states of

heightened vigilance or attention. The team found that a brain chemical associated with alertness, attention and learning alters brain connectivity and function not by acting directly on neurons, the cells known for their quick transmission of information, but through the work of astrocytes, another, slower-acting type of brain cell that is often overlooked in the field of neuroscience.

The discovery, published in *Science*, fundamentally changes current understanding about the determinants of brain network communication and activity. It also calls for greater focus on astrocytes as therapeutic targets in the treatment of attention, memory and emotional disorders.

"Textbooks tell us that neuromodulators like norepinephrine fine-tune neurons directly—in fact, textbooks tell us that everything in the brain is about neurons," said Thomas Papouin, Ph.D., assistant professor of neuroscience at WashU Medicine and the senior author of the study. "It seems that a lot of brain wiring and activity is probably orchestrated by astrocytes, on slower timescales. This is the type of discovery that profoundly reshapes our understanding of how the brain works."

## From the brain's wallflower to center stage

For the brain to dedicate itself to tasks that need attention, or to respond to unexpected stimuli like a fire alarm, it needs to be able to rewire itself by changing how brain cells communicate. This process is driven by the release of chemicals known as neuromodulators, including norepinephrine, in the brain. How these neuromodulators reorganize communication in the brain is poorly understood. The assumption for the past 80 years has been that neuromodulator chemicals act on neurons.

Meanwhile, for at least 30 years, astrocytes have been shown to contact and interact with synapses, which are the specialized structures where neurons communicate with one another. Researchers have long suspected that astrocytes have the potential to rearrange communication between neurons, and therefore, the flow of information in the brain.

Because of their very fine and sprawling shape, these cells are ideally positioned to monitor and detect neuromodulators like norepinephrine. "We wanted to test the idea that perhaps neuromodulation of synapses by norepinephrine is an astrocyte business," Papouin said.

To do so, Papouin and his team stimulated norepinephrine secretion from mouse brain cells or exposed mouse brain slices to norepinephrine and found that norepinephrine weakened connections between neurons, as has been known for decades. However, researchers found that norepinephrine also triggered activity among surrounding astrocytes. Once triggered by norepinephrine, astrocytes produced a second chemical that they released onto synapses, which caused the dampening of synapse activity.

Even when neurons' ability to directly sense norepinephrine was removed, norepinephrine was still able to rearrange neuronal connections. When astrocytes' ability to sense or

respond to norepinephrine was taken offline, on the other hand, norepinephrine was unable to reorganize neuronal connectivity.

Their findings indicate that neuromodulators such as norepinephrine rearrange neuronal connections in the brain by signaling through astrocytes rather than directly onto neurons.

The results also suggest that targeting astrocytes could be an effective way to reshape brain activity to potentially treat brain disorders. Papouin's team has started looking at existing drugs that are believed to act on neurons, to see if they require astrocytes to be effective. If so, perhaps astrocytes could be targeted directly for therapeutic purposes.

"There are so many drugs out there that interfere with norepinephrine signaling in the brain, in particular in the treatment of ADHD or depression. I wonder how many of them require astrocytes to modify brain activity," said Papouin.

**More information:** Katheryn B. Lefton et al, Norepinephrine signals through astrocytes to modulate synapses, *Science* (2025). DOI: 10.1126/science.adq5480. www.science.org/doi/10.1126/science.adq5480
**Journal information:** Science
Provided by Washington University in St. Louis

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MAY 13, 2025

# Long working hours may alter brain structure, preliminary findings suggest

by British Medical Journal

Long working hours may alter the structure of the brain, particularly the areas associated with emotional regulation and executive function, such as working memory and problem solving, suggest the findings of preliminary research, published online in *Occupational & Environmental Medicine*.

Ultimately, overwork may induce neuroadaptive changes that might affect cognitive and emotional health, say the researchers.

Long working hours have been linked to heightened risks of cardiovascular disease, metabolic disorders, and mental health issues. And the International Labor Organization (ILO) estimates that overwork kills more than 800,000 people every year, note the researchers.

While the behavioral and psychological consequences of overwork are reasonably well understood, the underlying neurological mechanisms and anatomical changes aren't, they add.

To explore this further, the researchers deployed structural brain volume analysis to compare the impact of overwork on specific brain regions in health care workers routinely clocking up long working hours, defined as 52 or more a week.

They drew on data from the Gachon Regional Occupational Cohort Study (GROCS) and from MRI scans carried out for a research project on the effects of working conditions on brain structure.

Participants in GROCS were asked to have an additional MRI scan, and the final analysis included 110 people after excluding those with missing data or poor MRI image quality. Most were clinicians: 32 worked excessive weekly hours (28%); 78 worked standard hours.

Those putting in long working hours every week were significantly younger, had spent less time in work and were more highly educated than those clocking up standard hours.

Differences in brain volume were assessed using voxel-based morphometry (VBM)—a neuroimaging technique that identifies and compares regional differences in levels of gray matter—and atlas-based analysis, which uses pre-defined references to identify and label structures in images like brain scans.

Comparative analysis of the findings showed that people who worked 52 or more hours a week displayed significant changes in brain regions associated with executive function and emotional regulation, unlike participants who worked standard hours every week.

For example, atlas-based analysis revealed a 19% increase in the volume of the middle frontal gyrus among those clocking up long working hours compared with those working standard hours.

This part of the brain has a major role in various cognitive functions, particularly in the frontal lobe. It's involved in attention, working memory, and language-related processing.

VBM showed peak increases in 17 regions, including the middle frontal gyrus, the superior frontal gyrus, which is involved in attention, planning, and decision-making, and the insula.

The insula has a key role in integrating sensory, motor, and autonomic feedback from the body. It's involved in emotional processing, self-awareness, and understanding social context.

This is a small observational snapshot study, and as such, no firm conclusions can be drawn about cause and effect. And the researchers acknowledge that in the absence of

long-term data, it's unclear whether these structural changes are a consequence of overwork or a predisposing factor.

But they nevertheless point out, "While the results should be interpreted cautiously due to the exploratory nature of this pilot study, they represent a meaningful first step in understanding the relationship between overwork and brain health."

They add, "Notably, the increased brain volumes observed in overworked individuals may reflect neuroadaptive responses to chronic occupational stress, although the exact mechanisms remain speculative."

They continue, "The observed changes in brain volume may provide a biological basis for the cognitive and emotional challenges often reported in overworked individuals. Future longitudinal and multi-modal neuroimaging studies are warranted to confirm these findings and elucidate the underlying mechanisms."

And they conclude, "The results underscore the importance of addressing overwork as an occupational health concern and highlight the need for workplace policies that mitigate excessive working hours."

**More information:** Overwork and changes in brain structure: a pilot study, *Occupational and Environmental Medicine* (2025). DOI: 10.1136/oemed-2025-110057
**Journal information:** Occupational and Environmental Medicine
Provided by British Medical Journal

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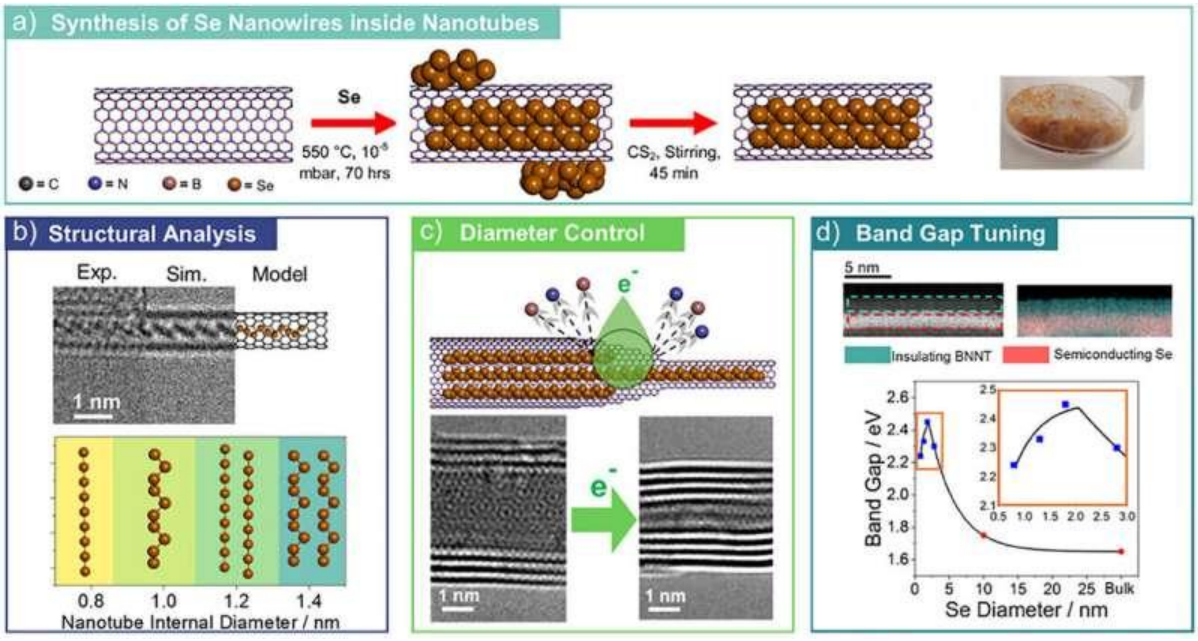
MAY 21, 2025

# Mind the band gap: Researchers create nanoscale forms of elementary semiconductor with tunable electronic properties

by University of Nottingham

edited by Sadie Harley, reviewed by Robert Egan




Sub-nanometer diameter control and bandgap analysis of individual selenium nanowires through electron microscopy. Credit: *Advanced Materials* (2025). DOI: 10.1002/adma.202501821

Researchers have demonstrated that by using a semiconductor with flexible bonds, the material can be molded into various structures using nano containers, without altering its composition. The discovery could lead to the design of a variety of customized electronic devices using only a single element.

Semiconductors are vital to our daily lives, as they are found in nearly every electronic device. One of the key characteristics of semiconductors is their band gap, which determines how they conduct electric current. The band gap is typically engineered for

specific applications by breaking chemical bonds or introducing additional elements into the material. However, these processes can be complex and energy-intensive.

Researchers from the University of Nottingham, the EPSRC SuperSTEM facility, Ulm University in Germany, and BNNT LLC in the U.S. imaged new forms of selenium using transmission electron microscopy, employing nanotubes as tiny test tubes. The study has been published in *Advanced Materials*.

Dr. Will Cull, research fellow in School of Chemistry, University of Nottingham, who carried out the experimental work, said, "Selenium is an old semiconductor with a rich history, having been used in the first solar cells. In our research, we have revitalized selenium by discovering new forms that can emerge when confined to the nanoscale."

Selenium can exist as nanowires, with its structure and bonding varying by diameter. Below a certain size, the bonding between selenium atoms changes, increasing bond angles. This causes straightening of the initially helical structure, ultimately constricting it into atomically thin wires.

Dr. Will Cull said, "We successfully imaged new forms of selenium using transmission electron microscopy, employing nanotubes as tiny test tubes. This approach allowed us to create a new phase diagram that connects the atomic structure of selenium to the diameter of the nanowires."

Electron microscopy movies of the selenium nanowire extrusion filmed in real time. Credit: University of Nottingham
The Nottingham group previously reported using nano test tubes to image chemical reactions of individual molecules and to observe phase transitions in semiconductors. This approach enables real-time filming of chemistry at the atomic level.

Dr. Will Cull said, "To our astonishment, we observed that the nano test tube became thinner as we imaged it! Before our very eyes, we witnessed the selenium nanowire inside the nanotube being squeezed like toothpaste, stretching and thinning.

"This serendipitous discovery allowed us to establish mechanisms for the transformation of one type of nanowire to another, which have implications for their electronic properties, with near-atomic precision."

The band gap is a crucial property of semiconductors that significantly impacts their use in various devices, including solar cells, transistors, and photocatalysts. Professor Quentin Ramasse, director of EPSRC SuperSTEM, said, "By utilizing atomically resolved scanning transmission electron microscopy coupled with electron energy loss spectroscopy, we were able to measure the band gaps of individual chains of selenium. These measurements enabled us to establish a relationship between the diameter of these nanowires and their corresponding band gaps."

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Professor Quentin Ramasse said, "Traditionally, carbon nanotubes have been used as nano test tubes; however, their outstanding energy absorption properties can obscure the electronic transitions of the material inside. In contrast, a newer type of nano test tube, boron nitride nanotubes, is transparent, allowing us to observe the band gap transitions in selenium nanowires contained within them."

The famous Moore's Law states that the number of transistors on an integrated circuit doubles approximately every two years. As a result, electronic components must become smaller.

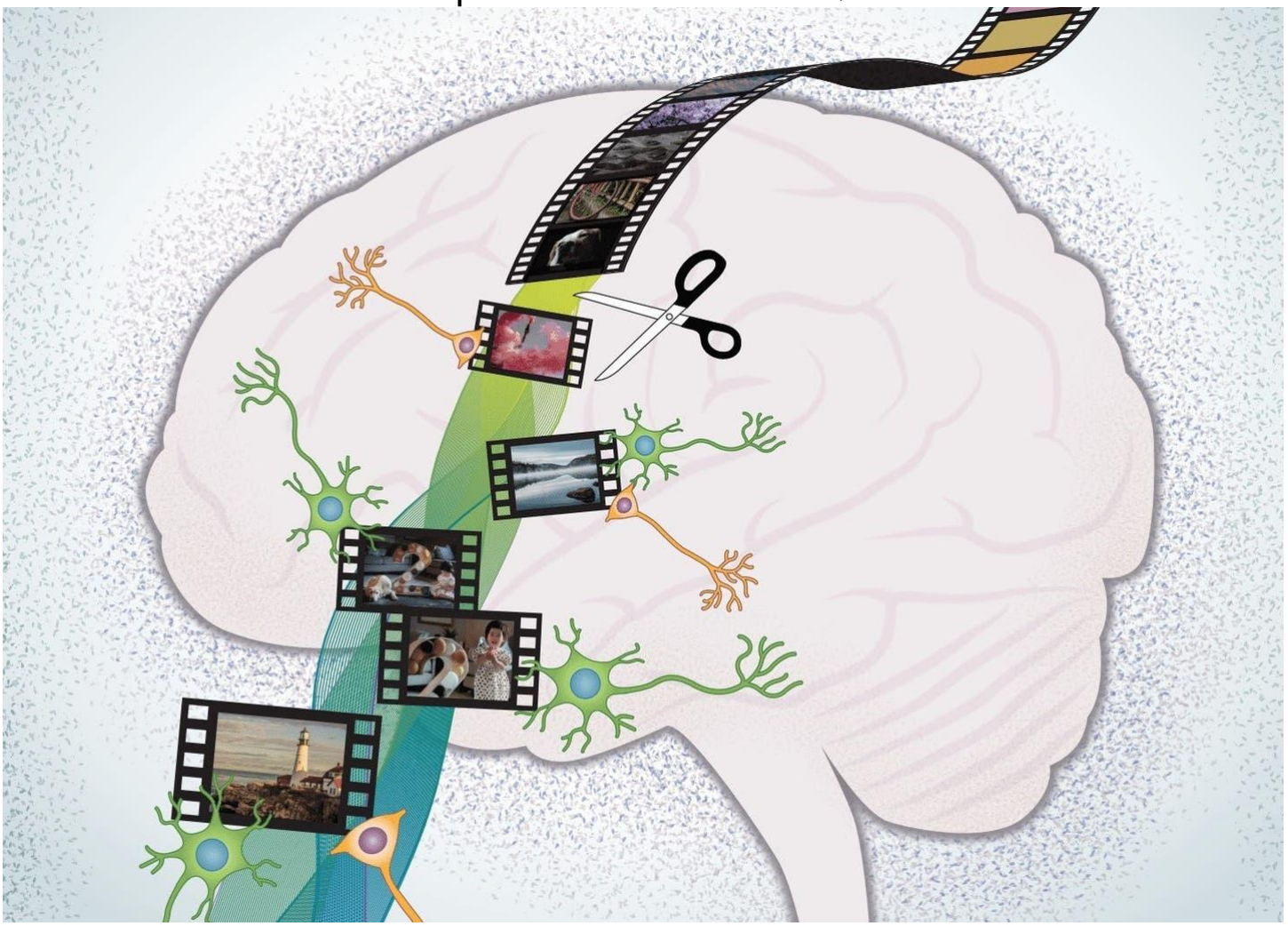
Professor Andrei Khlobystov, School of Chemistry, University of Nottingham, said, "We have investigated the ultimate limit for nanowire size while preserving useful electronic properties. This is possible for selenium because the phenomenon of quantum confinement can be effectively balanced by distortions in the atomic structure, thus allowing the band gap to remain within a useful range."

The researchers hope that these new materials will be incorporated into electronic devices in the future. Accurately tuning the band gap of selenium by changing the diameter of the nanowire could lead to the design of a variety of customized electronic devices using only a single element.

**More information:** William J. Cull et al, Flexible Selenium Nanowires with Tuneable Electronic Bandgaps, *Advanced Materials* (2025). DOI: 10.1002/adma.202501821
**Journal information:** Advanced Materials
Provided by University of Nottingham

# How does the brain make memories?

## In a Cedars-Sinai study, researchers have discovered two types of brain cells that play a key role in dividing continuous human experience. Published Mar 10, 2022 12:55



[Mar 10, 2022: Cara Martinez, Cedars-Sinai Medical Center]

Researchers have discovered two types of brain cells that play a key role in creating memories. (CREDIT: Sarah Pyle for Cedars-Sinai)

In a study led by Cedars-Sinai, researchers have discovered two types of brain cells that play a key role in dividing continuous human experience into distinct segments that can be recalled later. The discovery provides new promise as a path toward development of novel treatments for memory disorders such as dementia and Alzheimer's disease.

The study, part of a multi-institutional BRAIN Initiative consortium funded by the National Institutes of Health and led by Cedars-Sinai, was published in the peer-

reviewed journal Nature Neuroscience. As part of ongoing research into how memory works, Ueli Rutishauser, PhD, professor of Neurosurgery, Neurology, and Biomedical Sciences at Cedars-Sinai, and co-investigators looked at how brain cells react as memories are formed.

"One of the reasons we can't offer significant help for somebody who suffers from a memory disorder is that we don't know enough about how the memory system works," said Rutishauser, senior author of the study, adding that memory is foundational to us as human beings.

Human experience is continuous, but psychologists believe, based on observations of people's behavior, that memories are divided by the brain into distinct events, a concept known as event segmentation. Working with 19 patients with drug-resistant epilepsy, Rutishauser and his team were able to study how neurons perform during this process. Patients participating in the study had electrodes surgically inserted into their brains to help locate the focus of their epileptic seizures, allowing investigators to record the activity of individual neurons while the patients viewed film clips that included cognitive boundaries.

While these boundaries in daily life are nuanced, for research purposes, the investigators focused on "hard" and "soft" boundaries.

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"An example of a soft boundary would be a scene with two people walking down a hallway and talking, and in the next scene, a third person joins them, but it is still part of the same overall narrative," said Rutishauser, interim director of the Center for Neural Science and Medicine and the Board of Governors Chair in Neurosciences at Cedars-Sinai.

In the case of a hard boundary, the second scene might involve a completely different set of people riding in a car. "The difference between hard and soft boundaries is in the size of the deviation from the ongoing narrative," Rutishauser said. "Is it a totally different story, or like a new scene from the same story?"

When study participants watched film clips, investigators noted that certain neurons in the brain, which they labeled "boundary cells," increased their activity after both hard and soft boundaries. Another group of neurons, labeled "event cells," increased their activity only in response to hard boundaries, but not soft boundaries.

Rutishauser and his co-investigators theorize that peaks in the activity of boundary and event cells—which are highest after hard boundaries, when both types of cells fire—send the brain into the proper state for initiating a new memory.

"A boundary response is kind of like creating a new folder on your computer," said Rutishauser. "You can then deposit files in there. And when another boundary comes around, you close the first folder and create another one."

To retrieve memories, the brain uses boundary peaks as what Rutishauser calls “anchors for mental time travel.”

“When you try to remember something, it causes brain cells to fire,” Rutishauser said. “The memory system then compares this pattern of activity to all the previous firing peaks that happened shortly after boundaries. If it finds one that is similar, it opens that folder. You go back for a few seconds to that point in time, and things that happened then come into focus.”

To test their theory, investigators gave study participants two memory tests.

They first showed participants a series of still images and asked them whether or not they had seen them in the film clips they had viewed. Study participants were more likely to remember images that closely followed a hard or soft boundary, when a new “memory folder” would have been created.

Investigators also showed participants pairs of images from film clips they had viewed and asked which of the images appeared first. Participants had difficulty remembering the correct order of images that appeared on opposite sides of a hard boundary, possibly because the brain had segmented those images into separate memory folders.

Rutishauser said that therapies that improve event segmentation could help patients with memory disorders. Even something as simple as a change in atmosphere can amplify event boundaries, he explained.

