BRAIN INTRACRANIAL VOL 7

New research suggests our brains use quantum computation

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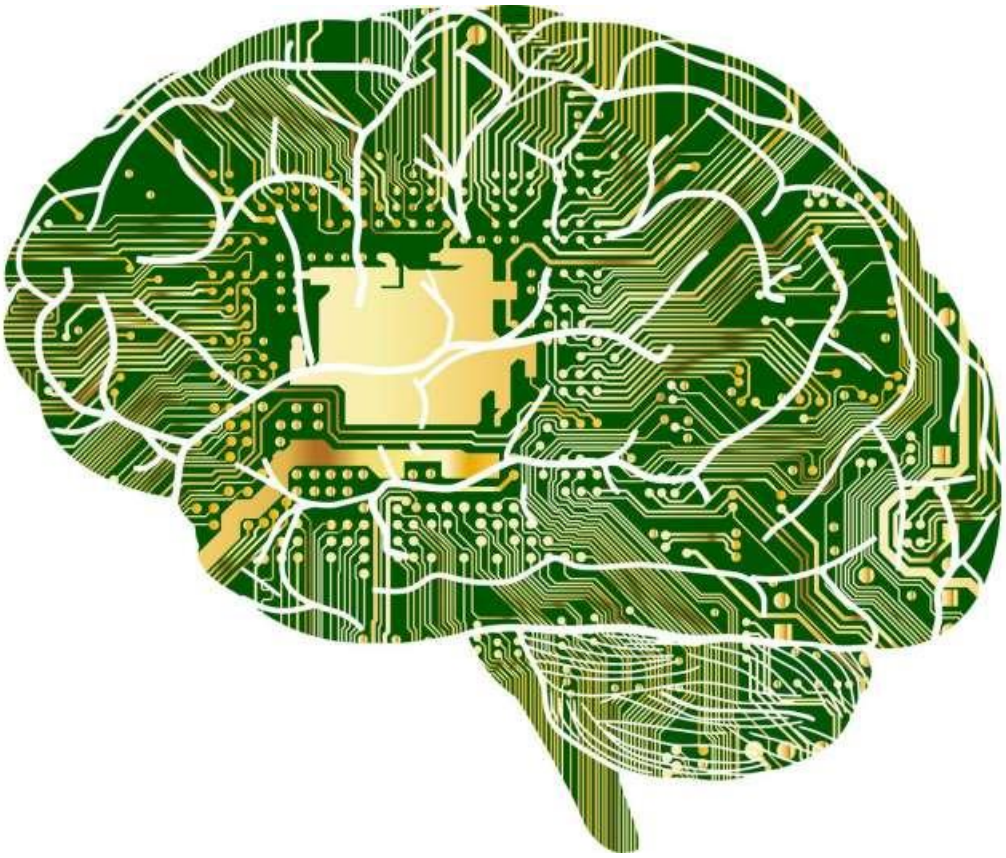
Scientists from Trinity College Dublin believe our brains could use quantum computation. Their discovery comes after they adapted an idea developed to prove the existence of



quantum gravity to explore the human brain and its workings.

The brain functions measured were also correlated to short-term memory performance and conscious awareness, suggesting quantum processes are also part of cognitive and conscious brain functions.

If the team's results can be confirmed—likely requiring advanced multidisciplinary approaches—they would enhance our general understanding of how the brain works and potentially how it can be maintained or even healed. They may also help find innovative technologies and build even more advanced quantum computers.

Dr. Christian Kerskens, lead physicist at the Trinity College Institute of Neuroscience (TCIN), is the co-author of the research article that has just been published in the *Journal of Physics Communications*. He said, "We adapted an idea, developed for experiments to prove the existence of quantum gravity, whereby you take known quantum systems, which

interact with an unknown system. If the known systems entangle, then the unknown must be a quantum system, too. It circumvents the difficulties to find measuring devices for something we know nothing about.

"For our experiments we used proton spins of 'brain water' as the known system. 'Brain water' builds up naturally as fluid in our brains and the proton spins can be measured using MRI (Magnetic Resonance Imaging). Then, by using a specific MRI design to seek entangled spins, we found MRI signals that resemble heartbeat evoked potentials, a form of EEG signals. EEGs measure electrical brain currents, which some people may recognize from personal experience or simply from watching hospital dramas on TV."

Electrophysiological potentials like the heartbeat evoked potentials are normally not detectable with MRI and the scientists believe they could only observe them because the nuclear proton spins in the brain were entangled.

Dr. Kerskens added, "If entanglement is the only possible explanation here then that would mean that brain processes must have interacted with the nuclear spins, mediating the entanglement between the nuclear spins. As a result, we can deduce that those brain functions must be quantum.

"Because these brain functions were also correlated to short-term memory performance and conscious awareness, it is likely that those quantum processes are an important part of our cognitive and conscious brain functions.

"Quantum brain processes could explain why we can still outperform supercomputers when it comes to unforeseen circumstances, decision making, or learning something new. Our experiments, performed only 50 meters away from the lecture theater where Schrödinger presented his famous thoughts about life, may shed light on the mysteries of biology, and on consciousness which scientifically is even harder to grasp."

More information: Christian Matthias Kerskens et al, Experimental indications of non-classical brain functions, *Journal of Physics Communications* (2022). DOI: 10.1088/2399-6528/ac94be
Provided by Trinity College Dublin

An approach to interfacing the brain with quantum computers: practical steps and caveats

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We report on the first proof-of-concept system demonstrating how one can control a qubit with mental activity. We developed a method to encode neural correlates of mental activity as instructions for a quantum computer. Brain signals are detected utilizing electrodes placed on the scalp of a person, who learns how to produce the required mental activity to issue instructions to rotate and measure a qubit. Currently, our proof-of-concept runs on a software simulation of a quantum computer. At the time of writing, available quantum computing hardware and brain activity sensing technology are not sufficiently developed for real-time control of quantum states with the brain. But we are one step closer to interfacing the brain with real quantum machines, as improvements in hardware technology at both fronts become available in time to come. The paper ends with a discussion on some of the challenging problems that need to be addressed before we can interface the brain with quantum hardware.

Are Brain–Computer Interfaces Feasible With Integrated Photonic Chips?

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PMCID: PMC8777191 PMID: 35069099

Abstract

The present paper examines the viability of a radically novel idea for brain–computer interface (BCI), which could lead to novel technological, experimental, and clinical applications. BCIs are computer-based systems that enable either one-way or two-way communication between a living brain and an external machine. BCIs read-out brain signals and transduce them into task commands, which are performed by a machine. In closed loop, the machine can stimulate the brain with appropriate signals. In recent years, it has been shown that there is some ultraweak light emission from neurons within or close to the visible and

near-infrared parts of the optical spectrum. Such ultraweak photon emission (UPE) reflects the cellular (and body) oxidative status, and compelling pieces of evidence are beginning to emerge that UPE may well play an informational role in neuronal functions. In fact, several experiments point to a direct correlation between UPE intensity and neural activity, oxidative reactions, EEG activity, cerebral blood flow, cerebral energy metabolism, and release of glutamate. Therefore, we propose a novel skull implant BCI that uses UPE. We suggest that a photonic integrated chip installed on the interior surface of the skull may enable a new form of extraction of the relevant features from the UPE signals. In the current technology landscape, photonic technologies are advancing rapidly and poised to overtake many electrical technologies, due to their unique advantages, such as miniaturization, high speed, low thermal effects, and large integration capacity that allow for high yield, volume manufacturing, and lower cost. For our proposed BCI, we are making some very major conjectures, which need to be experimentally verified, and therefore we discuss the controversial parts, feasibility of technology and limitations, and potential impact of this envisaged technology if successfully implemented in the future.
Keywords: ultraweak photon emission, brain-computer interface, photonic interferometry, pattern recognition, integrated photonic circuit, on-chip photon detection, quantum technology

1. Introduction

Brain–computer interface (BCI), or generally brain–machine interface (BMI), is a computer (machine)-based system that maps brain signals into computer (machine) commands or actions. This mapping may involve intermediate analysis and processing. Moreover, a closed-loop BCI is also possible, whereby the brain is stimulated via relevant neuro-bio-signals. The most common brain signals used in BCIs are electromagnetic, that is, of classical/non-quantum origin. Herein, we turn attention to an exciting and emergent literature that reveals the brain also emits “photons,” which are quanta of electromagnetic waves. The intensity of these emissions varies from a few photons to several hundred photons per second per square centimeter, mainly with spectral range of 200–800 nm (Salari et al., 2015). A caveat is that most single-photon sensitive detectors used in the experiments were only sensitive up to about 900 nm. Hence, observations with detector platforms that are sensitive in the 900–1,600 nm range, such as superconducting nano-wire single-photon detectors (SNSPDs) (Marsili et al., 2013), which also can be shaped as arrays (Wollman et al., 2019), may reveal hidden obscured about the UPE light.

The body of evidence for ultraweak photon emission (UPE) is fast growing and is being independently observed by different scientific communities/labs. Due to infancy of the research field, many different terms are used to describe this phenomenon, including biophotons, ultraweak photon emission, ultraweak bioluminescence, self-bioluminescent emission, photoluminescence, delayed luminescence, ultraweak luminescence, spontaneous chemiluminescence,

ultraweak glow, chemiluminescence, metabolic chemiluminescence, dark photobiochemistry, etc. (Salari et al., 2017; Esmaeilpour et al., 2020). In this report, we will henceforth adopt the term UPE. It has been evidenced that neurons and other living cells (e.g., in plants, animals, and humans) have spontaneous UPE (Cifra and Pospisil, 2014; Pospisil et al., 2014) mediated via their metabolic reactions associated with physiological conditions. In 1967, it was first reported that electric pulses in neurons can induce weak photon emission (in the visible region of the EM spectrum) due to chemical reactions accompanying pulses, while a dead-neuron does not exhibit any photon emission (Artem'ev et al., 1967). In 1984 (Imaizumi et al., 1984) and 1985 (Suzuki et al., 1985), it was demonstrated experimentally that after the induction of hypoxia states in a rat brain, UPE increases. Isojima et al. (1995) showed that there is a correlation between the intensity of UPE and neural metabolic activity in the rat hippocampal slice. In 1997, Zhang et al. (1997) revealed that the intensity of UPE from intact brains isolated from chick embryos was higher than the medium in which the brain was immersed. In 1999, Kobayashi et al. (1999b) detected spontaneous UPE in the rat's cortex *in vivo* without adding any chemical agent or employing external excitation and found that the UPE correlates with the electroencephalography (EEG) activity, cerebral blood flow, and hyperoxia, and the addition of glutamate increases UPE, which is mainly originated from the energy metabolism of the inner mitochondrial respiratory chain through the production of reactive oxygen species (ROS). Kataoka et al. (2001) detected spontaneous UPE from cultured rat cerebellar granule neurons in the visible range and demonstrated that the UPE depends on the neuronal activity and cellular metabolism. Then, a fascinating experimental discovery by Sun et al. revealed that photons can be conducted along neuronal fibers. In 2011, Wang et al. (2011) show-cased *in vitro* experimental evidence of spontaneous UPE and visible light-induced UPE (delayed luminescence) from freshly isolated rat's whole eye, lens, vitreous humor, and retina. Subsequently, in 2014 (Tang and Dai, 2014) Tang and Dai provided experimental evidence that the glutamate-induced UPE can be transmitted along the axons and in neuronal circuits in mouse.

These observations raise the following intriguing question: what are the underlying physiological processes that underpin UPE? Specifically, in the brain what are the associated neurophysiological processes? Although a complete picture has not been provided, it has been shown that the origin of UPE is in direct connection with the ROS. Moreover, its intensity has a direct correlation with thermal, chemical, and mechanical stress, the mitochondrial respiratory chain, cell cycle, neural activity, EEG activity, cerebral blood flow, cerebral energy metabolism, and release of glutamate. Experiments also show that cells can absorb photons by photochemical processes and slowly release these photons as delayed luminescence (Scordino et al., 2014). Interestingly, it has been shown that delayed luminescence emitted from the biological samples provide valid and predictive information about the functional status of biological systems (Musumeci et al., 2005; Niggli et al., 2005, 2008). All this opens novel

exciting mathematical and physical questions at the interface of quantum biology. For example, if we consider UPE in the context of metabolism, then there has been efforts to propose quantum-metabolism (Demetrius, 2003). As it is well-known, biological systems are essentially isothermal and as such energy flow in living organisms is mediated by differences in the turnover time of various metabolic processes in the cell, which occur cyclically. The mean cycle time (τ) of these metabolic processes (turnover of essentially redox reactions) are related to the metabolic rate (g), that is, the rate at which the organism transforms the free energy of nutrients into metabolic work. This is related to two coupled chains (electron-proton transport) of the ATP system in the mitochondria. In quantum-metabolism the main variables are metabolic rate, the entropy production rate, and the mean cycle time. Then the fundamental unit of energy is given by $E(\tau) = g\tau$, where g is related to the electron–proton transport. Noteworthy, this is in contrast, but has some correspondence to quantum thermodynamics, where the thermal energy per molecule is given by $E = K_bT$, which relates specific heat, Gibbs–Boltzmann entropy, and absolute temperature T. The difference is that biological systems work far from thermodynamic equilibrium, hence in quantum-metabolism the variables depend on fluxes (rates of change of energetic values). On top of this, Albrecht-Buehler (1995) hypothesized that the electron–proton transport releases photons ($E = hv$, where E is the photon energy, h is plank constant, and v photons frequency). Other researchers have contemplated at why UPE displays wide variety of frequencies, with Popp suggesting that these are coherent and mediated by DNA, thus it may regulate life processes of an organism (Popp et al., 1984, 1988). However, the coherence idea of UPE is still under debate (Salari and Brouder, 2011) and it is yet unclear if UPE is just a by-product in biological metabolism or it has some informational or functional role.

So far, UPE signals have only been studied in the context of basic science and has not been considered for experimental and clinical applications or novel technologies such as BCIs. The present article takes that first step forward and propose an implant BCI chip based on UPE. Since UPE is correlated to several sub-cellular, cellular, and neural tissue processes, there is also the potential that it can be used as a novel technological probe/bio-marker for both normal brain function and pathological conditions. In the subsequent sections, we will first briefly review the traditional classical methods in BCI and then we will focus our discussion toward UPE detection and pattern recognition for the development of a novel UPE-based skull implant BCI.

2. Classical Brain–Computer Interface Technology

In traditional BCI techniques, different types of signal acquisition may be used, depending on the application. In the following, we briefly review four types of brain signals, their properties, and the suitable machine interfaces.

- **Electroencephalography (EEG) signals**
  EEG is the most employed method to detect electrical activity of the brain by use of small electrodes attached to the scalp (Niedermeyer and da

Silva, 2004). These signals are recorded by a machine for tracing both normal brain function and diagnosing pathological conditions (e.g., epilepsy). In stimulus (e.g., visual cue) induced EEG, there is positive deflection of voltage with a latency (delay between stimulus and response) of roughly 250–500 ms, which is called event-related potentials (ERP). Examples of such ERP is the so-called P300 formed at time 300 ms, which is related to decision making. Indeed, cognitive impairment is often correlated with modifications in the P300 (Polich, 2007). It is considered an endogenous potential, as its occurrence links not to a stimulus' physical attributes, but a person's reaction to it. More specifically, the P300 is thought to reflect processes involved in stimulus evaluation or categorization. The presence, magnitude, topography, and timing of this signal are often used as metrics of cognitive function in decision-making processes and hence used in BCIs. The P300 has several desirable qualities for pattern recognition. First, the waveform is consistently detectable and is elicited in response to precise stimuli. The P300 waveform can also be evoked in nearly all subjects with little variation in measurement techniques, which help simplify interface designs and permit greater usability. The speed at which an interface can operate depends on how detectable the signal is despite “noise.” One negative characteristic of the P300 is that the waveform's amplitude requires averaging multiple recordings to isolate the signal. This and other post-recording processing steps determine the overall speed of a BCI interface (Donchin et al., 2000).

- **Magnetoencephalography (MEG) signals**
  MEG is a functional neuroimaging technique monitoring brain activity via magnetic fields of electrical currents in the brain, using SQUIDs (superconducting quantum interference devices), which are very sensitive magnetometers operated in a cryogenic environment. Another type of magnetometer is spin exchange relaxation-free (SERF) magnetometer (Hämäläinen et al., 1993), which can increase portability of MEG scanners, while it features sensitivity equivalent to that of SQUIDs. A typical SERF magnetometer is relatively small and does not require bulky cooling system to operate. It has been demonstrated that MEG could work with a type of SERF, i.e., chip-scale atomic magnetometer (CSAM) (Sander et al., 2012), where its development can be used efficiently for BCI. Basically, MEG may provide signals with higher spatiotemporal resolution than EEG, and therefore useful for an increased BCI communication speed.
- **Electrocorticography (ECoG) signals**
  ECoG uses electrodes placed directly on the surface of the brain to record electrical activity from the cerebral cortex, i.e., an invasive technology that involves removing a part of the skull to expose the brain surface to enable the implant of an electrode grid on the surface of the brain, i.e., called craniotomy, which is a surgical procedure performed either under general anesthesia or under local anesthesia if patient interaction is required for

functional cortical mapping. The spatial and temporal resolution of the resulting signal is higher and the signal to noise ratio (SNR) superior to those of EEG due to the closer proximity to neural activity. Thus, ECoG is a promising recording technique for use in BCI, especially for decoding imagined speech or music, in which users simply imagine words, sentences, or music that the BCI can directly interpret (Shenoy et al., 2007).

- **Functional near-infrared spectroscopy (fNIRS) signals**
  fNIRS is a non-invasive optical imaging technique that measures changes in hemoglobin (Hb) concentrations in the brain by means of the characteristic absorption spectra of Hb in the near-infrared (NIR) range (Scholkmann et al., 2014). fNIRS tomography makes use of the fact that light penetrates up to several centimeters into biological tissue, i.e., a safe technique that is minimally invasive and which relies on small, relatively inexpensive easy-to handle technology, and provides relatively low spatial resolution. The penetration range of light in tissue limits the size of the target tissue volume. fNIRS can be used in BCI for the restoration of movement capability for people with motor disabilities. fNIRS cannot afford high error rates for safety purposes, and must be fast enough to provide real-time control. Several fNIRS-BCI studies have tried to improve classification accuracies and information transfer rates (Naseer and Hong, 2015).

3. Potential Application of UPE in BCI

UPE is largely mediated by cellular metabolism and it is presently believed that it is merely a by-product (i.e., epiphenomenon). A tempting question is whether it is possible (or not) to retrieve information from stochastic emission of UPE? In previous sections, we already saw that there are different experimental reports on significant correlations between UPE emission and neuronal activity and associated metabolic processes (Isojima et al., 1995; Kobayashi et al., 1999b; Kataoka et al., 2001; Tang and Dai, 2013). Therefore, even if UPE is an epiphenomenon, its intensity can be a proxy for tracking the underlying neural information that dynamically changes under various conditions. Indeed, UPE seem to include information for monitoring physiological variations in a neuronal tissue. Note that for EEG signals we have a similar scenario. Indeed, EEG signals do not provide specific information about single neurons. Rather, it reflects a non-trivial summation of the synchronous activity of thousands of neurons and not that of a single neuron or dendrite. Thus, retrieving patterns as information from EEG is a data-science activity typically involving statistical comparisons between different brain states (e.g., normal and abnormal brain states).

Scholkmann (2015, 2016) hypothesized that UPE may be is used by neurosystems as an additional signal enabling cell-to-cell communication and coupling. Indeed, Sun et al. (2010) found that UPE can conduct along the neural

fibers. It has been hypothesized based on numerical simulations that neurons (or myelinated axons) may act as optical fibers and, hence, may conduct light associated with UPE (Kumar et al., 2016), and through these waveguides UPE may even mediate long-range quantum entanglement in the brain (Kumar et al., 2016; Zarkeshian et al., 2018; Simon, 2019). These myelinated axons are tightly wrapped by the myelin sheath, which has a higher refractive index (Antonov et al., 1983) than the inside of the axon and the interstitial fluid outside. Myelin is an insulating layer (sheath) around nerves, which is formed by two types of specialized glial cells, oligodendrocytes in the central nervous system (CNS) and Schwann cells in the peripheral nervous system (Simons and Trajkovic, 2006). Muller glia cells have also been suggested to guide photons within mammalian eyes (Franze et al., 2007; Agte et al., 2011; Reichenbach and Bringmann, 2013). These observations suggest that UPE and bioelectronic activities are not independent biological phenomena in the nervous system, and their synergistic action may take on considerable function in neural (quantum) signal and information processes (Salari et al., 2016b; Wang et al., 2016).

3.1. UPE Intensity From the Surface of the Human Brain

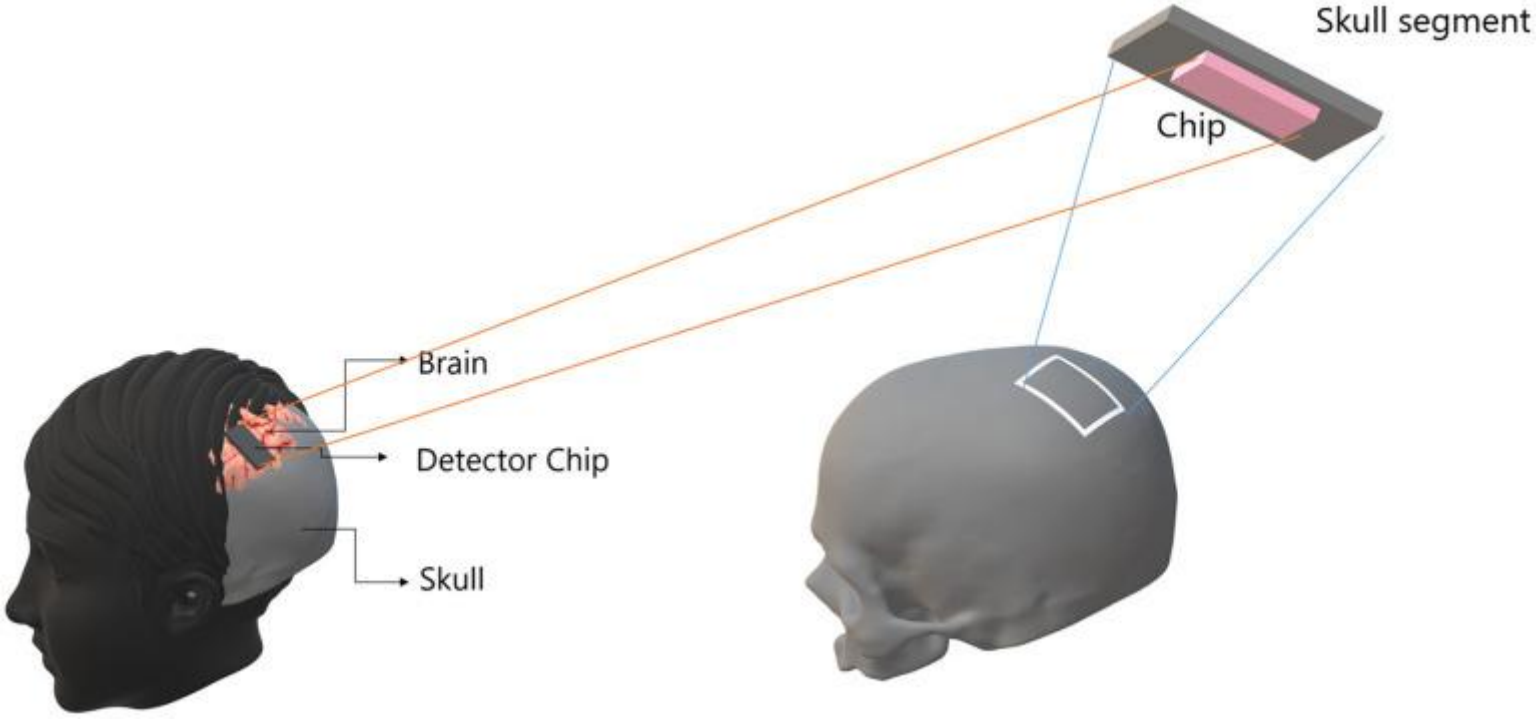
The UPE observed to date has been extremely weak. However, the true UPE intensity within neurons can be significantly higher than the one expected from the UPE measured a short distance away from the brain, as was done in all previous observations. Since photons are strongly scattered and absorbed in cellular or neural systems, the corresponding intensity of UPE within the organism or brain can even be two orders of magnitude higher (Slawinski, 1988; Chwirot, 1992). Based on the data from experiments with rat brain—employing a 2D photon-counting tube with a photocathode featuring a minimum detectable radiant flux density of $9.9 \times 10^{-17} W/cm^2$ under 1-s observation time—the intensity of UPE has approximately 100 countssec.cm2 from the cortex surface (Imaizumi et al., 1984; Adamo et al., 1989; Kobayashi et al., 1999a,b). Moreover, the limited quantum efficiency (QE) of the detector may impede the detection of UPE due to the limited SNR. Regarding the human brain, the neuronal density in V1 in visual cortex is 60 ×1⊠06⊠Neuronscm3 in postmortem human brains (Pakkenberg and Gundersen, 1987), It should be noted that postmortem studies use fixatives, which lead to shrinking of the tissue. The result is that the cell density is overestimated, while the volume of the extracellular space is underestimated. The reported number can be used only as an absolute best-case scenario for the interface. The V1 thickness is about 0.2 cm, and V1 surface area of one hemisphere is about 26 cm^2 in adult humans. At least, 10^6 neurons in object-related areas and 30×10^6 neurons in the entire visual cortex are activated by a single-object image (Levy et al., 2004). Based on a rough estimation, about 10^6 free radicals can be produced by each brain cell per second (Bokkon et al., 2010), which yields $10^6 \times 10^6 = 10^{12}$ free radicals produced by human visual neurons per second in V1 of one hemisphere during perception of a single-object image. Since UPE mainly originates from free radicals, the actual UPE intensity inside neuronal cells is expected to be considerably higher than the intensity