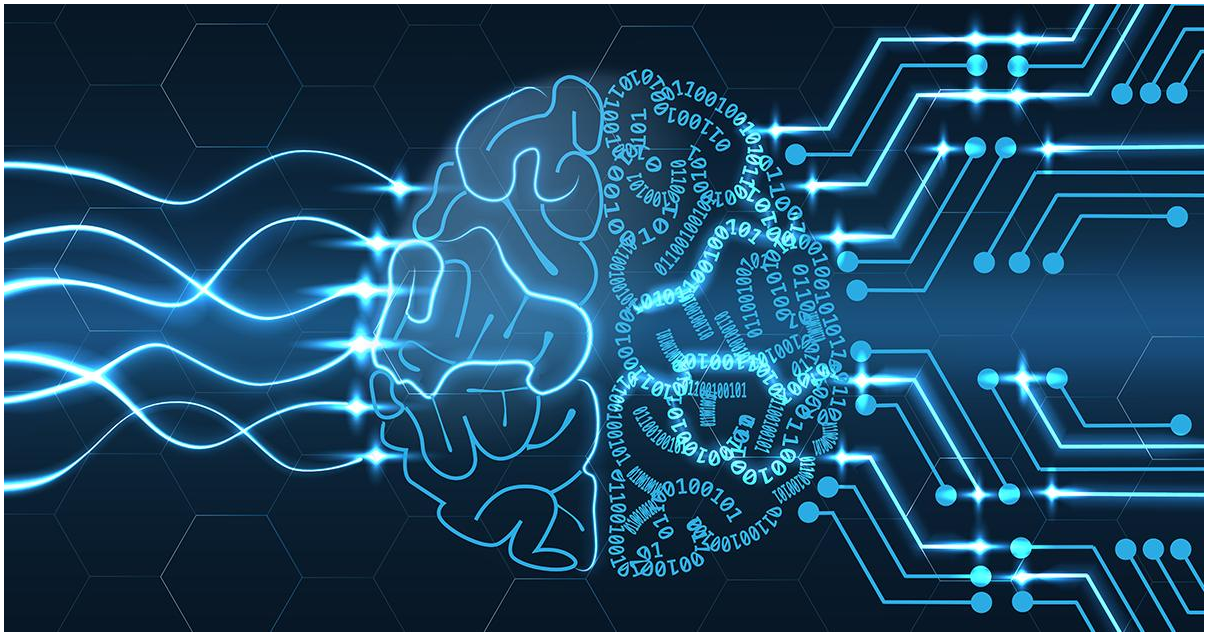
“The effect of context is actually quite strong,” Rutishauser said. “If you study in a new place, where you have never been before, instead of on your couch where everything is familiar, you will create a much stronger memory of the material.”

The research team included postdoctoral fellow Jie Zheng, PhD, and neuroscientist Gabriel Kreiman, PhD, from Boston Children’s Hospital; neurosurgeon Taufik A. Valiante, MD, PhD, of the University of Toronto; and Adam Mamelak, MD, professor of Neurosurgery and director of the Functional Neurosurgery Program at Cedars-Sinai.

In follow-up studies, the team plans to test the theory that boundary and event cells activate dopamine neurons when they fire, and that dopamine, a chemical that sends messages between cells, might be used as a therapy to strengthen memory formation.

Rutishauser and his team also noted during this study that when event cells fired in time with one of the brain’s internal rhythms, the theta rhythm—a repetitive pattern of activity linked to learning, memory and navigation—subjects were better able to remember the order of images they had seen. This is an important new insight because it shows that deep brain stimulation that adjusts theta rhythms could prove therapeutic for memory disorders.

“Theta rhythms are thought to be the ‘temporal glue’ for episodic memory,” said Zheng, first author of the study. “We think that firing of event cells in synchrony with the theta rhythm builds time-based links across



# Researchers find human learning can be duplicated in solid matter

## Researchers have found that learning — a universal feature of intelligence in living beings — can be mimicked in synthetic matter. Published Sep 28, 2021

[Sept 27, 2021: Rutgers University]
Rutgers researchers and their collaborators have found that learning -- a universal feature of intelligence in living beings -- can be mimicked in synthetic matter, a discovery that in turn could inspire new algorithms for artificial intelligence (AI). The study appears in the journal *PNAS*.
One of the fundamental characteristics of humans is the ability to continuously learn from and adapt to changing environments. But until recently, AI has been narrowly focused on emulating human logic. Now, researchers are looking to mimic human cognition in devices that can learn, remember and make decisions the way a human brain does.
Emulating such features in the solid state could inspire new algorithms in AI and neuromorphic computing that would have the flexibility to address uncertainties, contradictions and other aspects of everyday life. Neuromorphic computing mimics the neural structure and operation of the human brain, in part, by building artificial nerve systems to transfer electrical signals that mimic brain signals.
Researchers from Rutgers, Purdue and other institutions studied how the electrical conductivity of nickel oxide, a special type of insulating material, responded when its environment was changed repeatedly over various time intervals.

Rutgers researchers and their collaborators have found that learning -- a universal feature of intelligence in living beings -- can be mimicked in synthetic matter, a discovery that in turn could inspire new algorithms for artificial intelligence (AI). (Credit: Rutgers University-New Brunswick)

"The goal was to find a material whose electrical conductivity can be tuned by modulating the concentration of atomic defects with external stimuli such as oxygen, ozone and light," said Subhasish Mandal, a postdoctoral associate in the Department of Physics and Astronomy at Rutgers-New Brunswick. "We studied how this material behaves when we dope the system with oxygen or hydrogen, and most importantly, how the external stimulation changes the material's electronic properties."

The researchers found that when the gas stimulus changed rapidly, the material couldn't respond in full. It stayed in an unstable state in either environment and its response began to decrease. When the researchers introduced a noxious stimulus such as ozone, the material began to respond more strongly only to decrease again.

"The most interesting part of our results is that it demonstrates universal learning characteristics such as habituation and sensitization that we generally find in living species," Mandal said. "These material characteristics in turn can inspire new algorithms for artificial intelligence. Much as collective motion of birds or fish have inspired AI, we believe collective behavior of electrons in a quantum solid can do the same in the future.

"The growing field of AI requires hardware that can host adaptive memory properties beyond what is used in today's computers," he added. "We find that nickel oxide insulators, which historically have been restricted to academic pursuits, might be interesting candidates to be tested in future for brain-inspired computers and robotics."

The study included Distinguished Professor Karin Rabe from Rutgers and researchers from Purdue University, the University of Georgia and Argonne National Laboratory.

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# “Math neurons” identified in the human brain

## The findings indicate that some of the neurons detected are active exclusively during additions, while others are active during subtractions

Published Feb 14, 2022

[Feb 14, 2022: Johannes Seiler, University of Bonn]

Using ultrafine electrodes - implanted in the temporal lobes of epilepsy patients, researchers can visualize the activity of brain regions. (CREDIT: Christian Burkert/Volkswagen-Stiftung/University of Bonn)

The brain has neurons that fire specifically during certain mathematical operations. This is shown by a recent study conducted by the Universities of Tübingen and Bonn. The findings indicate that some of the neurons detected are active exclusively during additions, while others are active during subtractions. They do not care whether the

calculation instruction is written down as a word or a symbol. The results have now been published in the journal Current Biology.

Most elementary school children probably already know that three apples plus two apples add up to five apples. However, what happens in the brain during such calculations is still largely unknown. The current study by the Universities of Bonn and Tübingen now sheds light on this issue.

The researchers benefited from a special feature of the Department of Epileptology at the University Hospital Bonn. It specializes in surgical procedures on the brains of people with epilepsy. In some patients, seizures always originate from the same area of the brain. In order to precisely localize this defective area, the doctors implant several electrodes into the patients. The probes can be used to precisely determine the origin of the spasm. In addition, the activity of individual neurons can be measured via the wiring.

## Some neurons fire only when summing up

Five women and four men participated in the current study. They had electrodes implanted in the so-called temporal lobe of the brain to record the activity of nerve cells. Meanwhile, the participants had to perform simple arithmetic tasks. "We found that different neurons fired during additions than during subtractions," explains Prof. Florian Mormann from the Department of Epileptology at the University Hospital Bonn. It was not the case that some neurons responded only to a "+" sign and others only to a "-" sign: "Even when we replaced the mathematical symbols with words, the effect remained the same," explains Esther Kutter, who is doing her doctorate in Prof. Mormann's research group. "For example, when subjects were asked to calculate '5 and 3', their addition neurons sprang back into action; whereas for '7 less 4,' their subtraction neurons did."

This shows that the cells discovered actually encode a mathematical instruction for action. The brain activity thus showed with great accuracy what kind of tasks the test subjects were currently calculating: The researchers fed the cells' activity patterns into a self-learning computer program. At the same time, they told the software whether the subjects were currently calculating a sum or a difference. When the algorithm was confronted with new activity data after this training phase, it was able to accurately identify during which computational operation it had been recorded.

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Prof. Andreas Nieder from the University of Tübingen supervised the study together with Prof. Mormann. "We know from experiments with monkeys that neurons specific to certain computational rules also exist in their brains," he says. "In humans, however, there is hardly any data in this regard." During their analysis, the two working groups came across an interesting phenomenon: One of the brain regions studied was the so-

called parahippocampal cortex. There, too, the researchers found nerve cells that fired specifically during addition or subtraction. However, when summing up, different addition neurons became alternately active during one and the same arithmetic task. Figuratively speaking, it is as if the plus key on the calculator were constantly changing its location. It was the same with subtraction. Researchers also refer to this as "dynamic coding."
"This study marks an important step towards a better understanding of one of our most important symbolic abilities, namely calculating with numbers," stresses Mormann. The two teams from Bonn and Tübingen now want to investigate exactly what role the nerve cells found play in this.

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# Researchers find clues in the brain linking pain and food

## A new study suggests that circuitry in the brain responsible for motivation and pleasure is impacted when someone experiences pain.

Published Feb 14, 2022 12:55

[Feb 13, 2022: Kelsie Smith Hayduk, University of Rochester Medical Center]
A new study suggests that circuitry in the brain responsible for motivation and pleasure is impacted when someone experiences pain. (CREDIT: Creative Commons)
It has long been known that there is an association between food and pain, as people with chronic pain often struggle with their weight. Researchers at the Del Monte Institute for Neuroscience may have found an explanation in a new study that suggests that circuitry in the brain responsible for motivation and pleasure is impacted when someone experiences pain.
“These findings may reveal new physiological mechanisms linking chronic pain to a change in someone’s eating behavior,” said Paul Geha, M.D., lead author on the study published in *PLOS ONE*. “And this change can lead to the development of obesity.”
Finding pleasure in food comes from how our brain responds to what we are eating. In this study researchers were looking at the brain’s response to sugar and fat. Using a gelatin dessert and pudding researchers altered the sugar, fat, and texture of the foods. They found that none of the patients experienced eating behavior changes with sugar, but they did with fat. Those with acute lower back pain who later recovered were most

likely to lose pleasure in eating the pudding and show disrupted satiety signals – the communication from the digestive system to the brain – while those with acute lower back pain whose pain persisted at one year did not initially have the same change in their eating behavior. But chronic lower back pain patients did report that eventually foods high in fat and carbohydrates, like ice cream and cookies, became problematic for them over time and brain scans showed disrupted satiety signals.

"It is important to note, this change in food liking did not change their caloric intake," said Geha, who first authored a previous study published in PAIN that recent research is building on. "These findings suggest obesity in patients with chronic pain may not be caused by lack of movement but maybe they change how they eat."

Brain scans of the study participants revealed that the nucleus accumbens – a small area of the brain mostly known for its role in decision-making – may offer clues to who is at risk to experience a long-term change in eating behavior.

Researchers found the structure of this area of the brain was normal in of patients who initially experienced changes in their eating behavior but whose pain did not become chronic. However, patients whose eating behavior was normal, but whose pain became chronic had smaller nucleus accumbens. Interestingly, the nucleus accumbens predicted pleasure ratings only in chronic back pain patients and in patients who became chronic after an acute bout of back pain suggesting that this region becomes critical in motivated behavior of chronic pain patients.

Previous research by Geha, found a smaller nucleus accumbens can indicate if someone is at a greater risk of developing chronic pain.

Additional authors include Yezhe Lin, Ph.D., and Gelsina Stanley of the University of Rochester, Ivan de Araujo, Ph.D., of Icahn School of Medicine at Mount Sinai, and Dana Small, Ph.D., of Yale University. The research was funded by National Institute on Drugs Abuse.

# 'Super-vision' contact lenses let wearers see in the dark — even with their eyes closed

published May 22, 2025

Researchers have developed new contact lenses that enable vision in the near-infrared range, and they could restore color perception to people with color blindness.

A study participant places one of the night vision lenses in their eye. (Image credit: Yuqian Ma, Yunuo Chen, Hang Zhao)

Scientists have created night-vision contact lenses that they claim can grant people "super-vision."

The lenses — which use nanoparticles to absorb low-frequency light before emitting it in the visible spectrum — enable wearers to see infrared wavelengths that are otherwise invisible to the human eye.

And unlike traditional night-vision goggles, these lenses don't require a power source. The researchers described the new lenses May 22 in the journal Cell Press.

"Our research opens up the potential for non-invasive wearable devices to give people super-vision," senior author Tian Xue, a neuroscientist at the University of Science and Technology of China, said in a statement. "There are many potential applications right away for this material. For example, flickering infrared light could be used to transmit information in security, rescue, encryption or anti-counterfeiting settings."
First used in night combat during World War II, traditional night-vision goggles use an electronic image-intensifier tube to turn visible light or near-infrared photons into electrons. These electrons are then channeled onto a luminescent screen, causing it to glow green.

But these goggles typically need an energy source, which makes them bulky. Infrared goggles are also unable to precisely distinguish light across the infrared range, especially those at longer wavelengths.

To create the new lenses, the scientists embedded nanoparticles inside flexible, nontoxic polymers typically used in soft contact lenses. The nanoparticles — which consist of sodium gadolinium fluoride embedded with luminescent ytterbium, erbium and gold — absorb near-infrared photons in the 800- to 1,600-nanometer wavelength range before emitting them as visible light, wavelengths from around 380 to 750 nanometers

The researchers first tested their new lenses in mice. Mice sporting the new lenses favored dark boxes over those illuminated by infrared light, while those without the lenses showed no preference. (Mice are crepuscular animals that usually stick to dark environments to evade predators.) Additionally, the pupils of lens-wearing mice constricted in the presence of infrared light sources, with brain scans showing that their visual processing centers were firing.

Next, the team tried the lenses in humans. The people could perceive flickering infrared light and pick up on its direction. This infrared vision was enhanced when the participants closed their eyes, the researchers said.

"It's totally clear cut: without the contact lenses, the subject cannot see anything, but when they put them on, they can clearly see the flickering of the infrared light," Xue said. "We also found that when the subject closes their eyes, they're even better able to receive this flickering information, because near-infrared light penetrates the eyelid more effectively than visible light, so there is less interference from visible light."

The scientists replaced the nanoparticles embedded in the lenses with modified versions that mapped specific parts of the near-infrared spectrum to blue, green and red. The researchers suggested that this tweak could be used to aid people with color blindness.

"By converting red visible light into something like green visible light, this technology could make the invisible visible for color blind people," Xue said.

Despite these promising advances, more work is needed before the lenses see the light of day. Currently, they only pick up light projected from LED sources, which are incredibly bright, so the scientists will need to boost the lenses' sensitivity to pick up light of lower intensities.

The lenses' proximity to the retinas also may prevent them from detecting finer details, so the researchers have developed a wearable glass system for viewing objects at higher resolutions.

# New cells discovered in eye could help restore vision, scientists say published March 27, 2025

A new study suggests that never-seen-before stem cells in the human retina can restore vision in mice with a common eye disorder. But more work is needed to translate the treatment to people.

The findings of a new study may provide hope for patients with common eye diseases. (Image credit: abbestock via Getty Images)

Scientists have identified never-before-seen cells in the human eye that could potentially help reverse vision loss caused by common diseases, such as macular degeneration. The researchers discovered the cells in the retina, a light-sensitive structure at the back of the eye that is vital for vision. The cells were found in donated samples of fetal tissue.

The scientists also identified the same cells in lab-grown models of the human retina — and when they tried transplanting those models into mice with a common eye disorder, it restored the rodents' vision.

"This research not only deepens our understanding of retinal biology but also holds immense potential for advancing therapeutic interventions in RD [retinal degeneration] diseases," the researchers wrote in a paper describing the findings, which was published March 26 in the journal Science Translational Medicine.

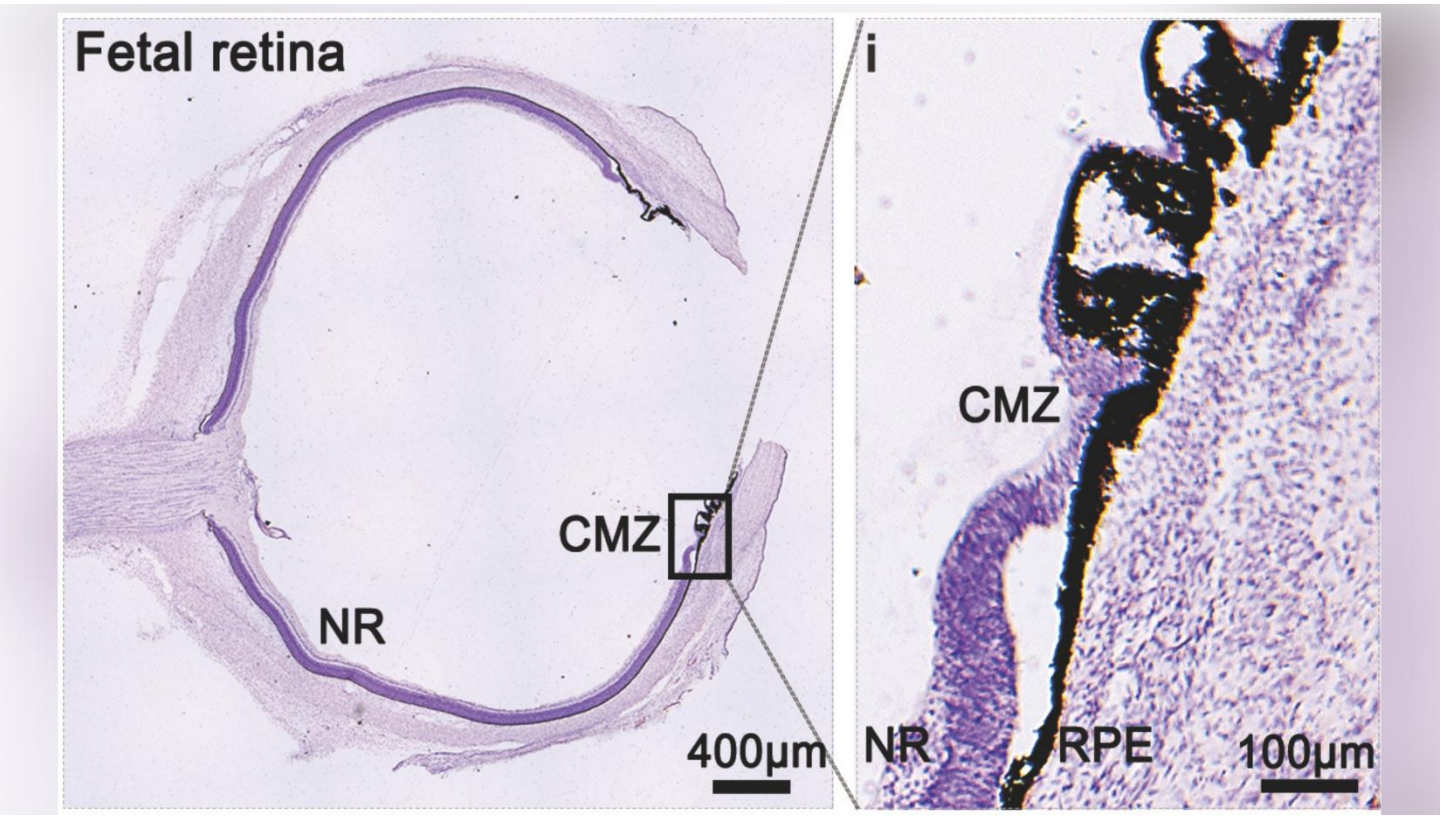
The retina detects light and converts it into signals that the brain can then interpret to determine what we're seeing. Deterioration of the retina is a leading cause of blindness worldwide. It can be triggered by many things, including aging, diabetes and physical

injury, and the degeneration can lead to common eye diseases, such as macular degeneration and retinitis pigmentosa.

Current treatments for these conditions focus mainly on reducing the rate at which retinal cells deteriorate, and protecting those that are still healthy. However, there are currently no effective therapies that promote repair of the retina, which would effectively reverse the deterioration.

A potential solution is to replace deteriorated cells with stem cells — cells that can mature to become any type of cell in the body under the right conditions. Yet, until now, scientists haven't found suitable stem cells in the human retina to achieve this, the authors of the new study wrote.

In the new research, the team analyzed the activity of cells in the fetal retinal samples in the lab. The scientists discovered two types of retinal stem cells with promising regenerative properties: human neural retinal stem-like cells (hNRSCs) and retinal pigment epithelium (RPE) stem-like cells.




This image shows retinal stem cells in dyed tissue from human fetuses. (Image credit: Jianzhong Su, State Key Laboratory of Eye Health, Eye Hospital, Wenzhou Medical University)

The researchers found that both types of cells, which were located in the outer edge of the retina, could clone themselves. However, only hNRSCs could turn into other types of retinal cells under the right conditions.

In a separate experiment, the researchers grew miniature replicas of the human retina in petri dishes. These 3D tissue models, known as organoids, better mimic the unique complexities of human organs than traditional animal models do.
An analysis of the cells within these organoids revealed that they contained hNRSCs similar to those found in the fetal tissue samples. The team also identified specific molecular chains of events that turned the stem cells into other retinal cells and regulated the repair process.

When transplanted into the retina of mice with a disease similar to retinitis pigmentosa, the stem cells from the organoids turned into the retinal cells needed to detect and process light signals. These new retinal cells ultimately improved the vision of the mice, compared with rodents that didn't receive any transplanted cells. This effect was seen for the duration of the experiment, up to 24 weeks.

Taken together, these early findings suggest that hNRSCs could be used to develop new treatments for retinal eye disorders in humans. But more research will be needed to confirm the potential of these cells for restoring the vision of human beings.