measured by a detector outside [e.g., 100 counts/(s.cm^2)]. If the QE of an ideal photodetector is close to 100%, we conjecture that it may measure the UPE intensity at the cortex surface at least on the order of 1,000 counts/(sec.cm^2) for an object visualization.

4. Skull-Implant Setup for the UPE-Based BCI

We now provide the complete design specification of a radically novel skull-implant that can facilitate a UPE-based BCI (see Figure 1). The envisaged BCI is not aimed for deep brain implants (although possible) but rather for intracranial brain surface implant (i.e., minimally invasive). The environment of a closed skull (after surgical implantation) is sufficiently dark and, therefore, a suitable environment for the detection of UPE signals. Once the UPE signals are detected, they are wirelessly relayed to a machine, computer, or smartphone. We also envisage alternative designs with closed-loop signals (photons) for modulating the metabolic processes of a neural tissue. However, herein we will only consider the read-out of UPE signals. The center-piece of the envisaged technology is the UPE-based integrated chip, which we will discuss at length in the subsequent sections. The integrated photonic chip is assembled from different component parts; specifically, a receiver optical plane (ROP), optical fibers, a photonic interferometery circuit, a complementary metal-oxide-semiconductor (CMOS) detector array, a battery, and a wireless system (see Figure 2). The use of the implantable CMOS image sensor has been described in recent years especially for optogenetic imaging (Tokuda et al., 2021).

Figure 1.



A detector chip can be installed on the interior surface of the skull without touching the brain tissue, i.e., non-invasive. The environment of the closed skull in the head is sufficiently dark and therefore it is a suitable environment for the detection of UPE with the installed chip. The intensity of UPE is stronger close to the surface of the brain, which can be captured by chip on the skull.

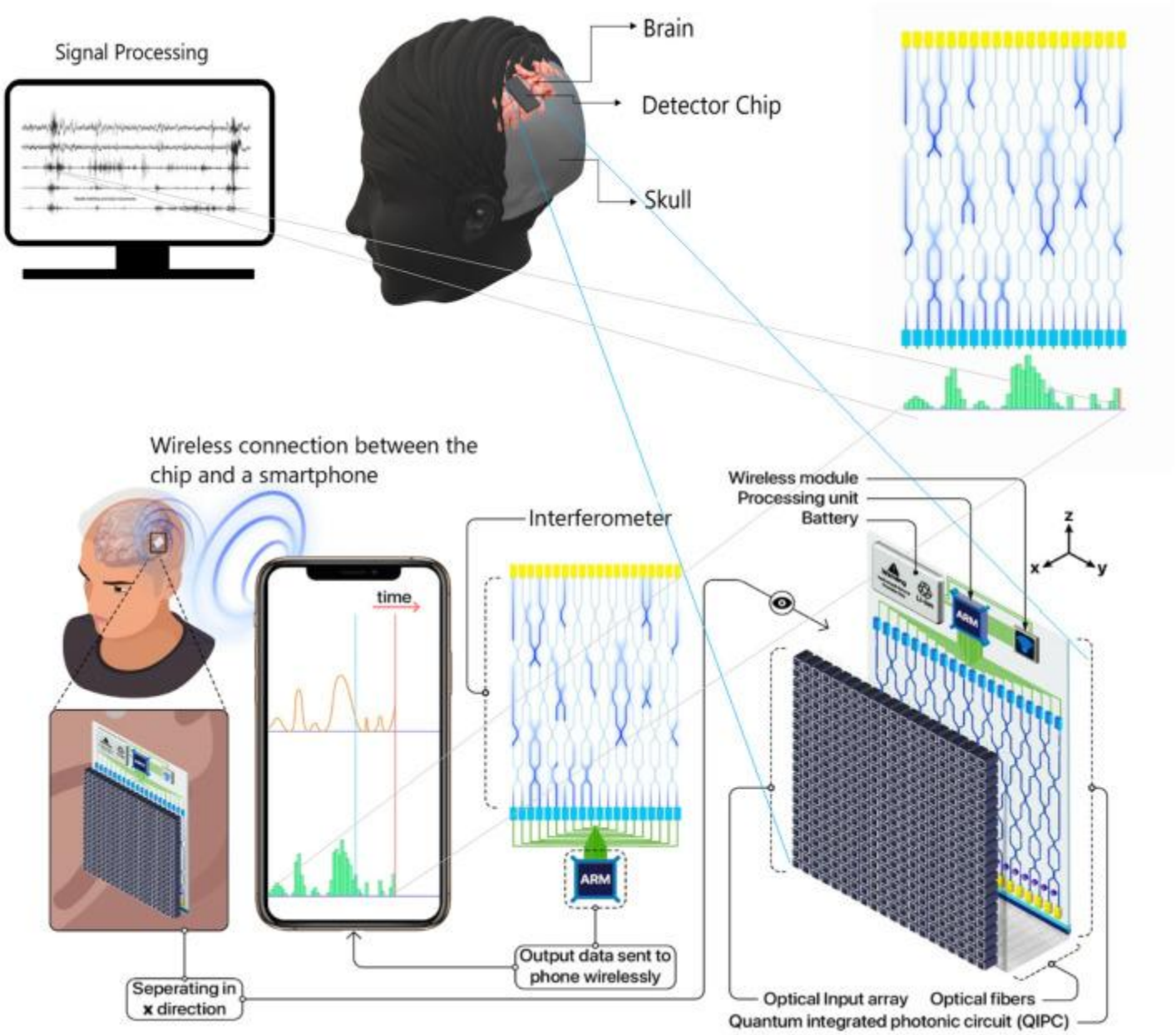
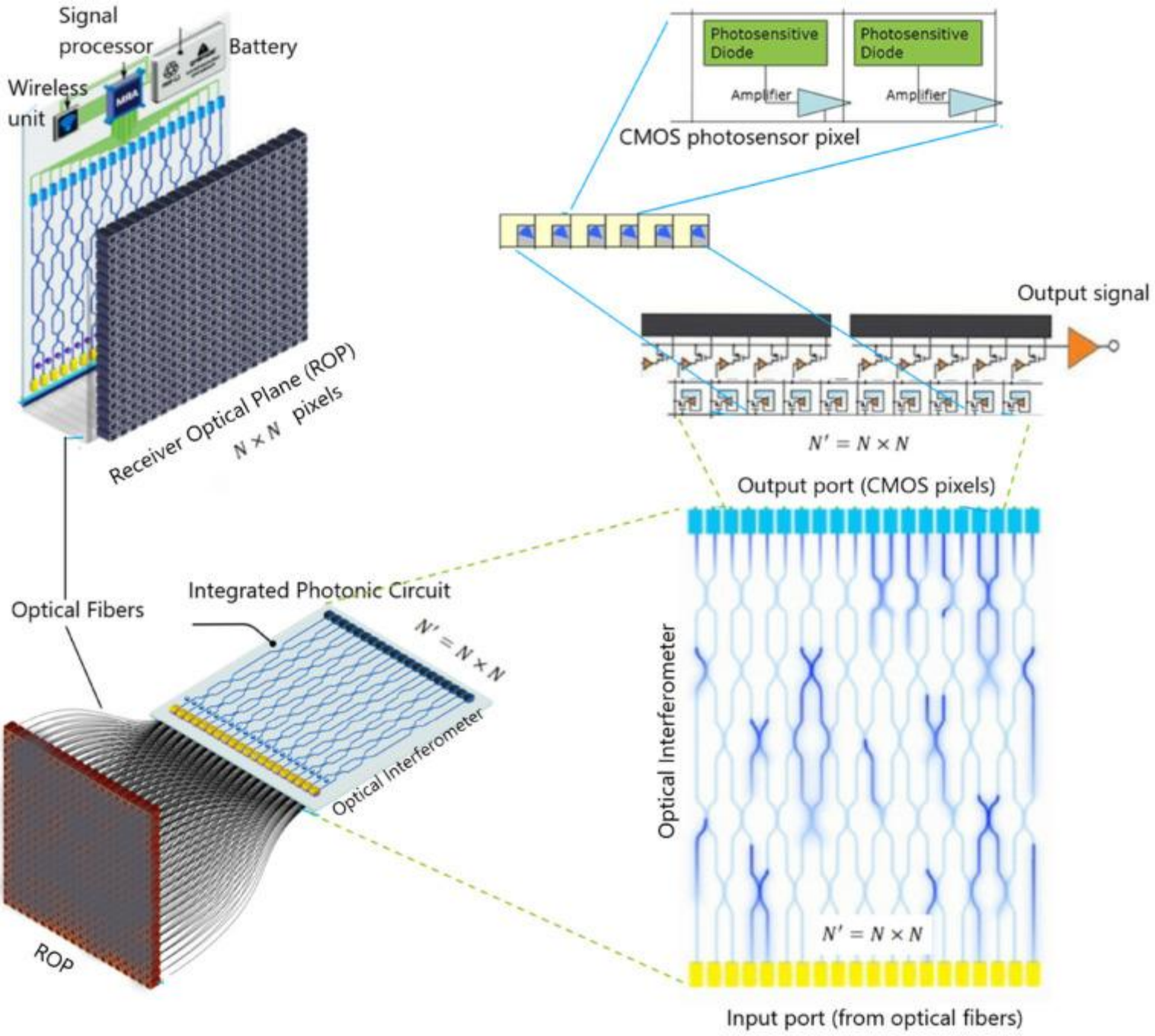


Figure 2.

In a brain–computer interface (BCI) proposal, an optical chip is implanted on the interior surface of the skull. A few number of ultraweak photon emission (UPE) photons interfere in a photonic chip and the results are detected as different single photon distributions at detectors vs. time. This results are communicated via wireless signals from the detector part of the chip to a receiver (e.g., smartphone or a computer).

The UPE photons first enter an ROP on the chip, which is essentially a photo-receiver array made up of optical fibers of size of $N \times N$, where N is the number of pixels (or fibers) in each row or column and each pixel is indeed an optical fiber that couples into a waveguide on the chip, using grating couplers (Cheng et al., 2020). Alternatively, the UPE light can be directly coupled to waveguides created by femto-second laser-writing and since these can be patterned at different depths in the chip (Nolte et al., 2003), and they can directly facilitate serialization step. Subsequently, the $N \times N$ pixels are serialized into a 1D vector (where $N' = N \times N$ is the number of optical fibers connected to the waveguides in the optical interferometer with N' input ports in a series and linear 1D form, and therefore N' CMOS pixels in a single row as the output port on the PIC). In fact, the received photons on ROP are guided to the optical interferometer via optical fibers. The advantage of an optical interferometer is that it may discriminate the emission patterns of photons. We estimate that UPE intensity ranges 10–1,000 counts per second per each cm^2 of the whole array, depending on how active a neuron or neural tissue is at a given time instant. In fact, we expect that similar and non-similar UPE emissions (in wavelength) generate different detection distributions, where interference will occur between photons with similar wavelength (i.e., emanating from the same-type neural processes). Thus, the detection distributions for similar-wavelength photons will be closer to an optical interference pattern, which is uniquely determined by the wavelength of these interfering photons. In this regard, one of the concerns may arise from the fact that UPE emission over a broad range of wavelengths can lead to the observation of different patterns at the same time, rendering an ambiguous combination of several independent patterns. Such complexity may bring disadvantages over the direct detection (i.e., no interferometer), or even could cause wrong interpretations. This potential problem can be alleviated by classifying those different wavelength patterns, again with pattern recognition techniques in machine learning, such as (PCA) (Jolliffe, 2002), which allows distinguishing the differences in an ensemble of patterns, and identifying each pattern according to the respective wavelength, after many sets of training data. The optical interferometer photons are then converted into electrical signal via the CMOS array (see Figure 6 for details). Finally, these signals are wirelessly linked to a smartphone or computer for pattern recognition/extraction. Noteworthy, since the number of detected photons is relatively low and because the data acquisition is in real time, the recognition of patterns should be done via machine learning protocols, e.g., convolutional neural networks (CCN), which is a powerful tool for 2D pattern recognition. We subsequently discuss in more detail each component part of the UPE-based electronic chip.



A typical on-chip ultraweak photon emission (UPE) detector can be built from an array of optical fibers connected to an integrated photonic circuit, which has an output gate composed of complementary metal-oxide-semiconductor (CMOS) photosensor array.

4.1. On-Chip Photonic Integrated Circuits

We base our proposed technology on photonic integrated circuits (PICs) (Coldren et al., 2012). These are chip that contains photonic components that operate with light (photons), where photons pass through optical components such as waveguides (equivalent to a resistor or electrical wire in an electronic chip). With electronic integrated circuits arriving at the end of their integration capacity, PICs have the potential to be the preferred technology. Nowadays, photonic platforms present several advantages for quantum information protocols enabling long coherence times, full connectivity, scalability, and operation in room temperature. Different photonic degrees of freedom including polarization, spectral, spatial, and temporal modes can be used to encode information, providing different experimental resources for a wide variety of quantum information tasks.

For our application, we consider a PIC containing an optical interferometer. A linear interferometer can be fabricated through silica-on-silicon or laser-written integrated interferometers, or electrically and optically interfaced optical chips (Szameit et al., 2007; Spring et al., 2012; Carolan et al., 2015), which makes a simple processor reducing the amount of physical resources needed for implementation.

4.2. Photons Statistics and Distributions

In the context of optics, coherence is a property of light. In a simplified picture, coherence is the ability of light to make interference, e.g., in the double-slit interference experiment light can create interference patterns (bright and dark bands) for both a wave (classical) and photon (quantum) picture. Thus, coherence of light can be both of a classical and quantum character. For example, thermal states of light can be described in the classical and the quantum framework, while other states, such as squeezed states, can only be described in the quantum framework. One of the essential conditions to show the coherence property of light is for its intensity/photon-number distribution to be a Poisson distribution. However, this condition is not sufficient to conclude that the light is certainly coherent. Other types of sources may yield a Poisson distribution, e.g., shot noise and dark noise. In the following paragraphs, we will introduce a couple of photon-number distributions in order to demonstrate how this measure provides insight into the nature of the UPE light being emitted.

The photocount statistics of coherent light is a Poisson distribution (Cifra and Brouder, 2015).

$$Pn(t,T)=\langle n\rangle nn!\times e-\langle n\rangle$$

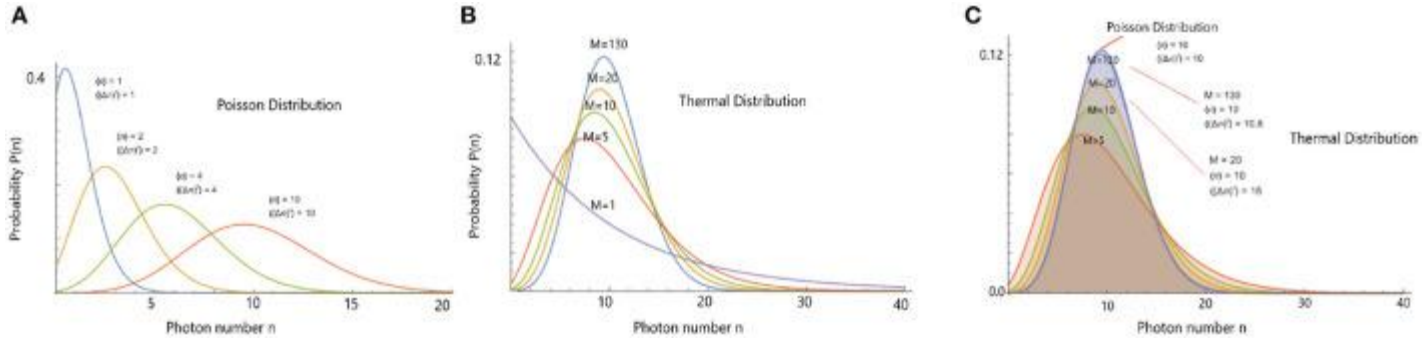
where $\langle n \rangle$ is the average number of photons measured between time t and time $t+T$. The variance of Poisson distribution is equal to its mean $\langle (\Delta n)^2 \rangle = \langle n \rangle$. The deviation of the photon-number distribution from the Poisson distribution is measured by the Fano factor F such that $\langle (\Delta n)^2 \rangle = \langle n \rangle F$, or by the Mandel parameter $Q = F-1$. A photocount statistics is said to be super-Poissonian if $F > 1$ and $Q > 0$, and sub-Poissonian (and therefore non-classical) if $F < 1$ and $Q < 0$. Hence, the shift from a Poisson distribution is a sign of non-classical (quantum) characteristics of the light (Cifra and Brouder, 2015) while a Poisson distribution is a sign of classicality.

The photocount statistics of a thermal source with M modes is approximated by the expression

$$P_n(t,T,M) = (n+M-1)!\, n!\, (M-1)!\, (1+M\langle n \rangle)^{-n} \times (1+\langle n \rangle M)^{-M}$$

where $\langle n \rangle$ is the average number of photons and M is the number of field modes (Cifra and Brouder, 2015). An important characteristic of these states is the relation between the variance and the mean $\langle (\Delta n)2 \rangle = \langle n \rangle + \langle n \rangle 2M$. The coefficient M is generally very large for chaotic sources. So that the relation between the variance and the mean is close to that of a coherent state, i.e., for large M, $P_n(t, T, M)$ approaches a Poisson distribution (see Figure 3). In relation to UPE, it is important to know whether the photocount statistics can distinguish between the coherent and thermal emissions, because photocount statistics of thermal light becomes equal to that of a coherent state when the number of modes M is large. Since the photocount statistics are not able to discriminate between a coherent and a thermal state with many modes.

Figure 3.



(A) Poisson distribution for four different average values of photon counts $\langle n \rangle$. **(B)** Demonstration of thermal field photocount distribution for different number of thermal modes for the average number of 10 photons. **(C)** Thermal

field photocount distribution (with similar $\langle n \rangle$) approaches Poisson distribution for a large number of modes M.

Another type of emission is super-radiance, which is the coherent emission of light by several sources, and its main characteristic is the fact that the intensity of the emitted light can vary with the square of the number of sources because they can emit in phase. The photocount statistics of super-radiant emission is sub-Poissonian (Cifra and Brouder, 2015), and the photon state of a super-radiant system is generally not a coherent state.

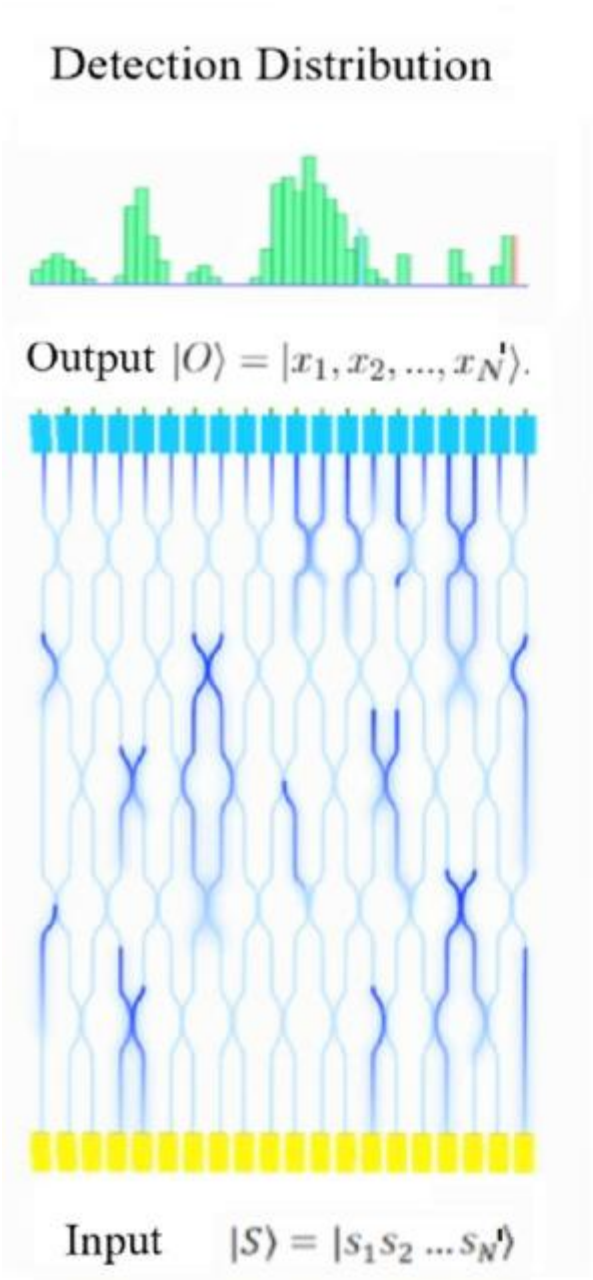
4.2.1. Photon Detection With Interference