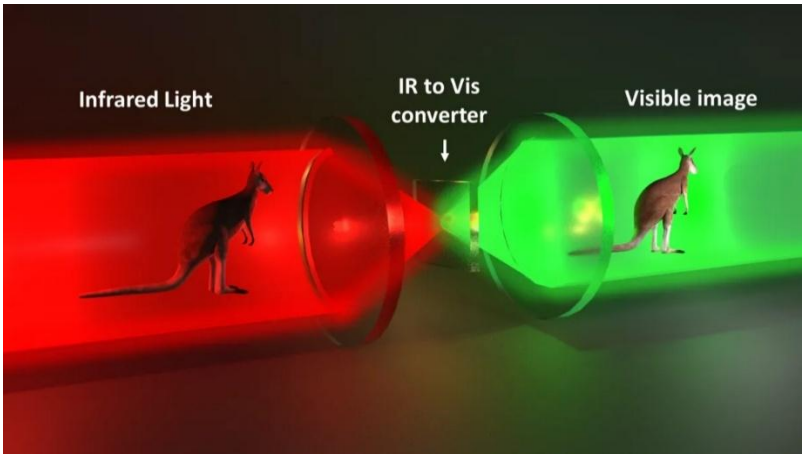
# 'Night vision lenses' could give you power to see in the dark using simple eyeglasses published June 28, 2024

Super-slim night-vision tech could be within reach thanks to a new material breakthrough that can capture infrared and visible light at the same time.

This breakthrough has opened the path to smaller, slimmer and more efficient night-vision systems for a variety of applications including the advent of night-vision filters that could be worn over eyeglasses to help people see at night. (Image credit: Pixsooz via Getty Images)

One day we could have everyday eyewear with night vision, thanks to an ultra-thin material that can capture infrared and visible light at the same time.

In a new study published May 23 in Advanced Materials, researchers in Australia have found that by using "metasurface-based up-conversion technology", you can create a night vision effect without the need for bulky light-processing and cryogenic cooling components.
"These results promise significant opportunities for the surveillance, autonomous navigation, and biological imaging industries, amongst others," chief investigator Dragomir Neshev from the Australian Research Council's Centre of Excellence for Transformative Meta-Optical Systems (TMOS) said in a statement. "Decreasing the size, weight and power requirements of night vision technology is an example of how meta-optics, and the work TMOS is doing, is crucial to Industry 4.0 and the future extreme miniaturisation of technology."
Traditional night-vision goggles work by visible light or infrared photons passing through a lens into an electronic image-intensifier tube consisting of a photocathode and a microchannel plate. The photocathode turns the photons into electrons, and these electrons then hit the microchannel plate, which has millions of holes that amplify their number. The electrons then interact with a phosphor-coated screen and exhibit a green glow, illuminating the scene that the wearer is viewing.




As the infrared photons only pass through a single resonant metasurface and are then mixed with a pump beam — a source of light used to amplify energy levels — night vision can be provided without the need to convert photons to electrons. (Image credit: Laura Valencia Molina, Australian National University)
The researchers explained that this current setup poses challenges due to its large size for a head-mounted device, thermal noise and the inability to augment infrared and visible imaging.

However, by using an "ultra-compact, high-quality-factor lithium niobate resonant metasurface" — a very thin photonic device that can modulate the behavior of electromagnetic waves — the researchers boosted the energy of the infrared photons, increasing their frequency so as to bring their wavelengths within the visual spectrum.

## Let there be visible light

As the infrared photons only pass through a single resonant metasurface and are then mixed with a pump beam — a source of light used to amplify energy levels — night vision can be provided without the need to convert photons to electrons. This then bypasses the need for multiple heavy optical and cooling components to reduce thermal noise; the up-conversion from IR to visible light via the metasurface takes place at room temperature. Furthermore, this up-conversion can capture both visible and nonvisible light in one image, which standard night-vision systems cannot as they must display images from each spectrum side-by-side. This leads to non-identical images. As such, the researchers found their approach offers direct imaging and edge detection via infrared simultaneously in a single view, enhancing the overall quality of a night-vision image.

This breakthrough has opened the path to smaller, slimmer and more efficient night-vision systems for a variety of applications, the scientists said. We could even see the advent of night-vision glasses or filters that could be worn over eyeglasses to help people see at night. Uses could range from helping keep track of a dog during an evening walk to making driving at night safer.

# Meta just stuck its AI somewhere you didn't expect it — a pair of Ray-Ban smart glasses

published May 11, 2024

Ray-Ban smart glasses will now use Meta AI virtual assistant software so that wearers can speak with their smart glasses and ask questions about what they're looking at.

Multimodal AI could super charge smart glasses. (Image credit: Meta / Ray-Ban)

Smart glasses have arguably failed to take off, but the addition of artificial intelligence (AI) could be the key to developing a truly transformational wearable technology.
In the US and Canada, Ray-Ban Meta smart glasses have received a rollout of multimodal AI technology with software called the "Meta AI virtual assistant." With multimodal AI — which means generative AI that can process queries that involve more than one medium (for example, both audio and imagery) — the device can better respond to queries based on what a wearer is looking at.

"Say you're traveling and trying to read a menu in French. Your smart glasses can use their built-in camera and Meta AI to translate the text for you, giving you the info you need without having to pull out your phone or stare at a screen," Meta representatives explained April 23 in a statement.
The device first takes a photo of what a wearer is looking at, then the AI taps into cloud-based processing to serve up an answer to a query, delivered by speech, such as "what type of plant am I looking at?"


(Image credit: Meta / Ray-Ban)

Meta first explored integrating multimodal AI into the Ray-Ban Meta smart glasses in a limited release in December 2023.
Testing the AI functionality in this device, a reporter from The Verge found that it mostly responded correctly when asked to identify the model of a car. It could also describe a type of cat, for example, and its features in an image snapped via the camera. But the AI ran into trouble in accurately identifying the species of plants belonging to one reporter and struggled to correctly identify a groundhog in their neighbor's backyard.

(Image credit: Meta / Ray-Ban)

## Multimodal machinations

AI-powered virtual assistants are nothing new, with the likes of the Google Assistant, Amazon Alexa and Apple's Siri all providing smart answers to queries in natural language. But the crux of the Meta AI in the Ray-Ban smart glasses is its multimodal functionality.

The ability to fuse and process data from multiple sensor modules — for example, cameras and microphones — means a multimodal AI can generate more accurate and sophisticated outcomes versus unimodal AI systems. Google's Gemini multimodal AI model , for example,can process a photo of some cookies and respond with the recipe.
Trained on identifying patterns in different types of data inputs through multiple neutral networks — collections of machine learning algorithms arranged to mimic the human brain — multimodal AIs can process input data from text, images, audio and more.

In smart glasses, it means an AI can make sense of the world the wearer is viewing by combining sensors on the glasses with these neural networks. As a result, the system can answer more sophisticated queries and offer smarter contextual information.

But in the case of the Ray-Ban Meta device, the AI has some distance to go before it meets the AI-processing capabilities found in the latest smartphones;  these benefit from more powerful chipsets and onboard sensor fusion – where data is taken from multiple sensors and processed together, for example to offer scene recognition in camera apps allowing for lighting and color balance to be intelligently adjusted, or combining data from thermometers and optical sensors in smartwatches to offer better feedback on one's workout.

# New AI model converts your thought into full written speech by harnessing your brain's magnetic signals published March 10, 2025

## An AI model can scan your brain with non-invasive equipment and convert your thoughts into typed sentences — with no implants required.

Two new studies shine a light on how we can convert thoughts into written sentences on a digital interface. (Image credit: Meta)

Scientists at Meta have used artificial intelligence (AI) and noninvasive brain scans to unravel how thoughts are translated into typed sentences, two new studies show.

In one study, scientists developed an AI model that decoded brain signals to reproduce sentences typed by volunteers. In the second study, the same researchers used AI to map how the brain actually produces language, turning thoughts into typed sentences.
The findings could one day support a noninvasive brain-computer interface that could help people with brain lesions or injuries to communicate, the scientists said.

"This was a real step in decoding, especially with noninvasive decoding," Alexander Huth, a computational neuroscientist at the University of Texas at Austin who was not involved in the research, told Live Science.
Brain-computer interfaces that use similar decoding techniques have been implanted in the brains of people who have lost the ability to communicate, but the new studies could support a potential path to wearable devices.

In the first study, the researchers used a technique called magnetoencephalography (MEG), which measures the magnetic field created by electrical impulses in the brain, to track

neural activity while participants typed sentences. Then, they trained an AI language model to decode the brain signals and reproduce the sentences from the MEG data.

The model decoded the letters that participants typed with 68% accuracy. Frequently occurring letters were decoded correctly more often, while less-common letters, like Z and K, came with higher error rates. When the model made mistakes, it tended to substitute characters that were physically close to the target letter on a QWERTY keyboard, suggesting that the model uses motor signals from the brain to predict which letter a participant typed.

The team's second study built on these results to show how language is produced in the brain while a person types. The scientists collected 1,000 MEG snapshots per second as each participant typed a few sentences. From these snapshots, they decoded the different phases of sentence production.

## Decoding your thoughts with AI

They found that the brain first generates information about the context and meaning of the sentence, and then produces increasingly granular representations of each word, syllable and letter as the participant types.

"These results confirm the long-standing predictions that language production requires a hierarchical decomposition of sentence meaning into progressively smaller units that ultimately control motor actions," the authors wrote in the study.

To prevent the representation of one word or letter from interfering with the next, the brain uses a "dynamic neural code" to keep them separate, the team found. This code constantly shifts where each piece of information is represented in the language-producing parts of the brain.

That lets the brain link successive letters, syllables, and words while maintaining information about each over longer periods of time. However, the MEG experiments were not able to pinpoint exactly where in those brain regions each of these representations of language arises.

Taken together, these two studies, which have not been peer-reviewed yet, could help scientists design noninvasive devices that could improve communication in people who have lost the ability to speak.

Although the current setup is too bulky and too sensitive to work properly outside a controlled lab environment, advances in MEG technology may open the door to future wearable devices, the researchers wrote.

"I think they're really at the cutting edge of methods here," Huth said. "They are definitely doing as much as we can do with current technology in terms of what they can pull out of these signals."

# Mind-reading brain implant converts thoughts to speech almost instantly: 'breakthrough' published April 3, 2025

Researchers have used a mind-reading brain implant to continuously play a paralyzed person's thoughts through a speaker, allowing them to talk again.

The brain-computer interface can provide a synthetic voice to those unable to speak. (Image credit: Noah Berger)

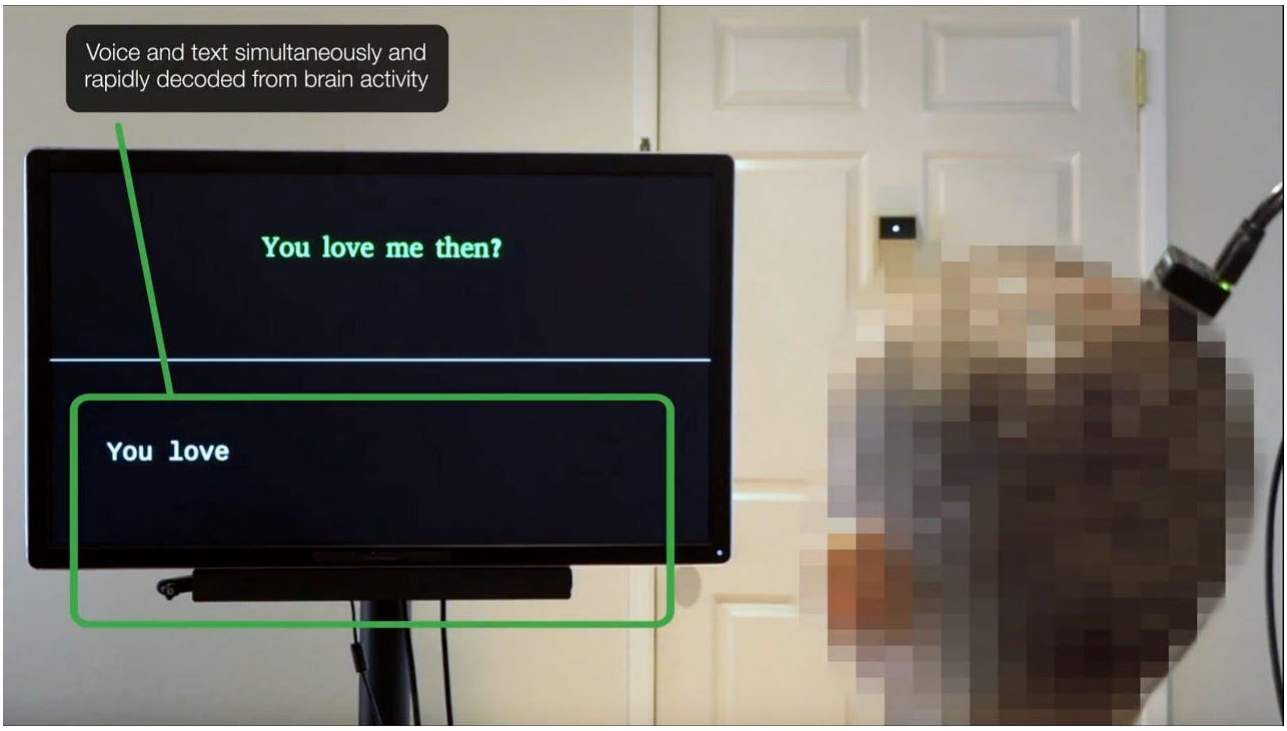
A brain implant that uses artificial intelligence (AI) can almost instantaneously decode a person's thoughts and stream them through a speaker, new research shows. This is the first time researchers have achieved near-synchronous brain-to-voice streaming.

The experimental mind-reading technology is designed to give a synthetic voice to people with severe paralysis who cannot speak. It works by putting electrodes onto the brain's surface as part of an implant called a neuroprosthesis, which allows scientists to identify and interpret speech signals.

The brain-computer interface (BCI) uses AI to decode neural signals and can stream intended speech from the brain in close to real time, according to a statement released by

the University of California (UC), Berkeley. The team previously unveiled an earlier version of the technology in 2023, but the new version is quicker and less robotic.

A streaming brain-to-voice neuroprosthesis to restore naturalistic communication - YouTube




Watch On

"Our streaming approach brings the same rapid speech decoding capacity of devices like Alexa and Siri to neuroprostheses," study co-principal investigator Gopala Anumanchipalli, an assistant professor of electrical engineering and computer sciences at UC Berkeley, said in the statement. "Using a similar type of algorithm, we found that we could decode neural data and, for the first time, enable near-synchronous voice streaming."

Anumanchipalli and his colleagues shared their findings in a study published Monday (March 31) in the journal Nature Neuroscience.

The first person to trial this technology, identified as Ann, suffered a stroke in 2005 that left her severely paralyzed and unable to speak. She has since allowed researchers to implant 253 electrodes onto her brain to monitor the part of our brains that controls speech — called the motor cortex — to help develop synthetic speech technologies.

"We are essentially intercepting signals where the thought is translated into articulation and in the middle of that motor control," study co-lead author Cheol Jun Cho, a doctoral student in electrical engineering and computer sciences at UC Berkeley, said in the statement. "So what we're decoding is after a thought has happened, after we've decided what to say, after we've decided what words to use and how to move our vocal-tract muscles."

AI decodes data sampled by the implant to help convert neural activity into synthetic speech. The team trained their AI algorithm by having Ann silently attempt to speak

sentences that appeared on a screen before her, and then by matching the neural activity to the words she wanted to say.

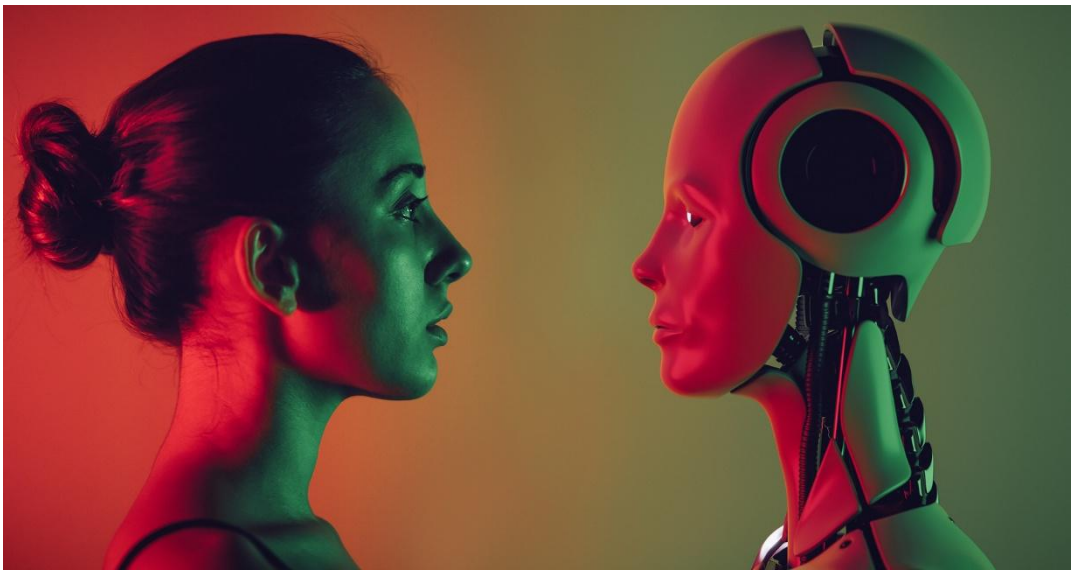
The system sampled brain signals every 80 milliseconds (0.08 seconds) and could detect words and convert them into speech with a delay of up to around 3 seconds, according to the study. That's a little slow compared to normal conversation, but faster than the previous version, which had a delay of about 8 seconds and could only process whole sentences.

The new system benefits from converting shorter windows of neural activity than the old one, so it can continuously process individual words rather than waiting for a finished sentence. The researchers say the new study is a step toward achieving more natural-sounding synthetic speech with BCIs.

"This proof-of-concept framework is quite a breakthrough," Cho said. "We are optimistic that we can now make advances at every level. On the engineering side, for example, we will continue to push the algorithm to see how we can generate speech better and faster."

# Scientists discover major differences in how humans and AI 'think' — and the implications could be significant published April 1, 2025

Study finds that AI fundamentally lacks the human capability to make creative mental connections, raising warning signs for how we deploy AI tools.



AI models struggle to form analogies when considering complex subjects, like humans can, meaning their use in real-world decision making could be risky. (Image credit: imaginima/Getty Images)

We know that artificial intelligence (AI) can't think the same way as a person, but new research has revealed how this difference might affect AI's decision-making, leading to real-world ramifications humans might be unprepared for.

The study, published Feb. 2025 in the journal Transactions on Machine Learning Research, examined how well large language models (LLMs) can form analogies.
They found that in both simple letter-string analogies and digital matrix problems — where the task was to complete a matrix by identifying the missing digit — humans performed well but AI performance declined sharply.

While testing the robustness of humans and AI models on story-based analogy problems, the study found the models were susceptible to answer-order effects — differences in responses due to the order of treatments in an experiment — and may have also been more likely to paraphrase.

Altogether, the study concluded that AI models lack “zero-shot” learning abilities, where a learner observes samples from classes that weren't present during training and makes predictions about the class they belong to according to the question.

Co-author of the study Martha Lewis, assistant professor of neurosymbolic AI at the University of Amsterdam, gave an example of how AI can't perform analogical reasoning as well as humans in letter string problems.
"Letter string analogies have the form of 'if abcd goes to abce, what does ijkl go to?' Most humans will answer 'ijkm', and [AI] tends to give this response too," Lewis told Live Science. "But another problem might be 'if abbcd goes to abcd, what does ijkkl go to? Humans will tend to answer 'ijkl' – the pattern is to remove the repeated element. But GPT-4 tends to get problems [like these] wrong."

## Why it matters that AI can't think like humans

Lewis said that while we can abstract from specific patterns to more general rules, LLMs don't have that capability. "They're good at identifying and matching patterns, but not at generalizing from those patterns."

Most AI applications rely to some extent on volume — the more training data is available, the more patterns are identified. But Lewis stressed pattern-matching and abstraction aren't the same thing. "It's less about what's in the data, and more about how data is used," she added.

To give a sense of the implications, AI is increasingly used in the legal sphere for research, case law analysis and sentencing recommendations. But with a lower ability to make analogies, it may fail to recognize how legal precedents apply to slightly different cases when they arise.

Given this lack of robustness might affect real-world outcomes, the study pointed out that this served as evidence that we need to carefully evaluate AI systems not just for accuracy but also for robustness in their cognitive capabilities.

# Are groovy brains more efficient?

University of California, Berkeley researchers find deeper brain grooves enhance connectivity, improving reasoning and cognitive functions.

From University of California – Berkeley 22/05/25 (first released 21/05/25)

Illustration by Superinnovators

Many grooves and dimples on the surface of the brain are unique to humans, but they're often dismissed as an uninteresting consequence of packing an unusually large brain into a too-small skull.

But neuroscientists are finding that these folds are not mere artifacts, like the puffy folds you get when forcing a sleeping bag into a stuff sack.

The depths of some of the smallest of these grooves seem to be linked to increased interconnectedness in the brain and better reasoning ability.

In a study published May 19 in *The Journal of Neuroscience*, University of California, Berkeley, researchers show that in children and adolescents, the depths of some small grooves are correlated with increased connectivity between regions of the brain — the lateral prefrontal cortex and lateral parietal cortex — involved in reasoning and other high-level cognitive functions.

The grooves may actually bring those areas closer together in space, shortening the connections between them and speeding communications.

The implication, the researchers say, is that variability in these small grooves, which are called tertiary sulci (pronounced sul'-sigh), may help explain individual differences in cognitive performance, and could serve as diagnostic indicators or biomarkers of reasoning ability or neurodevelopmental disorders.

"The impetus for this study was having seen that sulcal depth correlated with reasoning across children and adolescents," said Silvia Bunge, professor of psychology and a member of UC Berkeley's Helen Wills Neuroscience Institute (HWNI).

"Given our previous findings, our former postdoctoral fellow Suvi Häkkinen aimed to test if sulcal depth was correlated with reasoning performance and to test if patterns of coordinated

activity within a lateral prefrontal-parietal network could explain this relation between sulcal depth and reasoning."

"We had explicit predictions about which tertiary sulci in the lateral prefrontal cortex would be functionally connected to tertiary sulci in the lateral parietal cortex, and that panned out," added Kevin Weiner, UC Berkeley associate professor of psychology and of neuroscience and a member of HWNI.