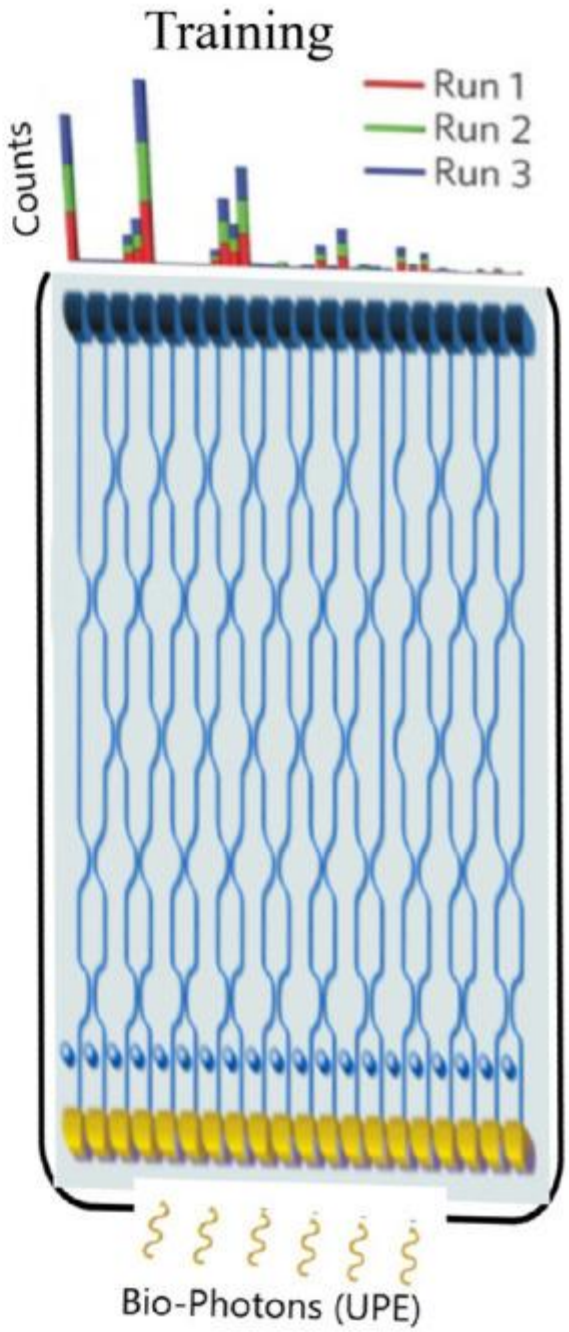
The photons collected onto our chip will then be propagated through a PIC featuring several interference paths and other components. The model of the effect of the PIC on the incident photons aims to predict the probability distribution of photons at the detector following their propagation and interference in a linear interferometer. The experimental setup only requires photodetectors and linear optical elements, i.e., beam splitters and phase shifters. Suppose the chip is injected with an input state of single photons of UPE, $|S\rangle = |s1, s2, ..., s'N\rangle$ where s_k are the number of UPE emitted photons in the kth mode and injected into the chip. The output state of the chip can be written as $|O\rangle = |x1, x2, ..., x'N\rangle$. For the sake of simplicity, suppose that there are four outputs on the chip. Therefore, probabilities of output detection for $N = 1$ input photons in case there is no dissipation in the circuit are $P_{|1000\rangle}$, $P_{|0100\rangle}$, $P_{|0010\rangle}$, $P_{|0001\rangle}$, and for $N = 2$ input photons the probabilities at the output are $P_{|1001\rangle}$, $P_{|1010\rangle}$, $P_{|1100\rangle}$, $P_{|0110\rangle}$, $P_{|0011\rangle}$, $P_{|0101\rangle}$, $P_{|2000\rangle}$, $P_{|0200\rangle}$, $P_{|0020\rangle}$, $P_{|0002\rangle}$. Now, we consider a general case for N' outputs. The signal processing and the interpretation of the signals require machine learning techniques. As the signal acquisition is performed through an interferometer, different interference patterns may form. We suggest a pattern recognition approach via convolutional neural networks (CNNs) (Fukushima, 1980) for an efficient interpretation of output signals on the photonic interferometer chip. Here, the conjecture is that a synchronous activity in a specific region of cortex makes synchronous similar metabolism with similar chemical reactions producing similar ROS by-products simultaneously, and therefore the probability of detection of similar photons (even with a low probability of interference in the interferometer) during a specific brain activity is higher than the normal state with stochastic photon emissions. Discrimination between the interference pattern of active and normal states will be non-trivial but tractable via machine learning. This conjecture is expected to be reasonable based on highly synchronized brain activities for different specific cognitive tasks. In fact, the photonic chip continuously produces data under normal and active states of the brain. The patterns can be recognized by studying the data and classifications via discrimination between the signals of

normal and active states. In such a state, both supervised and unsupervised learning can be performed on software. This can be an advantage of the method.

The idea of using UPE signals for BCI applications still remains at the level of conjecture, relying on a mere fact that UPE shows correlations with some brain activities. Therefore, from a BCI point of view, such correlations are very important because for almost all types of brain signals for BCI applications, it is hardly possible to extract specific information from the signals directly. With an analysis of signals over thousands of training trials, it will be possible to obtain an average pattern with specific features (for feature extraction) that finally make it easy for a specific algorithm to recognize the pattern in the next acquisition signals directly. Here, we suggest using a machine-learning algorithm to discriminate variations and extraction of features by enhancement of training data. A deep-learning algorithm becomes stronger in learning with increasing the training data to a specific level. This is a benefit for an implanted chip since it is always creating thousands of patterns easily to be processed by software on a computer or a smartphone. There is no need to perform separate experiments each time for training. Therefore, a deep-learning algorithm can learn how to understand features from UPE signals and interpret them according to the relevant cognitive task. Thus, data analysis of the output UPE signals of the chip can be performed via machine learning in general and deep learning specifically. For instance, a possibility is via deep learning method called CNN technique, which enables high-resolution pattern recognition. Since CNNs are ideal for 2D imaging processing, then the UPE signals detected at the receiver optical plane pixel-array can be readily adapted for CNN (see Figure 4). The pattern analysis can be enhanced depending on the details our architecture. CNN error minimization methods are used to optimize convolutional networks in order to implement quite powerful pattern transformations. This is very useful when the input is spatially or temporally distributed. The first layer of a CNN generally implements non-linear template-matching at a relatively fine spatial resolution, extracting basic features of the data. Subsequent layers learn to recognize particular spatial combinations of previous features, generating “patterns of patterns” in a hierarchical manner. If down-sampling is implemented, subsequent layers perform pattern recognition at progressively larger spatial scales, with lower resolution. A CNN with several down-sampling layers enables processing of large spatial arrays, with relatively few free weights. As we discussed before, an ensemble of wavelengths may make different patterns at the same time and obscure the interference patterns, where a PCA algorithm (Jolliffe, 2002) can find the differences between different patterns in the overlapped patterns, and classify each pattern for the relevant wavelength after many sets of training data.

Figure 4.





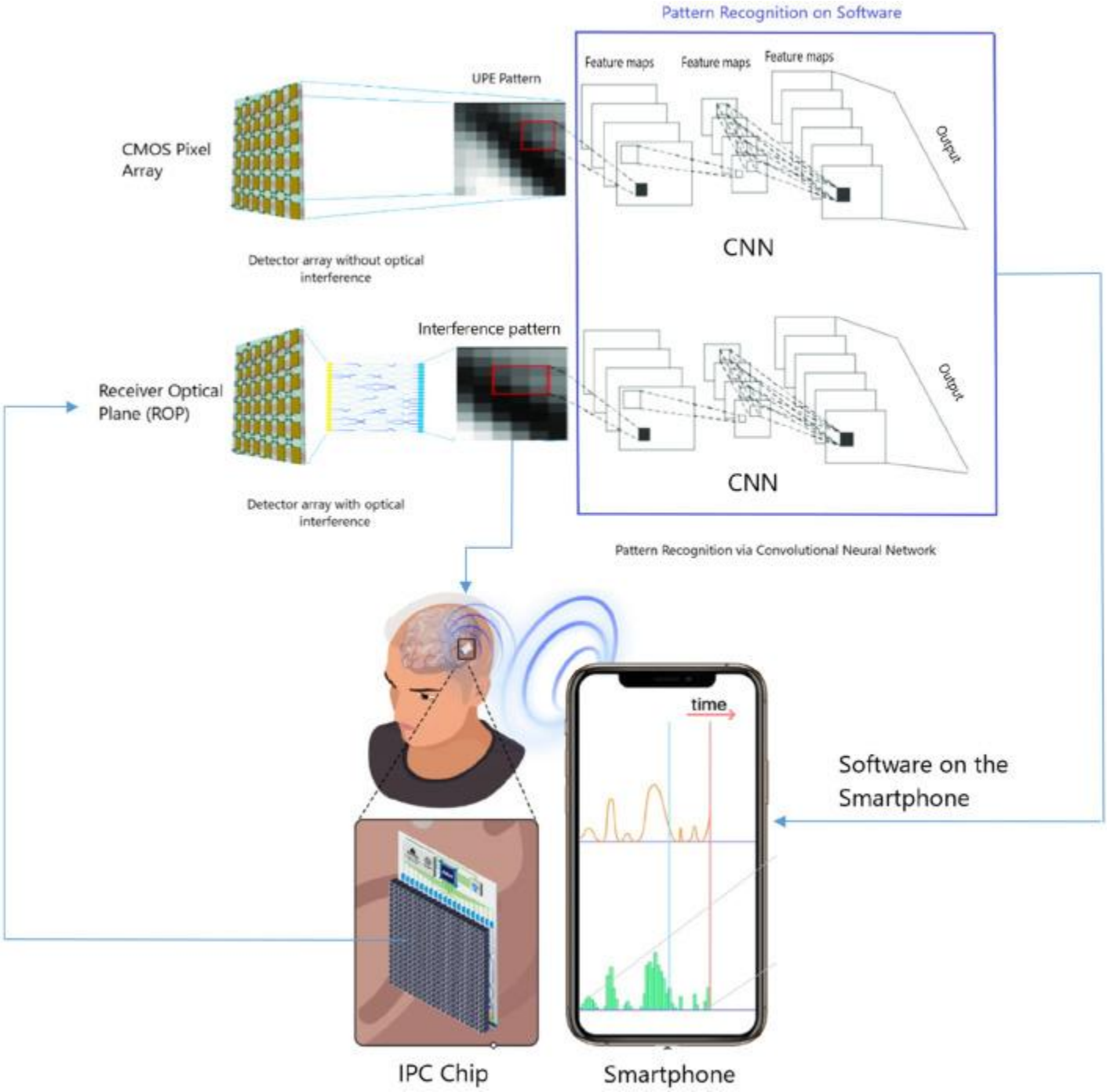
On-chip optical interferometer with N' inputs and N' outputs. The output patterns can be processed for feature extraction via machine learning techniques. It is expected that for each cognitive task or decision making, a similar pattern (in average) forms after many runs under training for specific tasks. The features of

the average pattern can be recognized by deep learning methods, or specifically by convolutional neural networks (CNNs) on a software.

4.3. Implementation Feasibility

We now discuss the feasibility of fabricating all elements of our envisaged skull-implant UPE-based BCI (to be followed with Figure 5).

Figure 5.



Feature extraction and pattern recognition of detected ultraweak photon emission (UPE) by a chip composed of complementary metal-oxide-semiconductor (CMOS) array via convolutional neural network (CNN) on a software installed on a computer, machine, or smartphone; **(top)** direct UPE detection without optical

interferometer, and **(bottom)** UPE detection after the interferometer. The existence of optical interferometer is to discriminate UPE wavelengths, since interference of similar photons (in wavelength) make a different pattern with non-similar photons. One of the advantages of such an interferometer is to have a simple “spectrometry” over similar wavelengths. However, an ensemble of wavelengths may make different patterns at the same time and obscure the interference patterns which may not make advantage over a direct detection, but one can classify those ensemble patterns with pattern recognition techniques such as PCA, which can find the differences between different patterns in the overlapped patterns, and classify each pattern for the relevant wavelength after many sets of training data. The direct detection of UPE by CMOS array and indirect detection after an optical interferometer both can be used for UPE data acquisition.

4.3.1. Chip Ingredients

The design and fabrication of PICs is a mature technology, which is realized on a variety of material platforms, which are tailored to the needs and requirements of the application at hand. Available platforms for lithography-based fabrication include silicon photonics [Silicon on Insulator (220 nm and 3 μm SOI), Si-based silica on silicon (SiO_2, also known as PLC), and silicon nitride (SiN and TriPleX)], III-V photonics such as indium phosphide (InP), gallium arsenide (GaAs) and derivatives, and finally lithium niobate ($LiNbO_3$) and other more exotic materials (Liang and Bowers, 2009; Washburna and Bailey, 2011; Fang and Zhao, 2012; Arakawa et al., 2013; Chrostowski and Hochberg, 2015; Muñoz et al., 2017; Boes et al., 2018; Zhu et al., 2021). It should be noted that the SIO platform is not a suitable candidate for the UPE in the visible spectrum as the relatively small band-gap of silicon renders it completely opaque below a wavelength of about 1,000 nm. SiN, which, on the other hand, is transparent in the visible wavelength-range and features compatibility with CMOS technology (Romero-Garcia et al., 2013), appears to be a strong candidate as a PIC platform for our proposed BCI. As an alternative to the lithography-based PIC, femto-second laser-written waveguides (FLWs) in SiO_2 (glass) have in recent years been used to successfully implement advanced PICs (Davis et al., 1996; Marshall et al., 2009). The unique advantage of FLWs is that the ability to define waveguides in three dimensions, i.e., including at different depths in the chip. This allows more complex routing, such as the crossing of waveguides (Marshall et al., 2009).