"Prefrontal and parietal cortices aside, the hypothesis is that the formation of sulci leads to shortened distances between connected brain regions, which could lead to increased neural efficiency, and then, in turn, individual differences in improved cognition with translational applications."

"The cortex is sort of haphazardly crunched up into the brain — that's what I was always taught," Bunge said.

"Kevin came along and changed my mind about sulci."

**The hills and valleys of the brain**

The brains of most animals, mammals included, have smooth surfaces.

Primates have hills and valleys covering their cerebral cortex.

While one group of primates, the New World monkeys called marmosets, have shallow, barely perceptible sulci, those of humans are deeply incised, with between 60% and 70% of the cortex buried in these folds.

The cortical folding patterns in humans also change with age, establishing their final structure late in prenatal development while becoming less prominent in old age.

"While sulci can change over development, getting deeper or shallower and developing thinner or thicker gray matter — probably in ways that depend on experience — our particular configuration of sulci is a stable individual difference: their size, shape, location and even, for a few sulci, whether they're present or absent," said Bunge, who studies abstract reasoning in young people, from 6 years of age through young adulthood.

The smallest grooves, many of which are uniquely human, are called tertiary sulci because they appear last in prenatal development and are never as deep as the major or primary sulci that are most evident on the cerebral surface.

Scientists have speculated that the tertiary sulci emerge in parts of the human brain that have expanded the most throughout evolution and have a protracted development, and that they are likely associated with aspects of cognition — reasoning, decision-making, planning and self-control — that develop over a protracted adolescence.

But prior to this study, evidence was lacking for a connection between tertiary sulci and brain connectivity.

The UC Berkeley study is one of few, all within the past few years, to provide such proof.

**Sulci linked to cognition**

Weiner and Bunge said that, as undergraduates, they were never taught how to define tertiary sulci; they often examined scans of average brains that did not match any specific individual.

Weiner noticed this mismatch as an undergraduate.

“At the time, all I knew was that I had some cortical squiggles that weren’t in the average brain atlases that we had in the lab. So the question I asked my mentors, Sabine Kastner and Charlie Gross, was: Do I have different structures that aren’t in our atlases or are structures missing from these atlases?” he said.

“That sent me down a 15-year rabbit hole studying one particular tertiary sulcus in the visual cortex.”

That work showed that a specific sulcus, the mid-fusiform sulcus, varied in length from as small as 3 millimeters to as long as 7 centimeters in any given person.

Moreover, the longer the sulcus, the better a person was at processing and recognizing human faces.

“About 2% of individuals have developmental prosopagnosia, which means they can’t perceive faces, and they don’t have any brain damage,” he said.

“That sulcus, especially in the right hemisphere, is shorter and shallower in those folks than in what we refer to as neurotypical controls.”

Building on that rabbit hole, Bunge and Weiner wondered whether tertiary sulci in other regions of the brain, outside the visual processing units, also correlated with cognitive ability.

Upon moving to UC Berkeley in 2018, Weiner began investigating the prefrontal cortex — located in the front of the brain behind the forehead — in collaboration with Bunge, who wanted to test whether sulci in this area would be linked to reasoning.

In a 2021 paper, the two collaborated to define all the smaller sulci in the lateral prefrontal cortex and created a computer model that identified the tertiary sulci as contributing the most variation in reasoning ability.

“The model identified that there’s tertiary sulci in the lateral prefrontal cortex that are contributing to reasoning skills in kids,” Weiner said.

Expanding on that work in the new study, Weiner, Bunge and their colleagues painstakingly catalogued the tertiary sulci in the lateral parietal cortex, located under and just behind the crown of the skull, and investigated its functional connections with the sulci of the lateral prefrontal cortex.

For both studies, they studied 43 participants, 20 of them female, who ranged in age from 7 to 18.

While in a functional magnetic resonance imaging (fMRI) scanner, the participants were given a reasoning task.

The researchers focused on the brain activity in 21 sulci they had identified in each hemisphere of the brain, and the functional connections between these sulci — including, for the first time, tertiary sulci.

Across these individuals, greater depth for several of the sulci implicated in reasoning was associated with higher network centrality across the set of prefrontal and parietal sulci.

**Experience affects sulci**

Bunge pointed out that the association between depths of sulci and reasoning does not hold for all sulci, and that sulcal depth may change with experience.

“Do we think that an individual’s capacity for reasoning is set in stone based on their cortical folding? No!,” she said.

“Cognitive function depends on variability in a variety of anatomical and functional features and, importantly, we know that experience, like quality of schooling, plays a powerful role in shaping an individual’s cognitive trajectory, and that it is malleable, even in adulthood.”

Weiner’s lab is creating a computer program to help researchers identify tertiary sulci in the human brain.

Most programs only identify about 35 sulci, but when tertiary sulci are included, there are over 100, he said, including new ones that their labs have uncovered together.

They argue that sulci could serve as landmarks to compare brains between individuals, since brains vary so much.

“Dozens of brain maps have been proposed in just the last five years, but they disagree about the areas of associated regions in the cortex, and there are mismatches between areas at the group and individual level,” Weiner said.

“Examining network architecture based on individual sulcal morphology circumvents these disagreements and mismatches, with the opportunity to glean network-level insight from the local sulcal anatomy that is specific to a given individual.”

The MRI scans of nine participants in the study, all children, adolescents and young adults, show how varied the tertiary sulci (color patches) are among individuals. The patches are identified sulci in the lateral prefrontal and lateral parietal cortices of the left and right hemispheres of the brain. Credit: Hakkinen et al, UC Berkeley

*Aside from Bunge and Weiner, other UC Berkeley co-authors of the paper are former postdoctoral fellow Suvi Häkkinen, former graduate student Willa Voorhies, former undergraduates Ethan Willbrand and Jewelia Yao, and former visiting scholars Yi-Heng Tsai and Thomas Gagnant.*

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Research Articles, Behavioral/Cognitive

# Anchoring functional connectivity to individual sulcal morphology yields insights in a pediatric study of reasoning

Suvi Häkkinen, Willa I. Voorhies, Ethan H. Willbrand, Yi-Heng Tsai, Thomas Gagnant, Jewelia K. Yao, Kevin S. Weiner and Silvia A. Bunge

Journal of Neuroscience 19 May 2025, e0726242025; https://doi.org/10.1523/JNEUROSCI.0726-24.2025

## Abstract

A salient neuroanatomical feature of the human brain is its pronounced cortical folding, and there is mounting evidence that sulcal morphology is relevant to functional brain architecture and cognition. However, our understanding of the relationships between sulcal anatomy, brain activity, and behavior is still in its infancy. We previously found that the depth of three small, shallow sulci in lateral prefrontal cortex (LPFC) was linked to reasoning performance during development (Voorhies et al., 2021). These findings beg the question: what is the linking mechanism between sulcal morphology and cognition? Here, we investigated functional connectivity among sulci in LPFC and lateral parietal cortex (LPC) in participants from the same sample as our previous study. We leveraged manual parcellations (21 sulci/hemisphere, total of 1806) and functional magnetic resonance (fMRI) data from a reasoning task from 43 participants aged 7–18 years (20 female). We conducted clustering and classification analyses of individual-level functional connectivity among sulci. Broadly, we found that 1) the connectivity patterns of individual sulci could be differentiated – and more accurately than rotated sulcal labels equated for size and shape; 2) sulcal connectivity did not consistently correspond with that of probabilistic labels or

large-scale networks; 3) sulci clustered together into groups with similar patterns, not dictated by spatial proximity; and 4) across individuals, greater depth was associated with higher network centrality for several sulci under investigation. These results illustrate how sulcal morphology can be relevant for functional connectivity, and provide proof of concept that using sulci to define an individual coordinate space for functional connectomes is a promising future direction.

**Significance Statement** A salient, and behaviorally relevant, feature of the human brain is its pronounced cortical folding. However, the links between sulcal anatomy and brain function are still poorly understood – particularly for small, shallow, individually variable sulci in association cortices. Here, focusing on the functional connectivity between individually defined sulci in lateral prefrontal and parietal regions in a pediatric sample, we demonstrate for the first time a link between functional network centrality and sulcal morphology. This result, along with control analyses, provide proof of concept that defining functional brain networks in relation to sulcal anatomy is a promising way forward.

## Footnotes

- The authors declare no competing financial interests.
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# Dancing brainwaves: How sound reshapes your brain networks in real time

What happens inside your brain when you hear a steady rhythm or musical tone? According to a new study from Aarhus University and the University of Oxford, your brain doesn't just hear it--it reorganizes itself in real time.

*Date:*

June 2, 2025

*Source:*

Aarhus University

*Summary:*

What happens inside your brain when you hear a steady rhythm or musical tone? According to a new study, your brain doesn't just hear it -- it reorganizes itself in real time.

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## What happens inside your brain when you hear a steady rhythm or musical tone? According to a new study from Aarhus University and the University of Oxford, your brain doesn't just hear it -- it reorganizes itself in real time.

Every beep, tone and new sound you hear travels from the ear to registering in your brain. But what actually happens in your brain when you listen to a continuous stream of sounds? A new study from Aarhus University and University of Oxford published in *Advanced Science* reveals that the brain doesn't simply register sound: it dynamically reshapes its organization in real time, orchestrating a complex interplay of brainwaves in multiple networks.

The research, led by Dr. Mattia Rosso and Associate Professor Leonardo Bonetti at the Center for Music in the Brain, Aarhus University, in collaboration with the University of Oxford, introduces a novel neuroimaging method called *FREQ-NESS* -- Frequency-resolved Network Estimation via Source Separation. Using advanced algorithms, this method disentangles overlapping brain networks based on their dominant frequency. Once a network is identified by its unique frequency, the method can then trace how it propagates in space across the brain.

"We're used to thinking of brainwaves like fixed stations -- alpha, beta, gamma -- and of brain anatomy as a set of distinct regions," says Dr. Rosso. "But what we see with FREQ-NESS is much richer. It is long known that brain activity is organized through activity in different frequencies, tuned both internally and to the environment. Starting

from this fundamental principle, we've designed a method that finds how each frequency is expressed across the brain."

**Opens the door to precise brain mapping**

The development of FREQ-NESS represents a major advance in how scientists can investigate the brain's large-scale dynamics. Unlike traditional methods that rely on predefined frequency bands or regions of interest, the data-driven approach maps the whole brain's internal organization with high spectral and spatial precision. And that opens new possibilities for basic neuroscience, brain-computer interfaces, and clinical diagnostics.

This study adds to a growing body of research exploring how the brain's rhythmic structure shapes everything from music cognition to general perception and attention, and altered states of consciousness.

"The brain doesn't just react: it reconfigures. And now we can see it," says Professor Leonardo Bonetti, co-author and neuroscientist at Center for Music in the Brain, Aarhus University, and at the Centre for Eudaimonia and Human Flourishing, University of Oxford. "This could change how we study brain responses to music and beyond, including consciousness, mind-wandering, and broader interactions with the external world."

A large-scale research program is now underway to build on this methodology, supported by an international network of neuroscientists. Due to the high reliability across experimental conditions and across datasets -- FREQ-NESS might also pave the way for individualized brain mapping, explains Professor Leonardo Bonetti.

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**Story Source:**

Materials provided by **Aarhus University**. Original written by Vibe Bregendahl Noordeloos. *Note: Content may be edited for style and length.*

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**Journal Reference**:

1. Mattia Rosso, Gemma Fernández-Rubio, Peter Erik Keller, Elvira Brattico, Peter Vuust, Morten L Kringelbach, Leonardo Bonetti. **FREQ-NESS Reveals the Dynamic Reconfiguration of Frequency-Resolved Brain Networks During Auditory Stimulation**. *Advanced Science*, 2025; 12 (20)
DOI: 10.1002/advs.202413195

# Overlooked cells might explain the human brain's huge storage capacity

*Date:*

May 27, 2025

*Source:*

Massachusetts Institute of Technology

*Summary:*

Researchers have a new hypothesis for how brain cells called astrocytes might contribute to memory storage in the brain. Their model, known as dense associative memory, would help explain the brain's massive storage capacity.

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**FULL STORY**

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## The human brain contains about 86 billion neurons. These cells fire electrical signals that help the brain store memories and send information and commands throughout the brain and the nervous system.

The brain also contains billions of astrocytes -- star-shaped cells with many long extensions that allow them to interact with millions of neurons. Although they have long been thought to be mainly supportive cells, recent studies have suggested that astrocytes may play a role in memory storage and other cognitive functions.

MIT researchers have now put forth a new hypothesis for how astrocytes might contribute to memory storage. The architecture suggested by their model would help to explain the brain's massive storage capacity, which is much greater than would be expected using neurons alone.

"Originally, astrocytes were believed to just clean up around neurons, but there's no particular reason that evolution did not realize that, because each astrocyte can contact hundreds of thousands of synapses, they could also be used for computation," says Jean-Jacques Slotine, an MIT professor of mechanical engineering and of brain and cognitive sciences, and an author of the new study.

Dmitry Krotov, a research staff member at the MIT-IBM Watson AI Lab and IBM Research, is the senior author of the open-access paper, which appeared May 23 in the *Proceedings of the National Academy of Sciences*. Leo Kozachkov PhD '22 is the paper's lead author.

**Memory capacity**

Astrocytes have a variety of support functions in the brain: They clean up debris, provide nutrients to neurons, and help to ensure an adequate blood supply.

Astrocytes also send out many thin tentacles, known as processes, which can each wrap around a single synapse -- the junctions where two neurons interact with each other -- to create a tripartite (three-part) synapse.

Within the past couple of years, neuroscientists have shown that if the connections between astrocytes and neurons in the hippocampus are disrupted, memory storage and retrieval are impaired.

Unlike neurons, astrocytes can't fire action potentials, the electrical impulses that carry information throughout the brain. However, they can use calcium signaling to communicate with other astrocytes. Over the past few decades, as the resolution of calcium imaging has improved, researchers have found that calcium signaling also allows astrocytes to coordinate their activity with neurons in the synapses that they associate with.

These studies suggest that astrocytes can detect neural activity, which leads them to alter their own calcium levels. Those changes may trigger astrocytes to release gliotransmitters -- signaling molecules similar to neurotransmitters -- into the synapse.

"There's a closed circle between neuron signaling and astrocyte-to-neuron signaling," Kozachkov says. "The thing that is unknown is precisely what kind of computations the astrocytes can do with the information that they're sensing from neurons."

The MIT team set out to model what those connections might be doing and how they might contribute to memory storage. Their model is based on Hopfield networks -- a type of neural network that can store and recall patterns.

Hopfield networks, originally developed by John Hopfield and Shun-Ichi Amari in the 1970s and 1980s, are often used to model the brain, but it has been shown that these networks can't store enough information to account for the vast memory capacity of the human brain. A newer, modified version of a Hopfield network, known as dense associative memory, can store much more information through a higher order of couplings between more than two neurons.

However, it is unclear how the brain could implement these many-neuron couplings at a hypothetical synapse, since conventional synapses only connect two neurons: a presynaptic cell and a postsynaptic cell. This is where astrocytes come into play.

"If you have a network of neurons, which couple in pairs, there's only a very small amount of information that you can encode in those networks," Krotov says. "In order to build dense associative memories, you need to couple more than two neurons. Because a single astrocyte can connect to many neurons, and many synapses, it is tempting to hypothesize that there might exist an information transfer between synapses mediated by this biological cell. That was the biggest inspiration for us to look into astrocytes and led us to start thinking about how to build dense associative memories in biology."

The neuron-astrocyte associative memory model that the researchers developed in their new paper can store significantly more information than a traditional Hopfield network -- more than enough to account for the brain's memory capacity.

**Intricate connections**

The extensive biological connections between neurons and astrocytes offer support for the idea that this type of model might explain how the brain's memory storage systems work, the researchers say. They hypothesize that within astrocytes, memories are encoded by gradual changes in the patterns of calcium flow. This information is conveyed to neurons by gliotransmitters released at synapses that astrocyte processes connect to.

"By careful coordination of these two things -- the spatial temporal pattern of calcium in the cell and then the signaling back to the neurons -- you can get exactly the dynamics you need for this massively increased memory capacity," Kozachkov says.

One of the key features of the new model is that it treats astrocytes as collections of processes, rather than a single entity. Each of those processes can be considered one computational unit. Because of the high information storage capabilities of dense associative memories, the ratio of the amount of information stored to the number of computational units is very high and grows with the size of the network. This makes the system not only high capacity, but also energy efficient.

"By conceptualizing tripartite synaptic domains -- where astrocytes interact dynamically with pre- and postsynaptic neurons -- as the brain's fundamental computational units, the authors argue that each unit can store as many memory patterns as there are neurons in the network. This leads to the striking implication that, in principle, a neuron-astrocyte network could store an arbitrarily large number of patterns, limited only by its size," says Maurizio De Pitta, an assistant professor of physiology at the Krembil Research Institute at the University of Toronto, who was not involved in the study.

To test whether this model might accurately represent how the brain stores memory, researchers could try to develop ways to precisely manipulate the connections between astrocytes' processes, then observe how those manipulations affect memory function.

"We hope that one of the consequences of this work could be that experimentalists would consider this idea seriously and perform some experiments testing this hypothesis," Krotov says.

In addition to offering insight into how the brain may store memory, this model could also provide guidance for researchers working on artificial intelligence. By varying the connectivity of the process-to-process network, researchers could generate a huge range of models that could be explored for different purposes, for instance, creating a continuum between dense associative memories and attention mechanisms in large language models.

"While neuroscience initially inspired key ideas in AI, the last 50 years of neuroscience research have had little influence on the field, and many modern AI algorithms have drifted away from neural analogies," Slotine says. "In this sense, this work may be one of the first contributions to AI informed by recent neuroscience research."

**Story Source:**

Materials provided by **Massachusetts Institute of Technology**. Original written by Anne Trafton. *Note: Content may be edited for style and length.*

**Journal Reference**:

1. Leo Kozachkov, Jean-Jacques Slotine, Dmitry Krotov. **Neuron–astrocyte associative memory**. *Proceedings of the National Academy of Sciences*, 2025; 122 (21) DOI: 10.1073/pnas.2417788122

JUNE 4, 2025

# Boosting brain's self-cleansing system helps clear Alzheimer's toxins in mice

by Columbia University Irving Medical Center

edited by Sadie Harley, reviewed by Robert Egan

Cleaning the brain. A green tracer fluid flows through the brain's glymphatic system, a recently discovered waste disposal system. The system moves waste along the outer edges of the brain's blood vessels (red). Credit: Kai Chen

Columbia scientists have found that boosting the performance of a self-cleansing system in the brain helps flush amyloid and tau toxins from the brains of mice and improves the animals' cognition.

Their study, published in *Neuron*, also found that the brain cleansing system can be enhanced with drugs called PERK inhibitors, already in clinical trials for cancer, and suggests the drugs may also be beneficial for Alzheimer's and other neurodegenerative diseases.

"The glymphatic system—often called the brain's dishwasher—was only discovered about a decade ago and has captured the attention of many scientists," says Guang Yang, associate professor of anesthesiological sciences at Columbia University's Vagelos College of Physicians and Surgeons, who led the study.

## Brain cleaning and Alzheimer's

Alzheimer's has been linked to a weak glymphatic system, so Yang and her team wanted to see how the two are connected, information that could yield new ways to treat or prevent the disease.

The researchers measured the performance of the brain's cleansing cycle by injecting a tracer into the cerebrospinal fluid of mice and using high-resolution microscopy to capture time-lapse images of the tracer in the glymphatic system.

In mice with Alzheimer's, the team found that the cleaning system becomes sluggish because channels that help drain metabolic waste from the brain are misplaced.

"It looks like the cells have enough of these AQP4 channels, but they're not in the right locations in the cells," Yang says.

Normally, the channels are located at the endfeet of the astrocytes, star-shaped brain cells that control the glymphatic system. But in mice and people with Alzheimer's, the researchers found the channels distributed all around the astrocytes, which hindered waste removal from the cells.

The channels are misplaced in mice, the team found, because a protein called PERK is overactive. The researchers found that deleting the PERK gene or inhibiting it with a drug restored the channels to their proper location, increased amyloid and tau clearance, and improved the animals' cognitive performance.

## A role for sleep?

Yang says there's still more to learn about the connection between the glymphatic system and Alzheimer's that could lead to new treatments. "This is just the starting point. We know PERK is important for controlling localization of the channel, but the details need to be worked out," she says.

Sleep may also help the glymphatic system clean the brain. Some studies suggest the glymphatic system is most active during sleep, and Alzheimer's is known to be associated with sleep disorders.

"We're looking to see if PERK activity is linked to sleep, which might help explain how poor sleep could increase Alzheimer's pathology," Yang adds.

"Glymphatic impairment may be a common pathway in all neurodegenerative diseases, so our findings may also apply to other conditions."