Choosing the right technology will be the starting point for having a successful integrated chip. By integrating all devices into a single chip, complex assembly, alignment, and stabilization processes are avoided, and packaging and testing are greatly simplified. Moreover, it is the only way to scale up complexity when moving over 20–30 components into a single package. The selection of the integration material will then determine the capabilities and limitations for the technology platform, making some of them more appropriate for certain

applications than others. This is thus a critical choice and needs to be carefully evaluated.

4.4. Noise and Loss in the PIC

Design of an PIC, testing and packaging from the beginning should be done carefully. The steps are device level (optical, thermal, and material simulations), circuit level (virtual lab to test performance), system level (PIC connected to a CMOS array), layout level (generate the design intent), verification, simulation of each process step, fabrication, and finally packaging. Moreover, a software should be designed to process the detected signals. Here, we would like to estimate the noise magnitude in the optical section of the PIC. The optical section is composed of receiver optical plane (ROP), optical fibers (OF), and optical interferometer (OI).

4.4.1. Noise and Loss in the Receiver Optical Plane

First, we note that blackbody radiation is not a significant source of photons in the visible wavelength range at body temperature. On our BCI, photons are directly coupled to the ROP's fibers that are very close (approximately in contact) with the cortex, thereby leading to a minimal coupling loss. In terms of noise, shot noise [also known as “quantum noise” (Gardiner and Zoller, 2004) or “photon noise”] is the most important contribution in the ROP. It describes the fluctuations of the number of photons received due to their occurrence independent of each other. Optical detection is said to be “photon noise limited” as only the shot noise remains. Just as with other forms of shot noise, the fluctuations in a photo-current due to shot noise scale as the square-root of the average intensity:

$$\mathrm{SN} := |\sqrt{(n - \langle n \rangle)2}\,|$$

4.4.2. Loss in Optical Fibers

The intensity of photons will become lower when traveling through the core of fiber optic. Thus, the signal strength becomes weaker. This loss of light power is generally called fiber optic loss or attenuation. This decrease in power level is described in dB. There are two types of loss in optical fibers known as intrinsic fiber core attenuation (mainly due to light absorption and scattering) and extrinsic fiber attenuation due to bending loss as well as splicing (or coupling) loss between the fibers and chip. Given that the length of the fibers are to be in centimeter scale, the former will be negligible. However, bending and splicing/coupling loss can be significant depending on the process of binding the fibers to the photonic chip. For example, based on subwavelength gratings, it has been shown that it is possible to couple broadband light with very low coupling

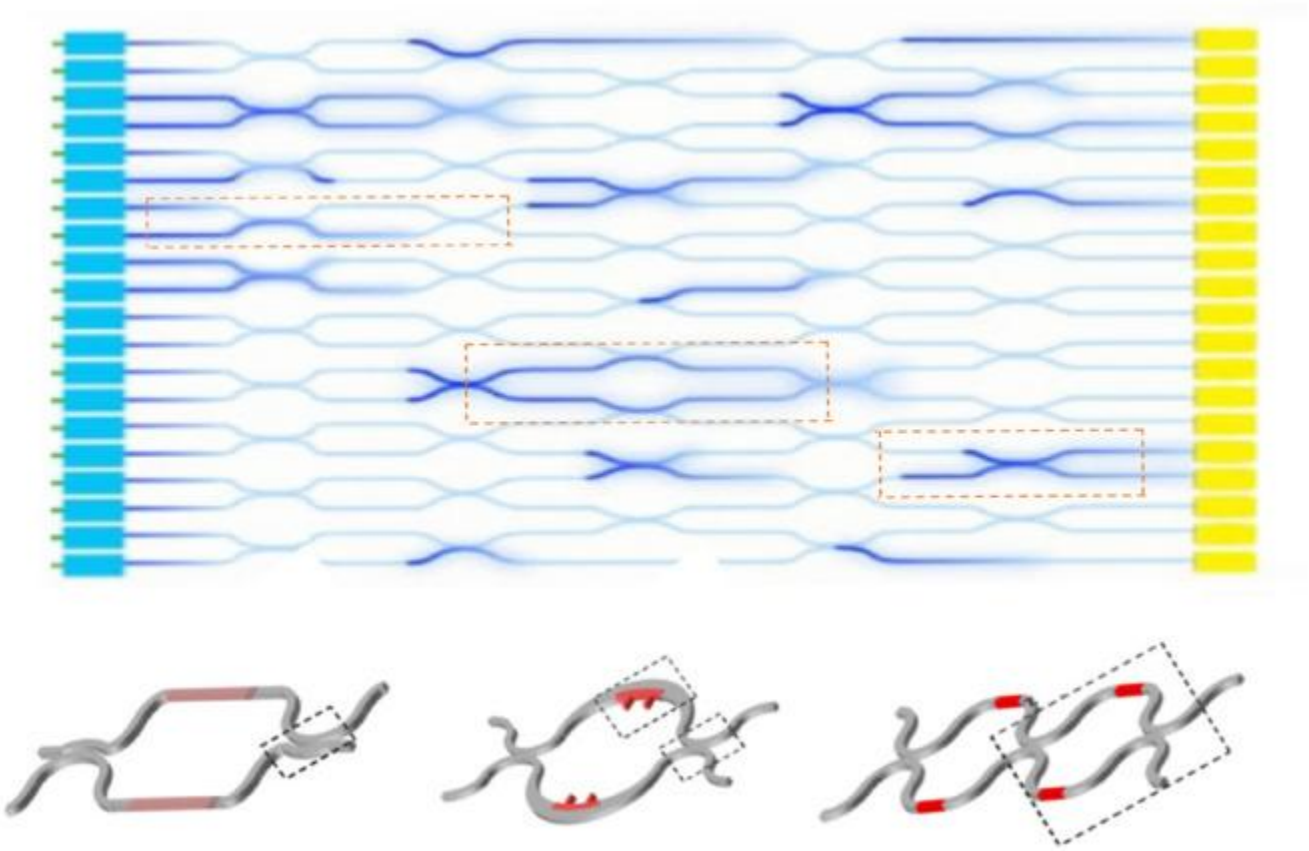
losses. Guiding of visible light in the wavelength range of 550–650 nm with losses down to 6 dB/cm is feasible using silicon gratings (having absorption of 13,000 dB/cm at this wavelength), which are fabricated with standard silicon photonics technology. This approach allows one to overcome traditional limits of the various established photonics technology platforms with respect to their suitable spectral range (Urbonas et al., 2021).

4.4.3. Noise and Loss in Optical Interferometer

The main elements of an optical interferometer on a photonic chip are couplers and optical modulators, as illustrated in Figure 7. There are different types of optical modulators such as MEMS, liquid crystal on silicon (LCOS), electro-optic $LiNbO_3$ waveguide, III-IV semiconductor optical amplifier (SOA), Mach-Zehnder interferometer (MZI), and micro-ring resonator (MRR) (Stefanov et al., 2020). Compared with the above technologies, the silicon photonic modulators based on silicon-on-insulator (SOI) platform attract more attention because of high device

density, whose volume is 1/1,000 of silicon dioxide devices, functional integration with active photonic devices and complementary metal oxide semiconductor (CMOS) circuit, and fabrication process compatible with a mature CMOS manufacturing technology. One of the state of art of the silicon photonic modulator engine that is very useful for quantum interference is MZI. A typical 2 × 2 MZI modulator cell consists of two 3 dB coupler and a dual-waveguide arm between them. One of the arms has a phase shifter based on the change of refractive index. Since the silicon has both strong thermo-optic (T-O) effect (1.86×10^{-4} K^{-1}) (Stefanov et al., 2020), the phase shifter can be categorized as T-O switch with a heater and electro-optic (E-O) switch with a p-i-n junction diode. The T-O switch has a response time of microsecond-scale to millisecond-scale, while the E-O switches have a response time of nanosecond-scale.

Figure 7.



Schematic of various of Mach-Zehnder interferometer (MZI) modulator cells in an optical interferometer. The undesirable attenuation of light in the waveguides and modulators depends on material of the chip platform as well as the dimension and structure of modulators (Stefanov et al., 2020), which determine bending and scattering loss.

The loss in on-chip optical interferometers arise from non-unity coupling from fiber to the input ports of the chips as well as attenuation through the waveguides patterned on the chip. As discussed above, the coupling loss can be significantly less than 1 dB through the advanced coupling methods. However, the waveguide propagation loss is given by the chip platform. Depending on the wavelength, this loss can vary substantially, in particular in the wavelength range of 300–700 nm, as shown in Table 1.

Table 1.

Data adapted from APL Photonics 5, 020903 (2020); Optica 6(3), 380-384 (2019); and Optics Express 14 (11), 4826-4834 (2006).

Loss vs. wavelength for various chip platforms

Loss (dB/cm)	300–400 nm	400–500 nm	500–600 nm	600–700 nm
Aluminum nitride (AlN)	40–50	40–50	30–40	20–30
Alumina (Al_2O_3)	~3	2	1	<1
Tantalum pentoxide (Ta_2O_3)	N/A	~4	~2	<1
Silicon-nitride (Si_3N_4)	N/A	5–20	<1	<1
Lithium niobate ($LiNbO_3$)	N/A	N/A	N/A	~0.06
Femto-second laser-written waveguides in glass (SiO_2)	N/A	N/A	N/A	~0.2

4.5. Noise and Loss in the CMOS Sensor Array

Noise can be produced by fluctuations in signal that makes uncertainty in detection. Essentially, the signal-to-noise ratio (SNR) is the ratio of pattern signal to the total noise. For larger SNR, it is easier to distinguish pattern from noise, which makes a higher confidence in measurements.

CMOS (Complementary metal–oxide–semiconductor) primary noise sources are shot (photon) noise (i.e., SN), dark noise (i.e., DN), and read noise (i.e., RN). Shot noise is due to physical property of light, regardless of sensor, and it is SN =√Signal. Dark noise is temperature dependent and higher for global shutter and its magnitude is obtained as DN =√Dark Current. Read noise includes Random Telegraph Noise (RTN), which is non-Gaussian, and depends on multiply column and pixel amplifiers, RN = ReadNoise. RTN is the most significant component of CMOS noise. The SNR for CMOS is obtained as follows:

$$\mathrm{SNR}=S\sqrt{\mathrm{SN}2+\mathrm{DN}2+\mathrm{RN}2}$$

where *S* is Signal=Photon flux × time × QE (Dragulinescu, 2012).

Scientific CMOS (sCMOS) sensor is a novel technology with room to grow, which allows for higher speed operation with larger pixel arrays than EMCCD and CCDs with similar noise performance to conventional CCDs.

4.5.1. Quantum Efficiency

QE is defined as

$$QE = \frac{\text{Converted photons to electrons}}{\text{Total incident photons}}$$

which is a measurement of sensitivity to light. As a ratio, QE is dimensionless, but it is closely related to the responsivity, which is expressed in amps (*A*) per watt (*W*). Since the energy of a photon is inversely proportional to its wavelength, QE is often measured over a range of different wavelengths to characterize a detector efficiency at each photon energy level.

The photodetector matrix consist of CMOS-compatible photodiodes (formed between drain diffusion and p-well) with associated readout and sensor selection circuits. The spectral measurements of the photodiode have exhibited a QE better than 60% at 650 nm, and better than 40% between 500 and 850 nm (Dragulinescu, 2012).

A chip design for UPE detection can be inspired by retina implants, but with bigger array size and significantly higher QE. The irradiance on the retina even under a bright daytime illumination does not exceed 1 μW mm^{-2}. At such illumination a 20 μm diameter photodiode (having even 100% QE) can provide only 40 pA of current (Palanker et al., 2005). Basically, each photoreceptor cell can produce 1 pA with a single photon absorption (Salari et al., 2016a). To provide stimulating current on the order of 1–2 μA, which would be minimal for physiological stimulation, current amplification by a factor of about 1,000 is required. Suitable current levels would require photodiodes more than 600 μm in diameter, so that ambient light cannot be used to power more than a token number of electrodes on a retinal chip. An additional source of power will be needed for any practical chip (Palanker et al., 2005). The stimulation current for an electrode of 10 μm in diameter is on the order of 1 μA. The photodiode converts photons into electric current with efficiency of up to 0.6 AW^{-1}, thus 1.7 μW of light power will be required for activation of one pixel. If light pulses are applied for 1 ms at 50 Hz, the average power will be reduced to 83 nW/pixel. With 18,000 pixels on the chip, the total light power irradiating an implant will be 1.5 mW (Palanker et al., 2005). In the case of skull-implant PIC chip, the main difference with the retina implant is that the retina implant should activate neurons with the currents produced by external light, which needs a relatively high intensity of light, while for the PIC chip there is no need to activate neurons, and a low light intensity even with a few numbers of photons is sufficient for the CMOS pixels activation to be reported to the software. In silicon, a single-photon

with a wavelength between 300 and 1,100 nm can generate only one electron–hole pair. Therefore, for visible and near-infrared light, the task of single-photon detection becomes a task of single-electron (or hole) detection. This is not easy due to the unavoidable readout noise of the sensor, which is usually too high for the reliable detection of a single electron. Another difficulty for room temperature applications are the thermal dark currents, because they are indistinguishable from photogenerated signals.

4.5.2. Chip Battery and Wireless Sectors

In order to have a dynamic chip for monitoring signals of the brain continuously, the chip requires a long lifetime battery. The size and lifetime of the battery is one of the major challenges in design of an implant chip for biomedical applications. As an alternative, replacing the battery with a miniaturized and integrated wireless power harvester aid the design of sustainable biomedical implants in smaller volumes (Masius and Wong, 2020). Currently, implanted batteries provide the energy for implantable biomedical devices. However, batteries have fixed energy density, limited lifetime, chemical side effects, and large size. Thus, researchers have developed several methods to harvest energy for implantable devices. Devices powered by harvested energy have longer lifetime and provide more comfort and safety than conventional devices. A solution to energy problems in wireless sensors is to scavenge energy from the ambient environment. Energies that may be scavenged include infrared radiant energy, wireless transfer energy, and RF radiation energy (inductive and capacitive coupling) (Hannan et al., 2014). Recently, a chip has been developed that is powered wirelessly and can be surgically implanted to read neural signals and stimulate the brain with both light and electrical current. The technology has been demonstrated successfully in rats and is designed for use as a research tool. The chip is capable of 16-ch neural recording, 8-ch electrical stimulation, and 16-ch optical stimulation, all integrated on a 5×3 mm^2 chip fabricated in 0.35-μm standard CMOS process. The trimodal SoC is designed to be inductively powered and communicated (Jia et al., 2020).

4.6. Biocompatibility of the Chip

Brain implants may induce side effects; for instance they may interact acutely and chronically with the brain tissue possibly causing blood–brain barrier (BBB) breach, vascular damage, micromotions, diffusion, etc. (Prodanov and Delbeke, 2016). The advantage of our suggested photonic chip is that it is minimally invasive compared to invasive implants (e.g., ECoG) since it does not need to penetrate the brain tissue.

Some of the key fundamental questions associated to brain implants are related to how long an implant can record useful neuronal signals and what degree of acquisition and decoding reliably can be achieved if the tissue is affected by chip

implant. Functional neural tissue survival, distance from the chip contact to target and long-term stability are essential parameters to be considered (Prodanov and Delbeke, 2016).

In the case of photonic chip, it should be installed on the inner surface of the skull and not to be implanted directly in the brain tissue. However, there is still the possibility of a close contact with the brain meninges (i.e., layered membranes that protect the brain and spine) due to the mechanical or volume changes of the brain. In this case, it has been shown that Silicone causes the least amount of inflammation relative to other materials tested at all sacrifice points, which makes it the leading standard neurosurgical implant material and an appropriate control for studies of brain biocompatibility (Mofid et al., 1997). Thus, we envisage to adopt silicone chips but we also expect that research in biocompatibility will provide alternative and advanced materials. However, since the photonic chip can be implanted in between the meninges and the skull, there can be concerns about the limitation of brain UPE detection due to the existence of meninges. The meninges layers of the human brain are composed of three main layers: dura, arachnoid, and falx. The key question is whether light can pass through these layers and if it does, then what are the scattering and absorption effects of photons? For instance, to have a reasonable data acquisition should the dura be open? The optical properties of the human brain and its meninges have been investigated decades ago. It has been shown that meninges is approximately transparent for the near-IR range, but almost half of emissions will not pass through it in the visible range, and less than 40% of emissions can pass through the meninges in the UV range (200–400 nm) (Eggert and Blazek, 1987). As a result, based on the high efficiency of the photonic chip in the near-IR range, the existence of meninges reduces the intensity of UPE but it does not lead to a significant limitation.

Additionally, because of the aqueous and biochemically aggressive nature of the body, the lifetime of brain implants strongly depends on packaging. There are different methods for packaging, which may be especially important for the case of traditional electric chips with wireless neuromodulatory implants with increasing electrode count to have an *in vivo* lifetime comparable to a sizable fraction of a healthy patient's lifetime (>10–20 years) (Shen and Maharbiz, 2021). For our suggested photonic chip, the situation is considerably better because the chip does not have electrodes in the wet biological tissue nor contact with that, and the environment between the meninges and skull is not aqueous, and therefore the probability of water leakage in the photonic chip is minimal. If there will be an injury in the meninges layers due to some impact or accident, then the aqueous leakage may occur, where the photonic chip should be investigated for packaging based on the materials used.

5. Discussion and Conclusion

We propose a radically novel BCI that is based on UPE from the brain. We describe its feasibility of fabrication based on integrated photonic circuits that be readily implemented in a lab. The envisaged BCI chip can be implanted on the interior surface of the skull to monitor in real-time UPE signals emanating from the cortex surface. The proposed chip is not only useful for BCI technology but also it can be used as a photonic sensor for imaging, spectroscopy, and sensitive measurements at low light levels in several applications from biological UPE to quantum optical processing (Salari et al., 2021). Although our proposed technology is, admittedly, at the level of conjecture, requiring comprehensive tests and investigations for verification, we still envision complementary features as well as certain advantages over established technologies, including ECoG. The inherent advantage of our proposed technology is that it is minimally invasive when compared to ECoG. Furthermore, there are certain side effects that may affect the quality of data acquisition over time in ECoG, whereas we expect a relatively stable long-term data acquisition in our proposed approach. In addition, if our suggested photonic chip-technology reaches a satisfactory detection performance based on our estimations, we anticipate that it can feature some other advantages. For example, it may provide additional information about brain functioning, such as an approximately real-time imaging (in slightly longer timescales, e.g., each 15, 20, 30, 60 min, or so) and open the door to studying metabolism variations, variation of ROS production, delayed luminescence but also undertake novel and complementary studies on object visualization studies, sleep studies, and neurodegenerative diseases (Breakspear et al., 2006; Fülöp et al., 2021). Indeed, the emphasis of our conjectural paper is to develop a novel technology and methods that could provide complementary information to improve our understanding of brain activity with potential applications for BCI technologies.

Now, we would like to discuss the advantages and limitations of our proposed technology vs. the current BCI methods. On-chip PICs offer advantages such as miniaturization, higher speed, low thermal effects, large integration capacity, and compatibility with existing processing flows that allow for high yield, volume manufacturing, and lower prices. In the case of UPE detection, there is no need for on-chip single-photon sources, which is one of the most difficult challenges in PICs for quantum computation and communication. In the suggested chip, single photons are produced naturally by metabolism in neurons and therefore a lower power with battery is needed for energy consumption on an implant PIC. Loss is low in NIR range (e.g., 2×10^{-6} dB/cm). In addition, photons are bosons, which do not interact and crosstalk is minimal. A PIC for optical interferometery is efficient for the wavelengths typically in the near infrared range, 800–1,650 nm. This makes a limitation for detection of UPE photons that are in the visible range and the overlapped part to NIR, 400–800 nm. For example, loss is high for the visible range (e.g., 0.6 dB/cm at 600 nm).

Moreover, it may look that the single-photon detections on a CMOS array have a low QE besides the dark current in room temperature, which may lose considerable amounts of UPE. Another concern may be that the output of CMOS is electrons, which are charged particles and fermions, and therefore electronic crosstalk is inherent. In fact, the CMOS QE is about 75%, which is about three times higher than the photo-multiplier tubes (PMTs) with QE about 25%. The SNR of a PMT at room temperature to detect UPE photons is about 1–2, thus a cooling system is required to cool down the PMT sensor to enhance the SNR to reach 3 and higher. Obviously, there is no cooling system on an PIC chip, but in this case, the QE of the CMOS sensor can compensate the lack of a cooling system. For a simple estimation, assuming a 1 × 1 cm chip and considering the length of each CMOS pixel is 4 μm, it is possible to have 2,500 CMOS pixels as the output port on the chip, including 50×50 pixels on the ROP. According the estimations in the main text, the amount of total photon loss from the receiver optical plane (ROP) to the output of the optical interferometer (OI) is about 50%, and the QE of CMOS at the output of the OI is estimated to be 25% in body temperature under the implant conditions on the skull to have a final SNR from 1 to 2. Consequently, it is estimated that only 10% of incident photons can be safely recognized in the output and reported wirelessly to the software on a computer or smartphone. Considering 10–1,000 incident photons per second received in the ROP under a cognitive task (e.g., an object visualization), there can be 1–100 photons per second efficiently detected in the output port, which are enough to have a relatively successful implant PIC chip for an acceptable pattern for UPE processing, where the size of the machine learning program is $N \times N$ sparse matrix, which is not a difficult task for a chip size number of pixels. To conclude, in this paper, we advance major conjectures regarding the relevance of UPE patterns and decision making as well as the feature extractions from UPE signals, which need to be experimentally verified. However, despite some probable limitations in chip fabrication and efficiency, it may be used for wireless BCI signal acquisition with several advantages vs. traditional counterparts such as speed, size, minimally invasive, cheap, scalability, etc. This can be a potential step forward for real-time brain imaging and biological information processing.

JANUARY 15, 2025

Repetitive transcranial magnetic stimulation enhances tai chi chuan–linked benefits, study claims

by Justin Jackson , Medical Xpress

Credit: Unsplash/CC0 Public Domain

Fujian University of Traditional Chinese Medicine in China has reported that repetitive transcranial magnetic stimulation (rTMS) boosts the effectiveness of tai chi chuan in improving sleep quality and cognitive function among older adults with sleep disorders and mild cognitive impairment (MCI).

Sleep disorders affect nearly half of adults over 60, exacerbating cognitive decline and increasing dementia risk by 30%. Current pharmacologic treatments yield unsatisfactory results, highlighting the need for effective nonpharmacologic interventions.

Tai chi chuan, a form of meditative calisthenics with roots in martial arts, is linked to enhancing sleep quality and delaying cognitive impairment, according to the researchers.

Adherence to tai chi chuan can present challenges for some as it requires prolonged moderate-intensity levels of aerobic activity.

rTMS is a technique that involves delivering repeated magnetic pulses to stimulate nerve cells in the brain. Magnetic stimulation appears to affect brain function and is often used in resistant forms of depression in hopes of awakening cells that remain dormant during depression. The mechanisms behind the result are still unclear. Other uses include migraine headache relief and smoking cessation therapy, again used only after traditional methods have failed.

In the current research, rTMS was investigated for its effects on the clinical benefits of tai chi chuan in older adults with sleep disorders and mild cognitive impairment.

In the study, "Repetitive Transcranial Magnetic Stimulation and Tai Chi Chuan for Older Adults With Sleep Disorders and Mild Cognitive Impairment: A Randomized Clinical Trial," published in *JAMA Network Open*, rTMS was investigated for its effects on the clinical benefits of tai chi chuan in older adults with sleep disorders and MCI.

In total, 110 participants aged 60 to 75 years were randomly assigned to either an experimental group receiving tai chi chuan and 1-Hz rTMS targeting the right dorsolateral prefrontal cortex or a group receiving tai chi chuan and sham rTMS. A 24-form Yang-style tai chi chuan routine was used.