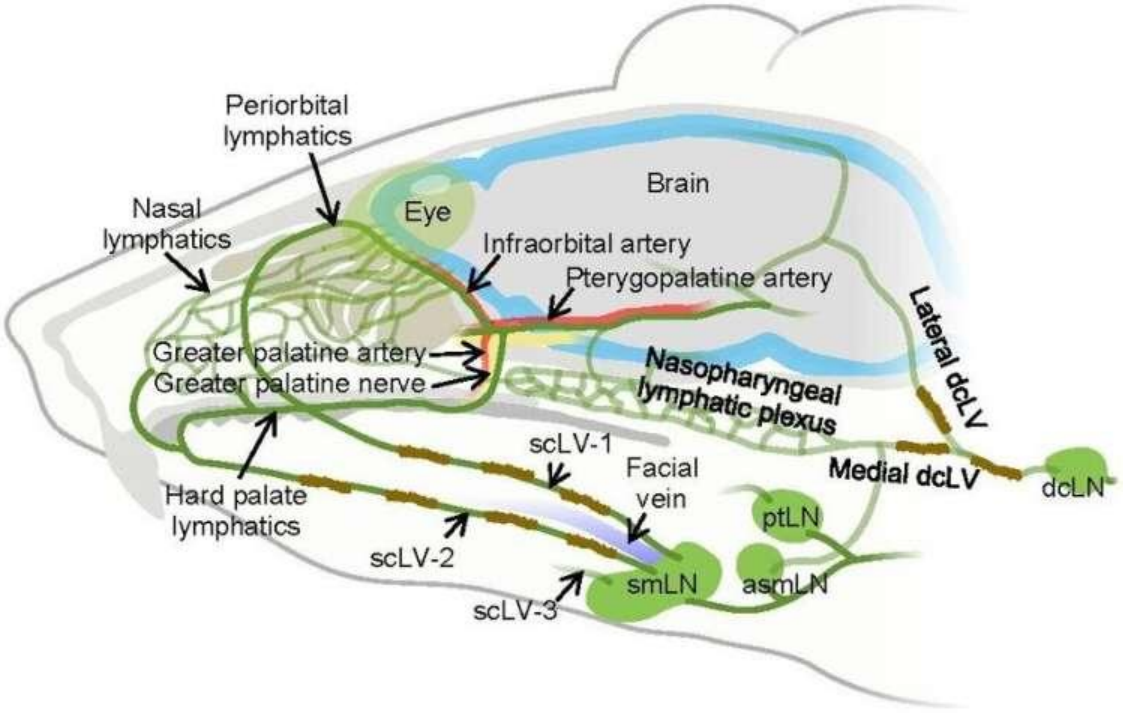
**More information:** Kai Chen et al, Selective removal of astrocytic PERK protects against glymphatic impairment and decreases toxic aggregation of β-amyloid and tau, *Neuron* (2025). DOI: 10.1016/j.neuron.2025.04.027
**Journal information:** Neuron
Provided by Columbia University Irving Medical Ce

JUNE 4, 2025

# Non-invasive mechanical stimulation can enhance brain waste clearance

by Institute for Basic Science

edited by Sadie Harley, reviewed by Robert Egan




This diagram shows the pathways cerebrospinal fluid (CSF) takes as it flows from the brain's surface through facial lymphatic vessels and into lymph nodes in the neck. Credit: Institute for Basic Science

Scientists at the Institute for Basic Science (IBS) have uncovered a non-invasive method to boost the brain's natural waste drainage system—a discovery that could open new avenues for tackling age-related neurological disorders.

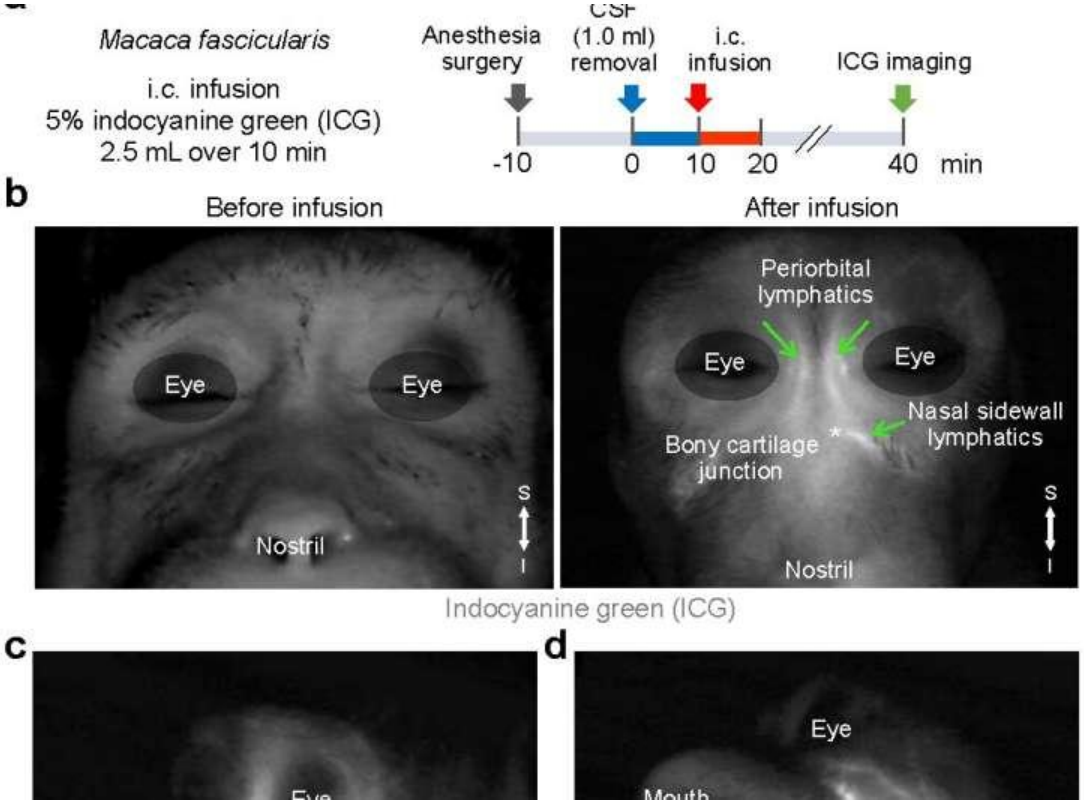
In a study published in *Nature*, researchers from the IBS Center for Vascular Research, led by Director Koh Gou Young, along with senior researchers Jin Hokyung, Yoon Jin-Hui, and principal researcher Hong Seon Pyo, demonstrate that precisely stimulating the lymphatics under skin on the neck and face can significantly enhance the flow of cerebrospinal fluid (CSF)—the liquid that cushions the brain and helps remove toxic waste—through lymphatic vessels.

This offers a new approach to clearing brain waste using safe, non-invasive mechanical stimulation, rather than relying on drugs or surgical interventions.

The human brain produces waste at a high rate compared to other organs, and clearing it efficiently is essential for healthy brain function. This clearance is primarily carried out by CSF, which removes harmful substances such as amyloid-β and tau proteins—key factors in Alzheimer's and other neurodegenerative diseases. However, as we age, this drainage slows down, contributing to cognitive decline.

The IBS Center for Vascular Research previously published landmark studies in *Nature* (2019 and 2024) demonstrating that CSF drains to deep cervical lymph nodes via meningeal lymphatic vessels at the base of the skull and the nasopharyngeal lymphatic plexus. They also showed that age-related degeneration of these lymphatics impairs CSF clearance.

Furthermore, the team found that CSF drainage could be enhanced or suppressed pharmacologically by targeting cervical lymphatic vessels outside the skull. However, clinical applications remained limited because these lymphatics are located too deep in the neck for non-invasive access.



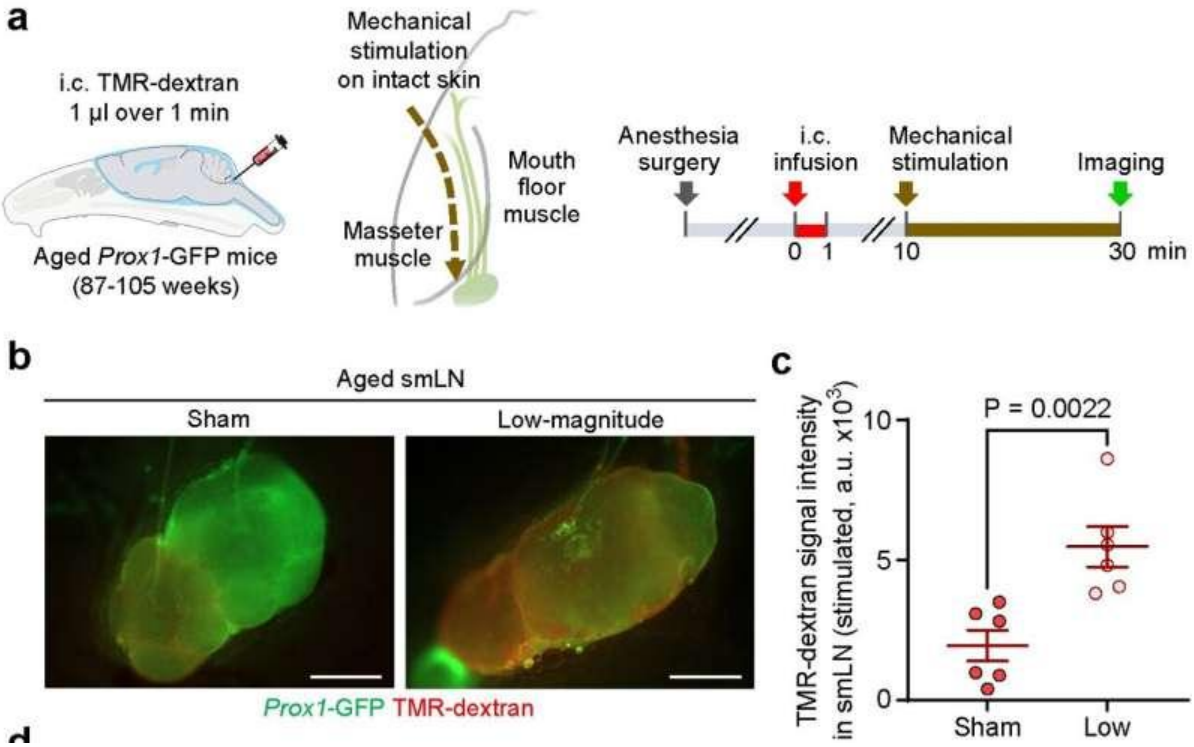
Images show how cerebrospinal fluid (CSF), labeled with a fluorescent tracer, travels through lymphatic vessels around the eyes, nasal area, hard palate, and neck following infusion into the brain. Credit: Institute for Basic Science

"This research not only completed the map of cerebrospinal fluid drainage pathways that clear brain waste, but also provided a new method to enhance CSF drainage from outside the brain," stated Koh Gou Young, Center Director and corresponding author. "We expect this will serve as a milestone for future research on neurodegenerative diseases, including dementia."

Now, using genetically modified mice and monkeys with fluorescent tracers, the researchers have mapped out a new CSF drainage route from the brain to superficial cervical lymph nodes—via a network of lymphatic vessels in the face, nose, and hard palate. In older animals, many of these routes had degenerated—except for the vessels just beneath the facial skin, which retained full functionality despite aging.

"We confirmed that lymphatic vessels beneath facial skin connect to submandibular lymph nodes through various pathways," explained Jin Hokyung, Senior Researcher and co-first author.

"Through these connections, we can regulate the reduced cerebrospinal fluid drainage function seen in aging and neurodegenerative diseases. Further research is needed to determine how this newly identified pathway can be applied in actual patients."




When researchers applied precise light mechanical stimulation to the skin of older mice, brain waste fluid (CSF) drained more efficiently into nearby lymph nodes and lymphatic vessels, as shown in these fluorescent images and supporting graphs. Credit: Institute for Basic Science

Recognizing this, the team developed a force-regulated mechanical stimulator—a handheld device that gently presses and strokes the skin in a controlled manner. When applied to aged mice, the device restored CSF clearance to youthful levels, dramatically improving drainage without disrupting natural lymphatic contractions.

"I am pleased that we found a safer and more effective method to enhance cerebrospinal fluid drainage from outside the skull," said Yoon Jin-Hui, co-first author and neurovascular physiologist. "We are conducting follow-up studies to investigate how this newly identified drainage pathway is altered in various brain disease patients and how this new stimulation method can be applied therapeutically."

This technique could pave the way for wearable or clinical devices that enhance brain waste clearance in older adults or patients with neurological conditions.

The team is now investigating how this drainage system behaves in diseases like Alzheimer's—and whether mechanical stimulation could serve as a preventive or therapeutic tool.

**More information:** Gou Young Koh, Increased CSF drainage by non-invasive manipulation of cervical lymphatics, *Nature* (2025). DOI: 10.1038/s41586-025-09052-5. www.nature.com/articles/s41586-025-09052-5

**Journal information:** Nature
Provided by Institute for Basic Science

JUNE 4, 2025

# Your left and right brain hear language differently. A neuroscientist explains how

by Hysell V. Oviedo, The Conversation

edited by Lisa Lock, reviewed by Andrew Zinin

Credit: Pixabay/CC0 Public Domain

Some of the most complex cognitive functions are possible because different sides of your brain control them. Chief among them is speech perception, the ability to interpret language. In people, the speech perception process is typically dominated by the left hemisphere.

Your brain breaks apart fleeting streams of acoustic information into parallel channels—linguistic, emotional and musical—and acts as a biological multicore processor. Although scientists have recognized this division of cognitive labor for over 160 years, the mechanisms underpinning it remain poorly understood.

Researchers know that distinct subgroups of neurons must be tuned to different frequencies and timing of sound. In recent decades, studies on animal models, especially in rodents, have confirmed that splitting sound processing across the brain is not uniquely human, opening the door to more closely dissecting how this occurs.

Yet a central puzzle persists: What makes near-identical regions in opposite hemispheres of the brain process different types of information?

Answering that question promises broader insight into how experience sculpts neural circuits during critical periods of early development, and why that process is disrupted in neurodevelopmental disorders.

## Timing is everything

Sensory processing of sounds begins in the cochlea, a part of the inner ear where sound frequencies are converted into electricity and forwarded to the auditory cortex of the brain.

Researchers believe that the division of labor across brain hemispheres required to recognize sound patterns begins in this region.

For more than a decade, my work as a neuroscientist has focused on the auditory cortex. My lab has shown that mice process sound differently in the left and right hemispheres of their brains, and we have worked to tease apart the underlying circuitry.

For example, we've found the left side of the brain has more focused, specialized connections that may help detect key features of speech, such as distinguishing one word from another. Meanwhile, the right side is more broadly connected, suited for processing melodies and the intonation of speech.

We tackled the question of how these left-right differences in hearing develop in our latest work, and our results underscore the adage that timing is everything.

We tracked how neural circuits in the left and right auditory cortex develop from early life to adulthood. To do this, we recorded electrical signals in mouse brains to observe how the auditory cortex matures and to see how sound experiences shape its structure.

Surprisingly, we found that the right hemisphere consistently outpaced the left in development, showing more rapid growth and refinement. This suggests there are critical windows of development—brief periods when the brain is especially adaptive and sensitive to environmental sound—specific to each hemisphere that occur at different times.

To test the consequences of this asynchrony, we exposed young mice to specific tones during these sensitive periods. In adulthood, we found that where sound is processed in their brains was permanently skewed. Animals that heard tones during the right hemisphere's earlier critical window had an overrepresentation of those frequencies mapped in the right auditory cortex.

Adding yet another layer of complexity, we found that these critical windows vary by sex. The right hemisphere critical window opens earlier in female mice, and the left hemisphere window opens just days later. In contrast, male mice had a very sensitive right hemisphere critical window, but no detectable window on the left. This points to the elusive role sex may play in brain plasticity.

Our findings provide a new way to understand how different hemispheres of the brain process sound and why this might vary for different people. They also provide evidence that parallel areas of the brain are not interchangeable: the brain can encode the same sound in radically different ways, depending on when it occurs and which hemisphere is primed to receive it.

## Speech and neurodevelopment

The division of labor between brain hemispheres is a hallmark of many human cognitive functions, especially language. This is often disrupted in neuropsychiatric conditions such as autism and schizophrenia.

Reduced language information encoding in the left hemisphere is a strong indication of auditory hallucinations in schizophrenia. And a shift from left- to right-hemisphere language processing is characteristic of autism, where language development is often impaired.

Strikingly, the right hemisphere of people with autism seems to respond earlier to sound than the left hemisphere, echoing the accelerated right-side maturation we saw in our study on mice. Our findings suggest that this early dominance of the right hemisphere in encoding sound information might amplify its control of auditory processing, deepening the imbalance between hemispheres.

These insights deepen our understanding of how language-related areas in the brain typically develop and can help scientists design earlier and more targeted treatments to support early speech, especially for children with neurodevelopmental language disorders.

Provided by The Conversation



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JUNE 5, 2025

# Brain mechanisms that distinguish imagination from reality discovered

by University College London

edited by Sadie Harley, reviewed by Robert Egan

Areas of the brain that help a person differentiate between what is real and what is imaginary have been uncovered in a new study led by UCL researchers.

The research, published in *Neuron*, found that a region in the brain known as the fusiform gyrus—located behind one's temples, on the underside of the brain's temporal lobe—is involved in helping the brain to determine whether what we see is from the external world or generated by our imagination.

The researchers hope that their findings will increase understanding of the cognitive processes that go awry when someone has difficulty judging what is real and what is not, such as in schizophrenia, and could eventually lead to advancement in diagnosing and treating these conditions.

Lead author, Dr. Nadine Dijkstra (Department of Imaging Neuroscience at UCL) said, "Imagine an apple in your mind's eye as vividly as you can. During imagination, many of the same brain regions activate in the same manner as when you see a real apple. Until recently, it remained unclear how the brain distinguishes between these real and imagined experiences."

For the study, researchers asked 26 participants to look at simple visual patterns while imagining them at the same time.

Specifically, participants were asked to look for a specific faint pattern within a noisy background on a screen and indicate whether the pattern was actually present or not. A real pattern was only presented half of the time.

At the same time, participants were also instructed to imagine a pattern that was either the same or different to the one they were looking for, and indicate how vivid their mental images were.

When the patterns were the same, and participants reported that their imagination was very vivid, they were more likely to say they saw a real pattern, even in trials in which nothing was presented. This means they mistook their mental images for reality.

While participants performed the tasks, their brain activity was monitored using functional magnetic resonance imaging (fMRI). This technology enabled the researchers to identify which parts of the brain showed patterns of activity that helped distinguish reality from imagination.

The team found that the strength of activity in the fusiform gyrus could predict whether people judged an experience as real or imagined, irrespective of whether it actually was real.

When activity in the fusiform gyrus was strong, people were more likely to indicate that the pattern was really there.

Usually, activation in the fusiform gyrus is weaker during imagination than during perception, which helps the brain keep the two apart. However, this study showed that sometimes when participants imagined very vividly, activation of the fusiform gyrus was very strong and participants confused their imagination for reality.

Senior author, Professor Steve Fleming (UCL Psychology & Language Sciences) said, "The brain activity in this area of the visual cortex matched the predictions from a computer simulation on how the difference between internally and externally generated experience is determined."

Dr. Dijkstra added, "Our findings suggest that the brain uses the strength of sensory signals to distinguish between imagination and reality."

The study also showed that the fusiform gyrus collaborates with other brain areas to help us decide what is real and what is imagined.

Specifically, activity in the anterior insula—a brain region in the prefrontal cortex (the front part of the brain that acts as a control center for tasks such as decision-making, problem solving and planning)—increased in line with activity in the fusiform gyrus when participants said something was real, even if it was in fact imagined.

Professor Fleming said, "These areas of the prefrontal cortex have previously been implicated in metacognition—the ability to think about our own minds. Our results indicate that the same brain areas are also involved in deciding what is real."

These results offer new insights into what might go wrong in the brain during psychiatric conditions like schizophrenia, where patients struggle to keep apart imagination and reality. The findings may also inform future virtual reality technologies by identifying how and when imagined experiences feel real.

The research was conducted in collaboration with Professor Peter Kok (Department of Imaging Neuroscience at UCL) and former UCL Masters student Thomas von Rein.

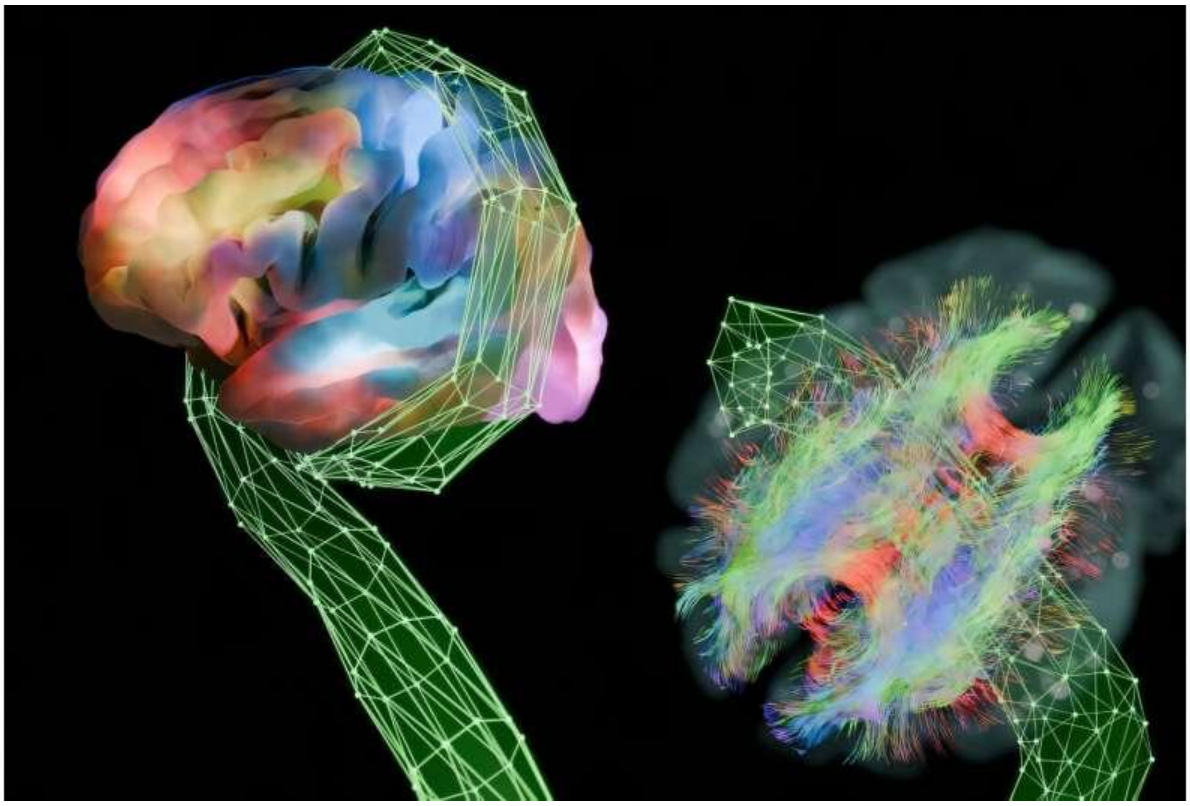
**More information:** A neural basis for distinguishing imagination from reality, *Neuron* (2025). DOI: 10.1016/j.neuron.2025.05.015. www.cell.com/neuron/fulltext/S0896-6273(25)00362-9
**Journal information:** Neuron
Provided by University College London

JUNE 5, 2025

# Algorithm maps the connections between the brain's structure and function

by Weill Cornell Medical College

edited by Lisa Lock, reviewed by Andrew Zinin



The Krakencoder's many arms align and fuse complementary maps of brain connectivity. Credit: Keith Jamison

Using an algorithm they call the Krakencoder, researchers at Weill Cornell Medicine are a step closer to unraveling how the brain's wiring supports the way we think and act.

The study, published June 5 in *Nature Methods*, used imaging data from the Human Connectome Project to align neural activity with its underlying circuitry.

Mapping how the brain's anatomical connections and activity patterns relate to behavior is crucial not only for understanding how the brain works generally but also for identifying biomarkers of disease, predicting outcomes in neurological disorders and designing personalized interventions.

## Addressing the elephant in the room

The brain consists of a complex network of interconnected neurons whose collective activity drives our behavior. The structural connectome represents the physical wiring of the brain, the map of how different regions are anatomically connected. The other piece of the puzzle is the functional connectome, which represents patterns of neuronal activity between different parts of the brain, highlighting regions that activate together during specific tasks or at rest. Surprisingly, scientists have found that regions that are "wired together" don't always "fire together."

"But we're still just scratching the surface of how brain networks relate to the tasks of everyday life, like solving a math problem, having a conversation with a friend or driving a car," said senior author Dr. Amy Kuceyeski, professor of mathematics in radiology and in neuroscience at Weill Cornell Medicine.

While many researchers are modeling the relationship between functional and structural connectomes, they come up with different maps. "Everybody uses different methods to take pictures of the brain's networks," Dr. Kuceyeski explained. For example, when using magnetic resonance imaging (MRI) for brain scans, different methods for processing the same raw images can generate different connectomes.

Dr. Kuceyeski likens this patchwork approach to examining an elephant in a dark room, where one person is touching the trunk, somebody a leg, someone else an ear. "Our fundamental assumption is that each set of choices in the imaging and processing pipelines provides a different view of the same underlying system," said Keith Jamison, the study's first author and a research associate in Dr. Kuceyeski's lab.

To get a more comprehensive representation, Dr. Kuceyeski and her team built a tool that could take the structural and functional connectomes produced by all of these disparate approaches and collapse them together to produce a more unified interpretation.

"In my head, I saw it as some sort of monster with multiple arms that could reach out and grab different brain representations and digest and congeal them into one unified connectome," Jamison said. The resulting program, an autoencoder that compresses and reconstructs more than a dozen different "flavors" of input data, thus came to be called the Krakencoder.

## Identifying connections that restore lost function

The team trained the Krakencoder on data collected from more than 700 subjects who participated in the National Institutes of Health's Human Connectome Project. As part of that study, volunteers underwent extensive structural and functional MRI scanning.

The researchers found that the Krakencoder allowed them to take an individual's structural connectome and correctly predict that person's functional connectome about 20 times more accurately than previously published approaches.

The Krakencoder's combined and compressed representation also predicted the individual's age, sex and their cognitive performance scores received on tests which had been administered along with their imaging scans. Such scores, Dr. Kuceyeski noted, are notoriously difficult to gauge based on brain imaging alone.

Being able to map functions like cognition to specific brain networks is key to understanding how anatomy and physiology give rise to our behaviors and abilities—and how diseases and injuries can impair our performance.

In the future, Dr. Kuceyeski and her colleagues plan to combine the Krakencoder with a network modification tool they call NeMo that will allow them to examine the connectomes of people whose brains have been damaged by diseases. Christie Gillies, a Ph.D. student in the Kuceyeski Lab, is using this approach to map outcomes following stroke.

"She's comparing the functional connectome produced by the NeMo + Krakencoder pipeline, based only on MRIs regularly collected in the clinic, to the actual functional MRI of a person. We found that our functional connectomes do a better job at predicting an individual's motor scores and language scores at follow up," Dr. Kuceyeski said.

These tools could also identify brain network connections associated with improved cognitive or motor performance. Boosting the activity of damaged circuits—for example, through transcranial magnetic stimulation, a treatment that uses magnetic pulses to stimulate nerve cells in the brain—could strengthen those connections and hasten recovery.

**More information:** Keith W. Jamison et al, Krakencoder: a unified brain connectome translation and fusion tool, *Nature Methods* (2025). DOI: 10.1038/s41592-025-02706-2
**Journal information:** Nature Methods
Provided by Weill Cornell Medical College

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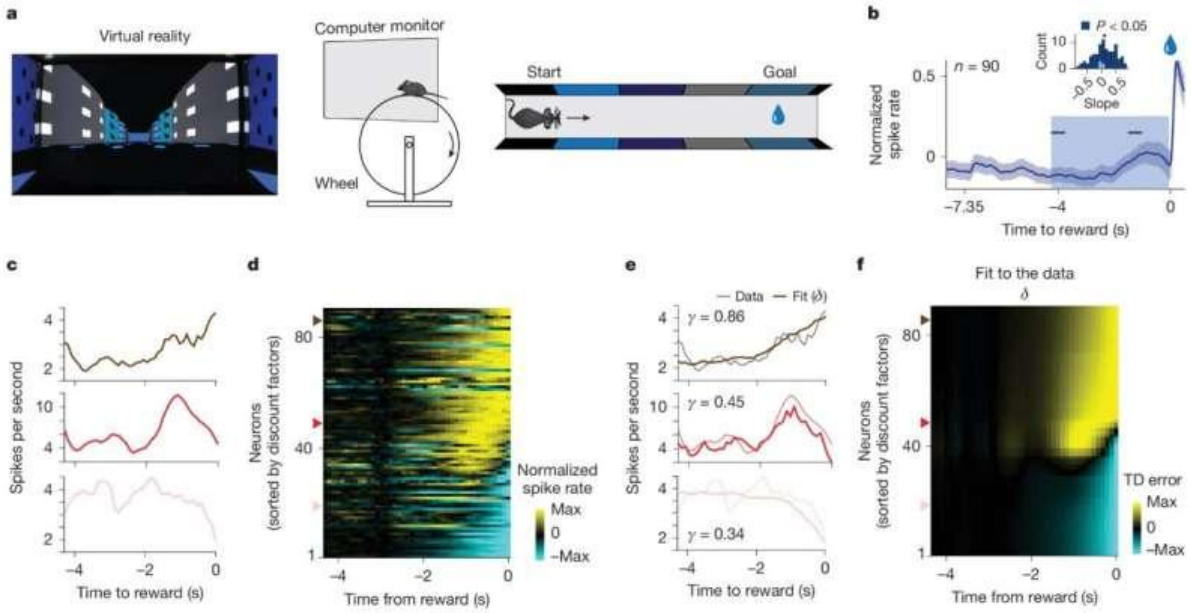
JUNE 5, 2025

# Algorithm reveals how a small region in our brain plays a key role in motivation

by University of Geneva

edited by Lisa Lock, reviewed by Robert Egan




The diversity of discount factors across dopaminergic neurons explains qualitatively different ramping activity. Credit: *Nature* (2025). DOI: 10.1038/s41586-025-08929-9

A small region of the brain, known as the ventral tegmental area (VTA), plays a key role in how we process rewards. It produces dopamine, a neuromodulator that helps predict future rewards based on contextual cues. A team from the universities of Geneva (UNIGE), Harvard, and McGill has shown that the VTA goes even further: It encodes not only the anticipated reward but also the precise moment it is expected.

This discovery, made possible by a machine learning algorithm, highlights the value of combining artificial intelligence with neuroscience. The study is published in the journal *Nature*.

The ventral tegmental area (VTA) plays a key role in motivation and the brain's reward circuit. The main source of dopamine, this small cluster of neurons sends this

neuromodulator to other brain regions to trigger an action in response to a positive stimulus.

"Initially, the VTA was thought to be merely the brain's reward center. But in the 1990s, scientists discovered that it doesn't encode reward itself, but rather the prediction of reward," explains Alexandre Pouget, full professor in the Department of Basic Neurosciences in the UNIGE Faculty of Medicine.

Experiments on animals have shown that when a reward consistently follows a light signal, for example, the VTA eventually releases dopamine not at the moment of the reward, but as soon as the signal appears. This response therefore encodes the prediction of the reward—linked to the signal—rather than the reward itself.

## A much more sophisticated function

This "reinforcement learning," which requires minimal supervision, is central to human learning. It's also the principle behind many artificial intelligence algorithms that improve performance through training—such as AlphaGo, the first algorithm to defeat a world champion in the game of Go.

In the recent study, Pouget's team, in collaboration with Naoshige Uchida of Harvard University and Paul Masset of McGill University, shows that the VTA's coding is even more sophisticated than previously thought. "Rather than predicting a weighted sum of future rewards, the VTA predicts their temporal evolution. In other words, each gain is represented separately, with the precise moment at which it is expected," explains the UNIGE researcher, who led this work.

"While we knew that VTA neurons prioritized rewards close in time over the ones further in the future—on the principle of a bird in the hand is worth two in the bush—we discovered that different neurons do so on different time scales, with some focus on the reward possible in a few seconds' time, others on the reward expected in a minute's time, and others on more distant horizons.

"This diversity is what allows the encoding of reward timing. This much finer representation gives the learning system great flexibility, allowing it to adapt to maximize immediate or delayed rewards, depending on the individual's goals and priorities."

## AI and neuroscience: A two-way street

These findings stem from a fruitful dialogue between neuroscience and artificial intelligence. Pouget developed a purely mathematical algorithm that incorporates the timing of reward processing. Meanwhile, the Harvard researchers gathered extensive neurophysiological data on VTA activity in animals experiencing rewards. "They then applied our algorithm to their data and found that the results matched perfectly with their empirical findings."

While the brain inspires AI and machine learning techniques, these results demonstrate that algorithms can also serve as powerful tools to reveal our neurophysiological mechanisms.

**More information:** Paul Masset et al, Multi-timescale reinforcement learning in the brain, *Nature* (2025). DOI: 10.1038/s41586-025-08929-9
**Journal information:** Nature
Provided by University of Geneva

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FAITH & SCIENCE NEUROSCIENCE & MIND

# Two Neuroscientists on Life, Death, Eternity, and What Really Matters June 5, 2025

This week, Michael Egnor, first author of the new book *The Immortal Mind* (Worthy 2025), did a podcast with a fellow neurosurgeon, Dr. Lee Warren, whose program is heard in over 70 countries.

Display "The Immortal Mind, with Dr. Michael Egnor (S12E48)" from YouTube

Warren is himself the author of *Hope Is the First Dose* (Waterbrook 2023), offering help in recovering from trauma, tragedy, and "other massive things." In addition, he is an inventor who "holds two U.S. patents for minimally invasive surgical equipment and is the inventor of numerous high-impact medical devices."

Despite the fact that both participants in the discussion are brain surgeons, it remained a lively and accessible chat about how the human mind is not simply the brain and can even survive death. Some excerpts:

## A Normal Conversation with a Patient While Removing Part of Her Brain (at 23:13)

***Egnor**: I have quite a few patients — and I'm sure you've seen the same thing, I think neurosurgeons encounter this — with missing parts of their brains who are really in pretty good shape. You know, obviously there are parts of your brain that you can't do without … there are parts that are very intolerant of injury but there are other parts that really you can do just fine without. That always struck me as bizarre and that wasn't in my neuroscience textbooks.*

*What really kind of brought it to a head was I was doing an awake brain operation many years ago. I don't do a lot of them; it's not my specialty within neurosurgery but I was doing it on a woman who had a left frontal lobe astrocytoma [tumor] which was lowgrade but it was infiltrating a lot of her left frontal lobe.*

*I wanted to make sure I protected her speech area so I did an awake procedure (you can do [24:02] brain surgery awake, of course, with local anesthesia so people don't feel pain. I'm mapping her frontal lobe by stimulating her brain and finding out where her speech area is so I can protect it.*

*As I remove the tumor — and I'm taking out a substantial portion of the frontal lobe to get the tumor out — I'm talking to her. I'm having a conversation with her and it's a perfectly normal conversation. We're talking about the weather, her family, the cafeteria food in the hospital, and it goes on for several hours as we're taking out the tumor.*

*And at the end of the case, she did very well. she did nicely, made a good recovery.*

*I was flabbergasted. I'm thinking, here I am, taking out a major part of this lady's brain. I might as well have been cutting her hair! I mean, she showed no response but my none of my textbooks explained that you could do that… So clearly, there was something different about the mind–brain relationship than what was in the textbooks. So I began looking at the neuroscience of it.*

This experience led Egnor to study, among other things, the work of pioneer neurosurgeon Wilder Penfield (1891–1976). Over many years of observations from neurosurgery, Penfield reached a similar conclusion to Egnor's. He had started by understanding the mind as a mere product of the brain but came to see it as distinct from the brain.

That journey resulted in *Mystery of the Mind* (Princeton 1975), in which he concluded, "The brain has not explained the mind fully." Many neuroscience discoveries and achievements later, Egnor finds the same thing.

## The Mind's Hope of Eternity (at 37:41)

The two neurosurgeons got into some really deep emotional stuff at this point:

***Warren**: For the person who's listening out there somewhere that's, say, going through something hard in their life — they've lost somebody — or a lot of our listeners will be like me, somebody who lost a child or somebody's going through something.*

***Egnor**: I'm so sorry. I'm so sorry. I — I lost a child too…*

***Warren**: I'm so sorry, yeah, But a lot of the listeners that find my work do so because they've read my books where I've talked about that. So there may be somebody out there who's listening and saying "Why does this stuff matter?" Like, why does it, how does it help me find hope to know that my mind and my brain aren't the same thing?*

***Egnor**: That's a great question, a great question, and it's a question that I think is really at the heart of what I'm doing. It's at the heart of what you're doing.*

*Pointing out that the scientific truth that we see is something that is not just an academic exercise. This is not something to just do in the musty halls of universities. This matters in people's lives. It matters enormously and it's given me enormous comfort.*

*As you mentioned, the loss of a loved one can really be a devastating event. And what helps me is the understanding — and I think this is absolutely true — that we have immortal souls, that when we die, our souls don't cease to exist. I believe that the Christian way of understanding eternity, of understanding our future, is true. So I know that my son, who passed away a few years ago, is in heaven and we will meet again. We will spend eternity together and it is unbelievably reassuring. It doesn't take all the pain away; there's still pain there but I know that death is not permanent. Death is a transition from this earthly life to a to a life with God, to a life where you go back to the source of love to the source of beauty and holiness.*

Chapter 5 of *The Immortal Mind* talks about veridical near-death experiences, where people report seeing things during NDEs that can later be verified. Chapter 6 addresses objections from skeptics. These experiences add to the evidence that the mind can act independently of the brain. Arguments for the immortality of the soul beyond that are addressed in Chapter 7.

*Cross-posted at Mind Matters News.*

ID THE FUTURE JUNE 11, 2025

# Michael Egnor Reads From His New Book The Immortal Mind

On this **ID The Future**, Dr. Michael Egnor reads the Introduction to his new book *The Immortal Mind: A Neurosurgeon's Case for the Existence of the Soul*, now available from Worthy Books.
In this reading, Dr. Egnor shares his journey from being a medical student who believed science could explain everything, including how consciousness emerges from the brain and whether we have a soul, to a neurosurgeon who questioned the conventional materialist view. He discusses how years of operating on and examining patients with brain damage led him to wonder how large parts of the brain could be removed without affecting a person's mind or their ability to think, reason, believe, and desire. His personal story, including a profound experience in a hospital chapel during a family crisis, became a turning point that challenged his atheism and led him to believe that the immaterial aspects of our minds are real and that nature is an open system, not a closed one. With the Introduction, Dr. Egnor sets the stage for his book's exploration of how modern neuroscience and medicine offer compelling scientific evidence for the existence of the human soul. He argues that some abilities of the mind are actually separate from the brain, that our souls do not cease to live when our bodies die, and that minds can continue to exist and function even when brains are severely damaged. After 40 years

of clinical practice and tens of thousands of patients, Dr. Egnor came to realize that “none of the materialist explanations we hear is the least bit credible.” It’s time to reject materialism as a model for the origin of mind and opt for the theory that better explains the scientific evidence: intelligent design.

Discover a neurosurgeon’s unique perspective, informed by over 7,000 brain operations, as he makes the case that human beings are spiritual, not merely physical creatures, and that science is compatible with the inference to God’s existence and the reality of the human soul.

## Michael Egnor

**PROFESSOR OF NEUROSURGERY AND PEDIATRICS**, STATE UNIVERSITY OF NEW YORK, STONY BROOK

Michael R. Egnor, MD, is a Professor of Neurosurgery and Pediatrics at State University of New York, Stony Brook, has served as the Director of Pediatric Neurosurgery, and is an award-winning brain surgeon. He was named one of New York’s best doctors by the *New York Magazine* in 2005. His book, *The Immortal Mind: A neurosurgeon’s case for the existence of the soul,* co-authored by Denyse O’Leary, was published by Worthy on June 3, 2025.

ID THE FUTURE JUNE 6, 2025

# Engineered Complexity in the Microbial World

On this **ID the Future** from the archive, host Jonathan Witt speaks to molecular biologist and professor Dustin Van Hofwegen about his research into the engineered complexity in microbial life. The two sat down at a previous Conference on Engineering in Living Systems to discuss the event, which brings together biologists and engineers to study how engineering principles can be applied to living things, as well as Hofwegen’s article in the *Journal of Bacteriology*, co-authored with Carolyn Hovde and Scott Minnich, based on research conducted at the University of Idaho.

Hofwegen shares his research on the famous decades-long E. coli evolution experiment conducted by Richard Lenski, which showed the sudden appearance of an ability to utilize citrate after many generations. However, Van Hofwegen's own experiments demonstrated that this "evolutionary innovation" could occur much faster and repeatedly under stressful conditions, suggesting it was not a random evolutionary leap but rather the activation of pre-existing genetic mechanisms, akin to flipping a switch. The discussion highlights that many biological "adaptations" may involve the use of innate abilities or the disruption of existing functions, rather than the creation of entirely new ones, supporting the idea of engineered complexity in microbial life.

## Dustin Van Hofwegen

**ASSISTANT PROFESSOR OF BIOLOGY & BIOCHEMISTRY**, UNIVERSITY OF NORTHWESTERN, ST. PAUL

Dustin Van Hofwegen, a biology professor at Azusa Pacific University in California, specializes in microbial genomics, bacterial evolution, and molecular mechanisms of gene regulation in bacteria. His research explores the role of post-transcriptional gene regulation mediated by small RNAs in bacterial model systems E. coli and Yersinia. He received his PhD from the University of Idaho and did postdoctoral research at Rocky Mountain Laboratories, the National Institute of Allergy and Infectious Diseases (NIAID), and the National Institutes of Health (NIH).

Image Credit: Monika Gruszewicz - Adobe Stock

ID THE FUTURE JUNE 9, 2025

# Jay Richards on the "Ground Clearing" Work of Jonathan Wells

Before the positive case for intelligent design can be received effectively, the case against the Darwinian evolutionary mechanism must be clearly laid out. One man who was instrumental in this initial "ground clearing operation" was biologist Dr. Jonathan Wells, our friend and colleague who

passed away in 2024 at the age of 82. On this **ID The Future**, host Andrew McDiarmid welcomes Dr. Jay Richards to the podcast to share his memories of Dr. Wells and discuss the significance of Wells's life and work. The conversation highlights Wells's early and deep understanding of biological complexity, even in the late 1990s. Richards recalls Wells explaining that the information in organisms goes "way beyond" the sequential information in DNA. Wells perceived "orders of information" and "extra sources of information" coordinating organismal development, which couldn't simply be located in DNA. He had a sense of the immateriality of the genome and anticipated the need for new categories and theories to account for what happens in organisms.

Dr. Richards also describes his experience working closely with Wells on the classic book *Icons of Evolution*. Wells's 2000 book was highly accessible and served as part of that necessary "ground clearing operation" showing that the reigning Darwinian explanation was inadequate by examining its pedagogical tools and claims, such as the infamous and long-known-inaccurate Haeckel's embryos. Wells argued in *Icons* that Darwinism made predictions contrary to evidence and was a "paradigm that's either spent or really never fit the facts."

The episode also covers Wells' intense work on *Getting the Facts Straight*, a viewer's guide to the 2001 PBS series *Evolution*, which failed to accurately represent shortcomings of Darwinian theory and dismissed its critics. Wells was the primary author on the viewer's guide, working diligently for weeks on it. The critique aimed to counter the series, especially because it was also turned into curriculum for use in public schools across America.

## Dig Deeper

- Dr. Wells's viewer's guide *Getting the Facts Straight* is available for free download.
- Learn more about Dr. Jonathan Wells' work and order his books at jonathanwells.org.

# Jay W. Richards

**SENIOR FELLOW** AT DISCOVERY, SENIOR RESEARCH FELLOW AT HERITAGE FOUNDATION

Jay W. Richards, Ph.D., is the Director of the DeVos Center and William E. Simon Senior Research Fellow at the Heritage Foundation, and a Senior Fellow at Discovery Institute. Richards is author or editor of more than a dozen books, including the *New York Times* bestsellers *Infiltrated* (2013) and *Indivisible* (2012); *The Human Advantage*; *Money, Greed, and God*, winner of a 2010 Templeton Enterprise Award; *The Hobbit Party* with Jonathan Witt; *The Privileged Planet* with Guillermo Gonzalez, coming out in a second edition in 2024; *The Price of Panic: How the Tyranny of Experts Turned a Pandemic Into a Catastrophe* with Douglas Axe and William Briggs; and *Eat, Fast, Feast*. His most recent book, with James Robison, is *Fight the Good Fight: How an Alliance of Faith and Reason Can Win the Culture War*.



INTELLIGENT DESIGN



LIFE SCIENCES

# The Most Unnatural Thing in the Universe

*Andrew McDiarmid* May 29, 2025

We usually think of life as the most natural thing there is — blooming plants, flowing water, the cycles of nature. But what if that perspective is fundamentally challenged by the very laws of physics that govern our

universe? On a new episode of *ID the Future*, I welcome physicist Dr. Eric Hedin to the podcast to discuss the compelling idea that life is the most "unnatural" thing in the universe. Dr. Hedin contends that the complex, organized nature of life defies the natural tendency of matter and energy towards disorder and equilibrium, suggesting that life requires something only an intelligent designer could provide.

If the natural state of matter is movement toward the lowest possible energy state, then why aren't all of us lumps of organic matter lying in a puddle on the ground? Dr. Hedin lays out two reasons living things are able to defy that fate. The first involves the specified complexity built into living things: "One is the extremely complex, specific functional mechanism of the living organism. Creating that in itself represents a far detour from any sort of equilibrium state. And so therefore nature would avoid it." Add to that the remarkable ability of living things to push back on the tendency toward lowest energy state by generating movement — be it running, flying, jumping, dancing, swimming, or eating — and you've got the makings of a formidable challenge to naturalism.

Dr. Hedin concludes that the unnatural qualities and complexity of life point to the necessity of an intelligent designer who can orchestrate the detour of matter into functional living forms. And although that detour seems temporary, Hedin also touches on how the argument for intelligent design in life can support a rational hope for the immortality of life beyond physical death, drawing on the idea of a transcendent origin for life. **Download the podcast or listen to it here**.

## Dig Deeper

- Dr. Hedin provides more evidence for intelligent design in living things in his book *Canceled Science*.
- Enjoy more conversation with Dr. Hedin here.

# ANDREW MCDIARMID

DIRECTOR OF PODCASTING AND SENIOR FELLOW
Andrew McDiarmid is Director of Podcasting and a Senior Fellow at the Discovery Institute. He is also a contributing writer to *Mind Matters*. He produces *ID The Future*, a podcast from the Center for Science & Culture that presents the case, research, and implications of intelligent design and explores the debate over evolution. He writes and

speaks regularly on the impact of technology on human living. His work has appeared in numerous publications, including the *New York Post*, *Houston Chronicle*, *The Daily Wire*, *San Francisco Chronicle*, *Real Clear Politics*, *Newsmax*, *The American Spectator*, *The Federalist*, *Technoskeptic Magazine*, and elsewhere. In addition to his roles at the Discovery Institute, he promotes his homeland as host of the Scottish culture and music podcast Simply Scottish. Andrew holds an MA in Teaching from Seattle Pacific University and a BA in English/Creative Writing from the University of Washington.

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JUNE 10, 2025

# CO-TENG: An origami-inspired self-powering sensor for smart wearables

by Shibaura Institute of Technology edited by Gaby Clark, reviewed by Robert Egan

Overview of O-TENG soft sensor. a) Configuration. O-TENG is constructed by laminating PTFE sheet as a charging layer and a copper sheet as an electrode layer on paper. b) Self-folding process. The paper automatically folds along the printed line, and creates an origami device. c) Operating process. The hinge has elastic memory properties and returns to its original shape after the force is released. d) Voltage generation mechanism. The electrical imbalance caused by the charged PTFE causes charges to move within the system, which generates a voltage. Credit: *Advanced Materials Technologies* (2025). DOI: 10.1002/admt.202500032

Origami, the Japanese art of paper folding, has evolved from a primarily ceremonial and decorative practice to an important tool in science and technology. With its applications ranging from solar panels in space to self-assembling robots, origami has revolutionized the design of modern engineering solutions.

One such notable solution is a corrugated origami triboelectric nanogenerator (CO-TENG), a smart, flexible energy-harvesting sensor that combines the triboelectric effect with self-folding technology for generating power. Triboelectric generation is the process of producing electricity by converting mechanical motion—such as contact and separation between materials—into electrical energy.

Recently, a team of researchers led by Associate Professor Hiroki Shigemune from Shibaura Institute of Technology, Japan, along with Mr. Haruki Higoshi and Mr. Daichi Naritomi from Shibaura Institute of Technology, Japan, developed a CO-TENG soft sensor to eliminate the need for batteries. In this study, the team laminated copper electrodes

(conductive layer) and a polytetrafluoroethylene sheet (triboelectric layer) onto paper. The self-folding solution was then printed in lines on the substrate using an inkjet printer.

By assembling the paper into a 3D structure, the researchers achieved a lightweight, low-cost, environmentally friendly, and self-powered sensor. This study was published online in the journal *Advanced Materials Technologies* on April 1, 2025.

Researchers from Japan have developed a novel CO-TENG sensor that utilizes paper self-folding technology and triboelectric power generation. This lightweight, low-cost, and environmentally friendly sensor holds significant potential for real-world applications in wearable health monitoring systems. Credit: Dr. Hiroki Shigemune from Shibaura Institute of Technology, Japan Source link: https://advanced.onlinelibrary.wiley.com/doi/10.1002/admt.202500032
"We were inspired by the structural elegance of origami and the rising need for sustainable, maintenance-free sensor solutions. So, we combined origami with the triboelectric effect to unlock a smart system that can build and power itself," says Dr. Shigemune.

The device operates by converting mechanical stress into electrical signals through friction between laminated conductive and dielectric materials. Since the sensor also utilizes self-folding paper technology, it does not need manual folding and minimizes the fabrication effort—offering a powerful tool for next-generation smart devices.

Once developed, the mechanical properties of the self-folding paper-based structures were thoroughly studied, analyzing how the printed line width and paper thickness affected fold angles and restoring force. They first tested the parameters for a single fold and then scaled it up to a multi-fold corrugated structure to enhance output performance. Notably, serial connection of multiple origami folds led to a significant enhancement in power output with excellent durability over 1,000 compression cycles.

Furthermore, the researchers demonstrated its real-world application in a smart cushioning system. Whenever an object was dropped onto the CO-TENG, it generated electrical signals corresponding to the compression force exerted by the object. These signals were analyzed using machine learning (LightGBM), and this enabled the system to identify the objects. The system could identify the objects with a remarkable 98.9% accuracy—highlighting its potential applications in logistics and smart packaging.

Researchers from Japan have developed a novel battery-free, lightweight, and low-cost sensor called CO-TENG that utilizes paper self-folding technology and triboelectric power generation. It holds significant potential for real-world applications as a smart cushioning sensor for logistics, wearable electronics, and sustainable packaging. Credit: Dr. Hiroki Shigemune from Shibaura Institute of Technology, Japan Source link: https://advanced.onlinelibrary.wiley.com/doi/10.1002/admt.202500032
"Smart cushioning could be a game-changer in logistics. By using the CO-TENG system, dropped objects can be automatically identified and monitored in real-time, offering new capabilities in shipment tracking and product integrity verification," explains Mr. Higoshi.

Apart from logistics, the developed nanogenerator also finds applications in the medical device and electronics industry. The high flexibility of the CO-TENG can be advantageous

for wearable devices for monitoring body motion, posture, or external impacts in real-time—especially for elderly care. Its compact design makes it ideal for soft, mobile, and on-demand devices with promising applications in IoT-based personalized health monitoring platforms.

Apart from its properties, the foldable nature of CO-TENG also reduces storage and transportation costs, which are essential for industrial applications and scalability.

**More information:** Haruki Higoshi et al, Self-Folded Corrugated Origami Sensor Based on Triboelectric Nanogenerator for a Smart Cushioning Device, *Advanced Materials Technologies* (2025). DOI: 10.1002/admt.202500032
**Journal information:** Advanced Materials Technologies
Provided by Shibaura Institute of Technology

JUNE 10, 2025

# Stem cell platform aims to recreate brain's immune system using lab-grown human microglia cells

by Harvard University edited by Gaby Clark, reviewed by Robert Egan

This image shows how human iPSCs in which the microglia-specifying six-TF cocktail is switched on (lower row), in contrast to iPSCs in which they remain switched off (upper row), abandon their pluripotency stage (marked by the protein OCT4) and adopt the fate of microglia cells (marked by the proteins CD11b, P2RY12, and CX3CR1). Credit: Wyss Institute at Harvard University

Microglia are a specialized type of immune cell that accounts for about 10% of all cells within the brain and spinal cord. They function by eliminating infectious microbes, dead cells, and aggregated proteins, as well as soluble antigens that may endanger the brain and, during development, also help shape neural circuits enabling specific brain functions.

When microglia don't function properly, they can trigger neuroinflammation and fail to clear away damaged cells and harmful protein clumps—such as the neurofibrillary tangles and amyloid plaques seen in Alzheimer's disease. This contributes to numerous neurodegenerative diseases, including Alzheimer's, Parkinson's and Huntington's disease, as well as amyotrophic lateral sclerosis (ALS), multiple sclerosis, and other disorders. In fact, neuroinflammation can occur even before proteins start to form pathogenic aggregates and, in turn, accelerates protein aggregation.

Researchers and drug developers aiming to better understand and target microglia functions in the brain are challenged by the fact that human microglia can only be obtained through biopsies, and rodents' microglia differ from their human counterparts in many critical features. This supply issue prompted them to work on methods to create microglia in the culture dish using stem cells as a starting point. However, to date, this process has remained inefficient, and requires weeks to complete at significant costs.

Now, a research team at the Wyss Institute at Harvard University and Harvard Medical School (HMS) led by Wyss Founding Core Faculty member George Church, Ph.D. has devised a solution for creating microglia with strong functional similarities to human microglia from induced pluripotent stem cells (iPSCs) within four days, compared to 35 days it takes to obtain similar, yet less fine-tuned cells in a conventional differentiation process.

Their approach builds on a previously developed technology known as TFome™ that can be used to drive multiple cell differentiation processes in the dish more efficiently than other methods can. In TFome™ technology, critical instructive proteins known as transcription factors (TFs) that orchestrate entire gene expression programs are expressed in iPSCs to specify their fate toward differentiated functional cell types.

In their new study, the team designed microglia-specific libraries of TFs, and then performed iterative rounds of screening distinct combinations of TFs for their ability to convert iPSCs to microglia-like cells. To investigate individual resulting cells, they used single cell RNA sequencing (scRNA-seq) technology to determine how similar their gene expression had become to that of actual microglia.

Through this process, they identified a potent cocktail of six TFs enabling the ultra-fast production of microglia-like cells. Their findings are published in *Nature Communications*.

"We advance transcription factor libraries as a platform technology here in a synthetic biology paradigm. By integrating it with single-cell RNA data-driven analysis and iterative rounds of optimization, we succeeded in creating much sought-after human microglia cells in the dish," said Church.

"This cell differentiation approach can open many avenues of brain disease-focused research and new therapeutic perspectives. Equally relevant, it can be applied to the generation of other hard-to-get and therapeutically relevant cell types that require complex transcriptional scenarios." Church is also Professor of Genetics at HMS and Professor of Health Sciences and Technology at Harvard and MIT.

FITC channel of microscopy analysis of the uptake of pHrodo-labeled S. aureus Bioparficles over fime. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-59596-3

# Organoid beginnings

In 2021, co-authors Alex Ng, Ph.D., and Parastoo Khoshakhlagh, Ph.D. had created a comprehensive library of 1,732 human TFs and their variants, a vital piece of the TFome™ platform technology, and identified individual TFs with the ability to generate specific cell types for potential use in the accelerated manufacturing of next-generation cell therapies.

Ng and Khoshakhlagh, together with Church and former HMS researchers Cory Smith, Ph.D., founded the startup GC Therapeutics to further commercialize their cell engineering technology to create next-generation cell therapy products. In this new study, Church's team at the Wyss and HMS further advanced the utility of their TFome™ platform.

In Church's group at the Wyss and HMS, the interest in microglia was initially sparked by earlier studies on lab-grown microtissues recapitulating functional and organizational features of the brain, also known as brain organoids.

"In our efforts to develop human brain organoids with features from patients who suffer from specific brain disorders, we were able to create tissue constructs containing iPSC-derived neuronal cells, oligodendrocytes, stromal and vascular cells, using TFome™ technology, but in order to capture aspects of neuroinflammation in our studies, we also needed to be able to incorporate microglia," said co-corresponding author Jenny Tam, Ph.D., the Director of the Wyss' Synthetic Biology platform headed by Church.

Church and Tam, together with co-author Katharina Meyer, Ph.D. and other Wyss researchers, are leveraging brain organoid and TFome™ technology in their CircaVent drug discovery platform for mental health conditions like bipolar disorder. "However, we knew that generating microglia would likely require a complex combination of TFs," said Tam.

"To create human microglia cells in vitro, using the TFome™ process, we realized that we don't have to screen the entire library but, based on a large body of earlier developmental and disease studies, could start by making a smart choice," said first-author Songlei Liu, Ph.D., who was a graduate student in Church's group.

"So, we came up with a collection of 40 TFs whose induced gene expression profiles were typical for primary human microglia and devised a strategy to express random combinations of five to seven of them in single iPSCs." Liu was the driving force behind the microglia project in Church's group and now is a platform technology scientist at nChroma Bio.

To determine which TF combinations most effectively induced the gene expression of differentiating microglia, the researchers teamed up with Soumya Raychaudhuri, M.D., Ph.D, a Professor of Medicine at the Brigham and Women's Hospital and of Biomedical Informatics at HMS and a co-corresponding author. Raychaudhuri with his former postdoctoral fellow Fan Zhang, Ph.D., and Li Li, Ph.D., a postdoctoral fellow in Church's group, applied statistical and computational methods that enabled the team to glean microglia-like gene expression changes in scRNA-seq data they acquired from thousands of single cells following only a few days of culture, and then rank the corresponding TF combinations. Zhang, who now is an Assistant Professor at University of Colorado, and Li are co-first authors on the publication.

The result of this first round of screening were three TFs (SPI1, CEBPA, and FLI1) that, together, turned on a microglia-specific differentiation program in iPSCs.

TFiMGLs differentiate quickly, are phagocytic and responsive to ADP stimulation.
Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-59596-3

# Next round is on the platform

Although the cells exhibited desired microglia-like transcriptional and morphological changes, the team realized that they still had not reached the functional maturity of actual primary human microglia.

"We argued that we could go through iterative rounds of this design-screen-validate cycle, meaning that adding new TFs in consecutive rounds could improve outcomes and lead to more superior TF combinations," said Liu.

By looking for additional TFs that were still expressed at lower levels in differentiating iPSCs that received the three-TF cocktail, compared to primary human microglia, and through different computational predictions, the researchers compiled a second set of 42 additional TFs. Their sc-RNA-seq and computational analysis pinpointed another three among them (MEF2C, CEBPB, and IRF8) that, in an expanded six-TF cocktail, advanced microglia differentiation even further.

Liu and the team tested whether the resulting cells, like actual microglia, could be activated by stimuli typical of brain infections and neurodegenerative diseases. They found that the cytokine interferon gamma (IFNg), which increase in the presence of infectious pathogens, induced a microglia-specific gene expression pattern in the differentiated cells.

Also, the so-called TDP-43 protein, which forms aggregates in ALS patients, caused human microglia-like gene expression changes. "Building on this proof-of-concept study, we believe that by identifying additional TFs, developing ways to further fine-tune the expression strength of individual TFs, and order of their appearance on the four-day time scale, we can further hone specific microglia identities and even create microglia subtypes with dedicated functions in the brain," said Liu.

Additional authors on the study are Mariana Garcia-Corral, Patrick Fortuna, Björn van Sambeek, Evan Appleton, Yuancheng Ryan Lu, James Cameron, Ricardo Ramirez, Yuting Chen, Chun-Ting Wu, Jeremy Huang, Yuqi Tan, George Chao, John Aach, and Elaine Lim.

**More information:** Songlei Liu et al, Iterative transcription factor screening enables rapid generation of microglia-like cells from human iPSC, *Nature Communications* (2025). DOI: 10.1038/s41467-025-59596-3
**Journal information:** Nature Communications
Provided by Harvard University

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JUNE 12, 2025

# Training robots without robots: Smart glasses capture first-person task demos

by Ingrid Fadelli, Phys.org edited by Lisa Lock, reviewed by Robert Egan

Human demonstrations are done with only black ovens (top). The policy transfers zero-shot to the robot with the same oven (middle) and also generalizes to a new oven instance (bottom). The points are color-coded to represent the correspondence. Credit: Liu et al.
Over the past few decades, robots have gradually started making their way into various real-world settings, including some malls, airports and hospitals, as well as a few offices and households.

For robots to be deployed on a larger scale, serving as reliable everyday assistants, they should be able to complete a wide range of common manual tasks and chores, such as cleaning, washing the dishes, cooking and doing the laundry.

Training machine learning algorithms that allow robots to successfully complete these tasks can be challenging, as it often requires extensive annotated data and/or demonstration videos showing humans the tasks. Devising more effective methods to collect data to train robotics algorithms could thus be highly advantageous, as it could help to further broaden the capabilities of robots.

Researchers at New York University and UC Berkeley recently introduced EgoZero, a new system to collect ego-centric demonstrations of humans completing specific manual tasks. This system, introduced in a paper posted to the *arXiv* preprint server, relies on the use of Project Aria glasses, the smart glasses for augmented reality (AR) developed by Meta.

"We believe that general-purpose robotics is bottlenecked by a lack of internet-scale data, and that the best way to address this problem would be to collect and learn from first-person human data," Lerrel Pinto, senior author of the paper, told Tech Xplore.

"The primary objectives of this project were to develop a way to collect accurate action-labeled data for robot training, optimize for the ergonomics of the data collection wearables needed, and transfer human behaviors into robot policies with zero robot data."

EgoZero, the new system developed by Pinto and his colleagues, relies on Project Aria smart glasses to easily collect video demonstrations of humans completing tasks while performing robot-executable actions, captured from the point of view of the person wearing the glasses.

These demonstrations can in turn be used to train robotics algorithms on new manipulation policies, which could in turn allow robots to successfully complete various manual tasks.

"Unlike prior works that require multiple calibrated cameras, wrist wearables, or motion capture gloves, EgoZero is unique in that it is able to extract these 3D representations with only smart glasses (Project Aria smart glasses)," explained Ademi Adeniji, student and co-lead author of the paper.

"As a result, robots can learn a new task from as little as 20 minutes of human demonstrations, with no teleoperation."

Architecture diagram. EgoZero trains policies in a unified state-action space defined as egocentric 3D points. Unlike previous methods, EgoZero localizes object points via

triangulation over the camera trajectory, and computes action points via Aria MPS hand pose and a hand estimation model. These points supervise a closed-loop Transformer policy, which is rolled out on unprojected points from an iPhone during inference. Credit: Liu et al.
To evaluate their proposed system, the researchers used it to collect video demonstrations of simple actions that are commonly completed in a household environment (e.g., opening an oven door) and then used these demonstrations to train a machine learning algorithm.

The machine learning algorithm was then deployed on Franka Panda, a robotic arm with a gripper attached at its end. Notably, they found that the robotic arm successfully completed most of the tasks they tested it on, even if the algorithm planning its movements underwent minimal training.

"EgoZero's biggest contribution is that it can transfer human behaviors into robot policies with zero robot data, with just a pair of smart glasses," said Pinto.

"It extends past work (Point Policy) by showing that 3D representations enable efficient robot learning from humans, but completely in-the-wild. We hope this serves as a foundation for future exploration of representations and algorithms to enable human-to-robot learning at scale."

The code for the data collection system introduced by Pinto and his colleagues was published on GitHub and can be easily accessed by other research teams.

In the future, it could be used to rapidly collect datasets to train robotics algorithms, which could contribute to the further development of robots, ultimately facilitating their deployment in a greater number of households and offices worldwide.

"We now hope to explore the tradeoffs between 2D and 3D representations at a larger scale," added Vincent Liu, student and co-lead author of the paper.

"EgoZero and past work (Point Policy, P3PO) have only explored single-task 3D policies, so it would be interesting to extend this framework of learning from 3D points in the form of a fine-tuned LLM/VLM, similar to how modern VLA models are trained."

*Written for you by our author Ingrid Fadelli, edited by Lisa Lock, and fact-checked and reviewed by Robert Egan—this article is the result of careful human work. We rely on readers like you to keep independent science journalism alive. If this reporting matters to you, please consider a donation (especially monthly). You'll get an* ***ad-free*** *account as a thank-you.*

**More information:** Vincent Liu et al, EgoZero: Robot Learning from Smart Glasses, *arXiv* (2025). DOI: 10.48550/arxiv.2505.20290
**Journal information:** arXiv

# BREAKTHROUGH STUDY SHEDS LIGHT ON THE RIDDLE OF HUMAN CREATIVITY

TIM MCMILLAN·AUGUST 12, 2024

Neuroscientists have pinpointed a specific brain region that plays a pivotal role in human creativity, according to the results of a groundbreaking new study.

Published in the journal *BRAIN*, the new study reveals that the brain's Default Mode Network (DMN) plays an instrumental role in driving one of humanity's most mysterious and defining characteristics—creativity.

“Our results suggest that DMN activity is flexibly modulated as a function of specific cognitive processes and supports its causal role in divergent thinking,” researchers wrote. “These findings shed light on the neural constructs supporting different forms of cognition and provide causal evidence for the role of DMN in the generation of original connections among concepts.”

Creativity has long been recognized as a hallmark of human intelligence, setting us apart from all other animals. It is the spark that has driven humanity to produce everything from masterpieces like Leonardo da Vinci’s Mona Lisa and William Shakespeare’s Hamlet to countless revolutionary technological innovations. However, the precise neural mechanisms underlying creativity have remained elusive despite its importance.

A recent study by researchers from the University of Utah Health and Baylor College of Medicine has provided compelling evidence that the brain’s Default Mode Network (DMN) is central to generating creative ideas.

The DMN is a large-scale interconnected network primarily composed of the dorsal medial prefrontal cortex, posterior cingulate cortex, precuneus, and angular gyrus regions of the brain. It is most known for being active when the conscious mind is at rest, such as during daydreaming or mindfulness meditation.

Previous research has shown that the DMN becomes deactivated during goal-oriented tasks, such as those requiring visual attention or working memory. These findings have led cognitive scientists to conclude that the network is crucial for the brain’s ability to generate thoughts independent of the immediate external environment, making it essential for imagination, creativity, and the ability to draw connections between seemingly unrelated ideas.

To better understand the mystery of how the brain generates creative ideas, researchers examined 13 study participants receiving treatment for epilepsy at Baylor St. Luke’s Medical Center that had Stereoelectroencephalography (sEEG) electrodes surgically implanted in their brains for seizure mapping.

By using participants with intracranial electrodes, researchers could record brain activity with exceptional temporal and spatial precision as they engaged in tasks designed to stimulate creative thinking.

These tasks included generating novel uses for everyday objects, a well-known test of creativity often called the "alternate uses task." Participants were also asked to engage in a "mind-wandering task," which involved focusing on neutral visual stimuli and allowing their thoughts to roam freely. Finally, participants were given a third "sustained attention task" as a control measure.

By comparing brain activity during these tasks, the researchers discovered that the DMN and brain regions, typically associated with introspection and daydreaming, were highly active during creative functions.

In addition to mapping the brain regions involved in creativity, the researchers also examined the specific types of brain waves that were most active during creative tasks. Specifically, they focused on two types of brain waves: theta and gamma.

Previous research has linked theta waves to long-range communication between brain regions and states of relaxation and meditation. Meanwhile, Gamma waves are often associated with local neural activity and are believed to be involved in moments of insight or the formation of unified perception.

Researchers found that during the creative tasks, there was a notable increase in gamma wave activity in the DMN, suggesting that this brain region is not only active during creative thinking but may also orchestrate and integrate different types of information necessary for creative insights.

Meanwhile, theta wave activity was also heightened, particularly in the moments leading up to the generation of a creative idea, indicating that a relaxed, open mental state might be a precursor to creativity.

These results suggest that the interplay between theta and gamma oscillations in the DMN is crucial for generating creative ideas. This

aligns with the notion that creativity involves a free flow of ideas, facilitated by a relaxed mental state, and the ability to synthesize these ideas into something new and useful, driven by more focused, integrative processes.

To confirm the DMN's role in creativity, researchers used electrical stimulation to temporarily disrupt activity in specific network regions. This approach allowed them to observe how reducing DMN activity affected participants' creative thinking.

The findings showed that participants' ability to generate creative ideas was significantly impaired when DMN activity was disrupted during "alternate uses tasks." However, intriguingly, disruptions to the neural network did not affect performance in mind-wandering tasks.

"Our results indicate that the thought processes occurring during daydreaming and mind wandering are more resilient to external perturbation of the system," researchers wrote. "It is possible that changes in the train of thoughts might be more difficult to detect given their "unconstrained" fluctuating nature, also in line with the subjective experience of a constant and coherent internal narrative."

The implications of this recent research are profound. Understanding the neural basis of creativity could lead to new ways of enhancing creativity in individuals, whether through educational techniques, cognitive training, or even brain stimulation technologies.

Moreover, this knowledge could inform the development of artificial intelligence systems that better mimic human creativity, potentially leading to more innovative and adaptable AI.

However, researchers caution that creativity is a complex, multifaceted phenomenon, and this latest research only focused on specific regions within the DMN. Previous studies have shown that creativity and divergent thinking can involve additional cognitive control networks.

"To better quantify the relationship between these various networks, future studies focused on measures of network synchrony, such as

cross-frequency coupling and phase synchronization, will be necessary," researchers wrote.

In the broader context, this understanding reinforces the idea that creativity is a defining feature of the human experience, rooted in the unique architecture of our brains.

Moreover, these findings challenge previous notions that the DMN plays a passive role in supporting mind-wandering and self-referential thoughts. Instead, the neural network is actively engaged in generating creativity and the imaginative thought process.

Ultimately, in a world where innovation is increasingly critical, this new understanding of how creativity arises in the brain could prove invaluable, offering new avenues for fostering creativity in individuals and societies.

# THE "HOLY GRAIL" OF NEUROSCIENCE? RESEARCHERS CREATE STUNNINGLY ACCURATE DIGITAL TWIN OF THE BRAIN

TIM MCMILLAN·APRIL 15, 2025

In a breakthrough that could revolutionize neuroscience, researchers have harnessed the power of artificial intelligence to create a highly accurate "digital twin" of the mouse brain. This advanced AI model can predict how neurons respond to entirely new visual stimuli—something no previous model has accomplished with such precision.

Recently published in *Nature*, the study—led by scientists from Baylor College of Medicine, Stanford University, and the Allen Institute for Brain Science—introduces a sophisticated artificial neural network called a "foundation model."

The model replicates brain activity and mirrors the intricate structural details of neural circuits, offering a powerful new tool for exploring the brain's inner workings.

Much like how ChatGPT and other large language models transformed natural language processing, this brain model could reshape how we study perception, behavior, or even consciousness.

“If you build a model of the brain and it’s very accurate, that means you can do a lot more experiments,” Stanford professor of ophthalmology and senior author of the study, Dr. Andreas Tolias, explained in a press release. “We’re trying to open the black box, so to speak, to understand the brain at the level of individual neurons or populations of neurons and how they work together to encode information.”

## A BRAIN DIGITAL TWIN THAT THINKS AHEAD

For decades, decoding the brain’s language has been one of science’s most enduring puzzles. Traditional neural network models, often trained to respond to specific data sets like object recognition tasks or motion detection, performed well but only within their comfort zones. These models struggle once unfamiliar data is introduced, such as new types of images or stimuli.

Inspired by the power of foundation models in AI—large-scale models trained on massive datasets that generalize remarkably well to new domains—neuroscientists set out to create something similar for the brain.

They recorded real-time neural responses in 14 awake mice as the animals watched natural videos and interacted with their environment. “It’s very hard to sample a realistic movie for mice because nobody makes Hollywood movies for mice,” Dr. Tolias said. “[However] mice like movement, which strongly activates their visual system, so we showed them movies that have a lot of action.”

These recordings captured visual stimuli, behavior (like eye movement and pupil dilation), and contextual variables across six visual brain areas. Over 900 minutes of data from the mice watching

clips of action movies, such as *Mad Max*, were fed into an artificial neural network (ANN).

The result was a four-part model: a "perspective" module to account for how a mouse's eye sees a stimulus, a "modulation" module to interpret behavioral signals, a "core" that processes the bulk of the sensory data, and a "readout" that translates that data into predictions of neural activity. Trained on just eight mice, the model proved startlingly robust—accurately predicting brain responses in new mice and across novel stimulus types it had never seen before.

The crown jewel of this ANN is what researchers call the "foundation core." Once trained, this shared internal representation of visual processing could be "transferred" to new individual mice with minimal additional data—sometimes as little as four minutes of new recordings. This dramatically reduced the amount of real-world data needed to accurately model a new brain.

Compared to previous leading models, the new foundation model achieved a 25–46% improvement in predictive accuracy, even in notoriously complex higher-order visual areas of the brain. These performance gains represent a blueprint for developing increasingly accurate models of the brain that can adapt quickly to new data without starting from scratch.

Remarkably, the model didn't stop at predicting how neurons would fire. It also inferred their physical characteristics—like where they sit in the brain and what kind of neuron they are.

In another major leap for neuroscience, researchers with the MICrONS project recently unveiled the most detailed functional map of the brain to date, offering unprecedented insight into how neurons connect, interact, and communicate. This feat was once considered "impossible."

Using data from the MICrONS project, researchers applied their model to more than 70,000 neurons. The model accurately predicted anatomical cell types, dendritic structures, and even synaptic

connectivity patterns despite never having been trained on anatomical data.

This suggests that the "functional barcodes" generated by the model—essentially, how a neuron processes visual information—can be used as fingerprints to reveal a cell's type and structure.

## UNLIMITED POTENTIAL, ZERO INVASIVENESS WITH DIGITAL TWINS

A key advantage of creating a digital twin of the brain is its scalability. Because the model can simulate neural responses inside a computer, researchers can now run unlimited experiments that would be time-consuming, invasive, or even impossible to perform on living brains.

For example, researchers tested how digital brains responded to classical vision experiments—like moving dots, Gabor patches, or flashing lights—and found that the digital neurons exhibited the same orientation or spatial selectivity as their real counterparts. In one test, simulated neurons matched the actual preferred orientation of live neurons within just 4 degrees, an extraordinary degree of precision.

## TOWARD A UNIFIED MODEL OF THE BRAIN

By leveraging similarities between brains, rather than treating each one as a separate puzzle, researchers can now model shared cognitive features while still accounting for individual quirks.

Additionally, what makes this recent breakthrough stand out isn't just the technical prowess—it's the philosophical leap. Foundation models, by their nature, don't just memorize; they internalize general principles. The hope is that a similar approach in neuroscience could eventually uncover a universal set of rules that governs how all brains process information.

By uncovering a shared set of rules that govern how neurons encode, process, and transmit information, scientists could be on the verge of establishing foundational laws of neuroscience, akin to the laws of physics that govern the natural world.

# IARPA RESEARCH ACHIEVES THE IMPOSSIBLE IN NEW BREAKTHROUGH REVEALING THE BRAIN'S BIGGEST MYSTERIES

TIM MCMILLAN·APRIL 14, 2025

In a scientific feat once deemed "impossible," researchers have mapped the most detailed wiring diagram and functional map of the brain to date, revealing a never-before-seen level of intricacy in how neurons connect and communicate.

In a groundbreaking study funded by the U.S. Intelligence Advanced Research Projects Activity (IARPA), scientists from the MICrONS Consortium harnessed advanced imaging and computational tools to uncover the intricate workings of the mouse visual cortex.

The breakthrough, recently published in *Nature*, represents a technical triumph and a transformative leap for neuroscience that could reshape our understanding of cognition, behavior, and brain disorders.

"The MICrONS advances published in this special issue of Nature are a watershed moment for neuroscience, comparable to the Human Genome Project in their transformative potential," Dr. David A. Markowitz, Ph.D., former IARPA program manager who coordinated this work, said in a release.

"IARPA's moonshot investment in the MICrONS program has shattered previous technological limitations, creating the first platform to study the relationship between neural structure and

function at scales necessary to understand intelligence. This achievement validates our focused research approach and sets the stage for future scaling to the whole brain level."

In 1979, Nobel laureate Dr. Francis Crick famously declared, "It is no use asking for the impossible, such as, say, the exact wiring diagram for a cubic millimeter of brain tissue and the way all its neurons are firing." However, today, that impossible dream has become a reality.

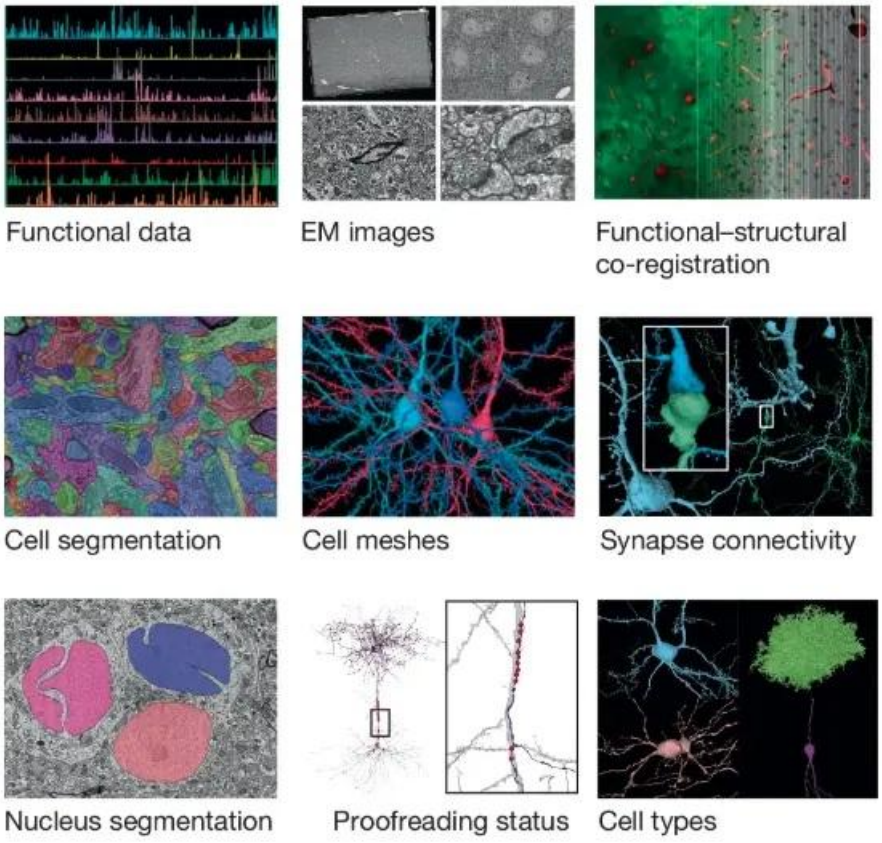
Using a combination of dense calcium imaging and serial-section electron microscopy (EM), scientists analyzed a cubic millimeter of mouse visual cortex. The result was a high-resolution dataset detailing over 200,000 cells and over 500 million synapses, with functional responses recorded from approximately 75,000 neurons in a living mouse. The achievement represents not just a leap in scale but a fusion of form and function, linking what neurons look like with what they do.

What sets the MICrONS project apart is its unprecedented integration of neuronal function and connectivity. The researchers were able to measure the responses of individual neurons to a wide range of visual stimuli, from natural scenes to artificially generated patterns. These responses were then co-registered with a dense 3D reconstruction of synaptic connections within the same brain volume.

The mapping was done across four areas of the mouse visual cortex—VISp, VISlm, VISrl, and VISal—covering all cortical layers except for the extremes of Layer 1. This allowed scientists to observe how neurons connect not only within an area but also across regions, uncovering feedforward and feedback loops crucial for visual processing.

The dataset includes pyramidal neurons, inhibitory neurons from many known classes (e.g., basket and chandelier cells), non-neuronal cells like astrocytes and microglia, and vasculature.

Each component is rendered in rich detail and publicly available through an open-access online platform, MICrONS Explorer.




Example of the types of data resources made publicly available by the MICrONS project (Image Source: the MICrONS project/Nature)

As Dr. Crick famously implied, creating this comprehensive map of neural connections in the brain was no trivial task. The tissue was sliced into nearly 28,000 serial sections, each 40 nanometers thick, and imaged over six months using five customized automated transmission electron microscopes. The resulting 2-petabyte dataset was stitched with advanced convolutional neural networks, identifying and tracing neurons and synapses with remarkable precision.

Example of the types of data resources made publicly available by the MICrONS project (Image Source: the MICrONS project/Nature)
As Dr. Crick famously implied, creating this comprehensive map of neural connections in the brain was no trivial task. The tissue was sliced into nearly 28,000 serial sections, each 40 nanometers thick,

and imaged over six months using five customized automated transmission electron microscopes. The resulting 2-petabyte dataset was stitched with advanced convolutional neural networks, identifying and tracing neurons and synapses with remarkable precision.

Beyond its technical novelty, the study revealed fundamental insights into how the brain organizes information. For instance, it confirmed the existence of a "like-to-like" connectivity principle, where neurons with similar functional properties tend to form stronger and more frequent connections. This finding helps explain how the brain efficiently processes sensory information.

Other discoveries include novel forms of neuronal invariance (where neurons respond consistently to the same stimulus despite changes in context) and patterns of connectivity that vary across cortical layers and cell types.

The data also helped define new computational principles underlying inter-areal communication, suggesting how visual information is integrated across different brain regions.

"Inside that tiny speck is an entire architecture like an exquisite forest," Dr. Clay Reid, a member of the IARPA MICrONS project and senior investigator at the Allen Institute, explained. "It has all sorts of rules of connections that we knew from various parts of neuroscience, and within the reconstruction itself, we can test the old theories and hope to find new things that no one has ever seen before."

Findings from this study hold transformative potential for medicine, artificial intelligence (AI), and beyond.

In neuroscience, understanding brain wiring at this scale can lead to better models of brain function, ultimately guiding treatments for disorders like epilepsy, schizophrenia, and autism, which are thought to stem from connectivity dysfunctions.

By providing a "ground truth" dataset, the IARPA MICrONS project enables more accurate simulations of brain activity, allowing researchers to test previously speculative hypotheses.

This breakthrough is more than just a detailed map of brain activity. Rather, it serves as a resource that will help answer long-standing questions about how the brain works and perhaps even how it goes wrong in disease.

In AI, the dataset could inspire the next generation of machine learning algorithms. Neural networks, after all, were inspired by the brain—but until now, they lacked detailed biological data for their design. Computer scientists can build more efficient and robust systems by studying how real neurons connect and process information.

"If you have a broken radio and you have the circuit diagram, you'll be in a better position to fix it." Dr. Nuno da Costa, an associate investigator at the Allen Institute, explained. "We are describing a kind of Google map or blueprint of this grain of sand. In the future, we can use this to compare the brain wiring in a healthy mouse to the brain wiring in a model of disease."

The MICrONS project has made its entire dataset available for public use. With tools like the Neuroglancer visualization platform and cloud-based APIs, professional and amateur scientists can explore and analyze the data without downloading terabytes of information.

Moreover, the researchers developed new tools to facilitate large-scale proofreading and analysis of neuron reconstructions, including the ChunkedGraph system and the NEURD error correction workflow. These innovations dramatically improve the speed and accuracy of working with such massive datasets.

Despite the achievement, challenges still remain. Proofreading and annotating such massive volumes of data is a labor-intensive process. While automated systems are improving, human oversight is essential for ensuring accuracy, especially in complex or ambiguous cases.

The IARPA MICrONS dataset stands as a powerful testament to what a multidisciplinary approach can achieve, transforming what once seemed "impossible" into reality. Researchers behind the project see

this accomplishment not as an endpoint but as the foundation for a new era of scientific discovery.

“This is the future in many ways,” Dr. Andreas Tolias, one of the IARPA project’s lead scientists at Baylor College of Medicine and Stanford University, said. “MICrONS will stand as a landmark where we build brain foundation models that span many levels of analysis, beginning from the behavioral level to the representational level of neural activity and even to the molecular level.”

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JUNE 13, 2025

# Autonomic nervous system is key driver of global fMRI signal, study finds

by Ingrid Fadelli, Phys.org edited by Sadie Harley, reviewed by Robert Egan

Global fMRI fluctuations are associated with systemic physiological changes. Credit: *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01945-y.
The activity of the human brain is known to be closely connected to other physiological signals, such as heart rate and breathing. A study by researchers at the University of California Los Angeles (UCLA) and other institutes reveals that a global spatiotemporal pattern in the brain (i.e. a pattern in brain activity that repeats itself across the brain and over time) is a central component of these brain-body interactions.

The same research team has now set out to further investigate this global signal, in the hope of identifying its underlying physiological and neural origins. Their findings, published in *Nature Neuroscience*, show that this unified pattern of brain-body activity is in great part driven by the autonomic nervous system, the part of the nervous system regulating arousal and other involuntary bodily functions.

"The inspiration for this project came from our previously published paper in *Nature Neuroscience* where we described prominent spatiotemporal patterns in brain functional magnetic resonance imaging (fMRI) signals," Taylor Bolt, first author of the paper, told Medical Xpress.

"Of these patterns there was one that dominates: the pattern known as the 'global signal.' It's easy to see when viewing an fMRI scan: suddenly the brain's fMRI signal 'lights up' with strong activity that seems to cover the entire brain—thus, the reason it's called the 'global signal.'"

The primary objective of this recent study by Bolt and his colleagues was to pin-point the underlying physiological and neural sources of the dominant pattern in fMRI signals observed in their earlier work.

To do this, they analyzed human fMRI data collected in previous studies and compiled them into readily available datasets, which are widely used to conduct neuroscience research.

"Most existing datasets are limited—pulse oximeter (PPG) on the finger and respiration belts—while others may collect more comprehensive recordings," explained Bolt.

"Catie Chang had gathered a comprehensive fMRI dataset with a wealth of physiological recordings that allowed us to track a range of bodily states and tie these back to what's going on in the brain, particularly the brain's 'global signal.' We also supplemented these analyses with several other fMRI datasets (with associated physiological recordings) to ensure the robustness of our findings."

The methods employed by the researchers were carefully designed to determine the extent to which the human body's physiological systems (e.g. heart, lungs, exocrine, etc.) track fluctuations in global fMRI signals. Moreover, if these systems are tightly connected, Bolt and his colleagues wished to determine which of them is responsible for the global fMRI fluctuations they observed.

"We found a robust association between the global fMRI signal and a host of autonomic-driven changes in the body that spanned cardiovascular, pulmonary, exocrine and smooth muscle systems under resting conditions," said Bolt.

"We also found that these co-fluctuations of brain and body observed at rest are induced by experimental manipulation of arousal, including a cued deep breath and intermittent auditory stimulation. Further, the same brain and body co-fluctuations were observed with spontaneous arousals during sleep (as measured by brief, aperiodic EEG activation)."

Overall, the findings gathered by Bolt and his colleagues suggest that the autonomic nervous system, which plays a central role in the regulation of arousal and wakefulness, is an important source of the global fMRI signal. Similarly, they also indicate that the global signal in the brain is a key component of the autonomic nervous system's arousal response.

"We would now like to dive into the functional significance of the global fMRI signal in the arousal response—what is it 'doing' for us, and what downstream mechanisms (or behaviors) are affected by this phenomena," added Bolt.

**More information:** Taylor Bolt et al, Autonomic physiological coupling of the global fMRI signal, *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01945-y.
**Journal information:** Nature Neuroscience