Each group underwent 30 sessions over six weeks, with assessments at baseline, post-intervention, and a 12-week follow-up. Primary outcomes measured sleep quality using the Pittsburgh Sleep Quality Index (PSQI) and cognitive function with the Montreal Cognitive Assessment (MoCA).

At the six-week mark, the experimental group showed significant 3.1-point lower PSQI scores and 1.4-point higher MoCA scores compared to the sham treatment group.

At the 12-week follow-up, the experimental group maintained these benefits, with PSQI scores remaining 2.1 points lower and MoCA scores remaining 0.9 points higher than those in the sham group.

Secondary outcomes showed enhancements in memory, anxiety, depression, and specific cognitive tasks. Adverse events were minimal and unrelated to the interventions.

Findings suggest that 1-Hz rTMS targeting the right dorsolateral prefrontal cortex significantly enhances tai chi chuan's benefits for sleep and cognitive functions in older adults with sleep disorders and MCI. The research team asserts that this may be related to alterations in neural plasticity, though it is unclear how this was investigated.

Incomplete reporting

The published article does not reflect the full scope of investigative measures registered for the trial, particularly when it comes to advanced neuroimaging and biochemical assays. Specifically, advanced neuroimaging methods such as fMRI, EEG, and fNIRS, along with biochemical assays like serum mass spectrometry neurotransmitter assays, were outlined in the clinical trial registration but were not reflected in the published findings.

The absence of these methods in the publication raises questions about whether they were utilized as per the registration or if they were excluded post-registration. Part of the reason clinical trials and methods are registered is to prevent "cherry picking" of favorable results and to offer transparency in study results. If indicators like fMRI or EEG were not utilized or the results were omitted, the authors should explicitly mention these exclusions in the study's limitations or discussion sections.

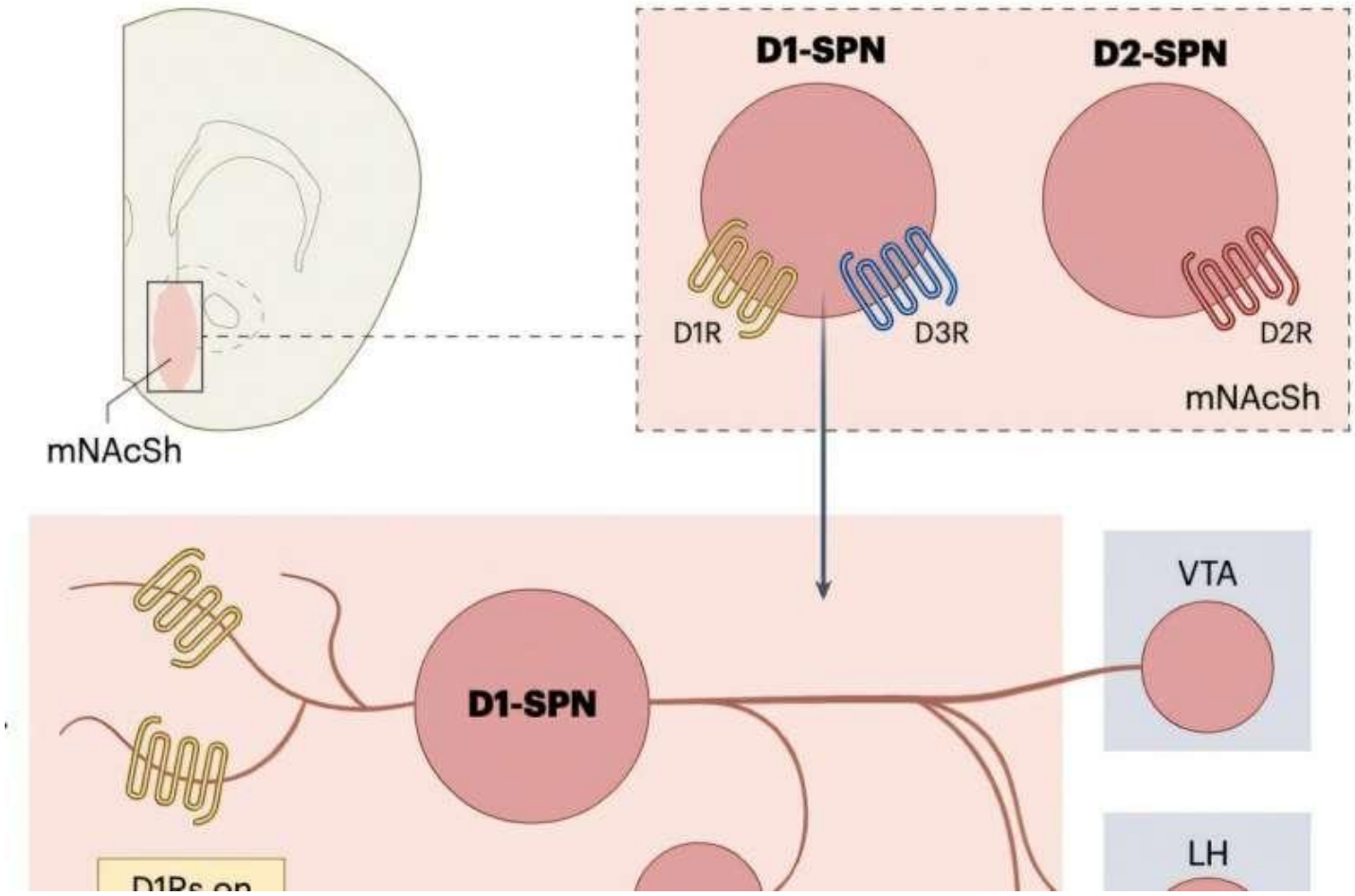
More information: Zhizhen Liu et al, Repetitive Transcranial Magnetic Stimulation and Tai Chi Chuan for Older Adults With Sleep Disorders and Mild Cognitive Impairment, *JAMA Network Open* (2025). DOI: 10.1001/jamanetworkopen.2024.54307

Giuseppe Lanza et al, Noninvasive Brain Stimulation and Holistic Therapies for Sleep and Cognition, *JAMA Network Open* (2025). DOI: 10.1001/jamanetworkopen.2024.54316
Journal information: JAMA Network Open

JANUARY 15, 2025

Dopamine acts on motivation and reinforcement learning via distinct cellular processes, study suggests

by Ingrid Fadelli , Medical Xpress



Credit: *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01820-2

Dopamine is a key neurotransmitter known to modulate motivation and reinforcement learning. While the role of dopamine in these reward-related processes is well-established, the cellular and neural circuit-level mechanisms underpinning its involvement in these processes is not yet fully understood.

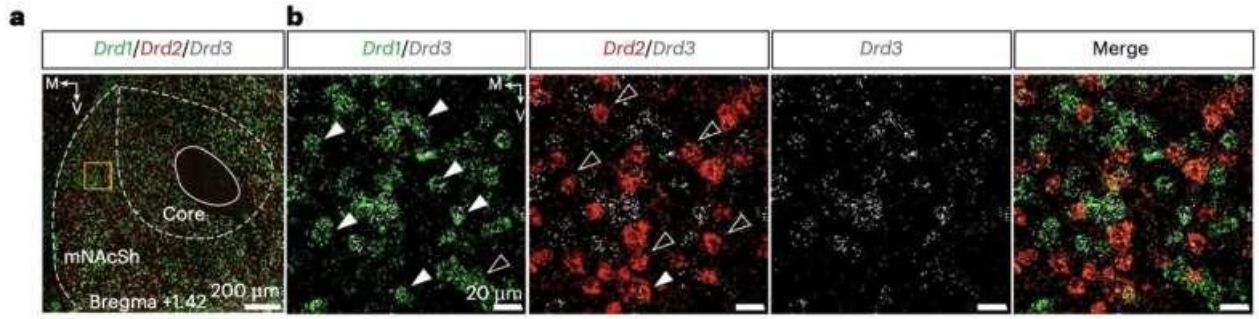
Researchers at the National Institute of Mental Health and other institutes carried out a study investigating the cellular processes via which dopamine supports motivation and the reinforcement of specific behaviors.

Their findings, published in *Nature Neuroscience*, suggest that different aspects of reward-related behavior are supported by two distinct dopamine receptors, namely D3 and D1.

"The previous literature clearly showed that dopamine is important for motivation and reinforcement," Hugo Tejeda, senior author of the paper, told Medical Xpress.

"This is an important topic since deficits in motivation or excessive motivation are cardinal symptoms in many mental disorders. The nucleus accumbens, a brain region where dopamine is thought to exert its effects, is uniquely enriched with a molecule that recognizes dopamine, the D3 receptor."

So far, the role of the D3 receptor in regulating motivation and reinforcement, as well as the relation between its functioning and that of other receptors, had remained elusive. The key objective of the recent study by Tejeda and his colleagues was to shed new light on the contribution of D3, while also exploring how it works with other dopamine receptors.



mNAcSh D3Rs are primarily expressed in D1-MSNs and D3-MSNs display D1-MSN projection pattern. A) Representative low-magnification confocal image of RNA in situ hybridization for Drd1 (green), Drd2 (red) and Drd3 (white) transcripts in the NAc. Orange inset shows the region targeted for zoomed images in b. b) Split high-magnification images of Drd1/Drd3, Drd2/Drd3 and Drd3 RNA expression in the mNAcSh. Credit: *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01819-9

As an initial step in addressing the role of D3, co-senior author Zachary Freyberg and his laboratory at the University of Pittsburgh developed a new mouse strain that enables cell-type-selective deletion of D3 receptors, including in the nucleus accumbens.

"Using a virus-based technique in mice, we were able to specifically genetically delete D3 receptors from the nucleus accumbens," said Tejeda. "Importantly, this technique left the other dopamine receptors in this region intact, as well as D3 receptors in other brain regions."

After they had genetically "deleted" D3 receptors in the nucleus accumbens of mice, the researchers examined how this experimental intervention had affected the animals'

motivation and reinforcement-related behaviors. To assess the animal's motivation, they particularly looked at the mice's willingness to exercise or work to attain food rewards.

"To determine the impact of deleting D3 receptors on reinforcement, we examined the mouse's ability to learn that an action generated an outcome," explained Tejeda. "On a cellular level, we used electrophysiology to show the effects of D3 receptors on neuron physiology in the nucleus accumbens and how it differed from the D1 receptor, which cells co-express with D3 receptors."Whole-brain imaging of D3-MSN projections. This video shows tdTomato-labeled fibers and Syn-GFP-labeled putative presynaptic terminals from Drd3-Cre MSNs of the mNAcSh. Different signals are shown separately to highlight the different nature of labeling. Credit: *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01819-9

Tejeda and his colleagues also developed a new set of "disconnection" procedures that allowed them to assess the contribution of D3 and D1 receptors individually. Using these procedures, they unveiled that D3 and D1 receptors regulate different aspects of reward-based learning via physiological processes occurring within nucleus accumbens neurons.

Specifically, D3 receptors were found to regulate motivation, while D1 receptors appeared to regulate reinforcement.

"Our findings provide the first evidence that dopamine exerts its actions on motivation and reinforcement through separable cellular processes in neurons that are part of the brain's reward circuitry," said Tejeda.

"There are important implications because medications that act on D3 receptors are used for the treatment of mood disorders. For example, cariprazine, a partial activator of the D3 receptor, was approved by the U.S. Food and Drug Administration for the treatment of mood disorders."

The recent work by this team of researchers introduced new experimental procedures that can be used to closely examine the cellular contribution of specific receptors in the mouse brain.

The results of their initial experiments contribute to the understanding of how dopamine supports different aspects of reward-based learning, which could inform the development of new treatments for mental disorders characterized by a lack of motivation.

"We want to investigate how dysfunction of D3 receptors contributes to motivation loss in some mental disorders," added Tejeda. "We also want to study the impact that D3 receptors have in conjunction with other dopamine receptors on computations in brain reward circuits."

More information: Juan Enriquez-Traba et al, Dissociable control of motivation and reinforcement by distinct ventral striatal dopamine receptors, *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01819-9

Nicolas X. Tritsch, Motivating interest in D3 dopamine receptors, *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01820-2
Journal information: Nature Neuroscience

JANUARY 14, 2025

Drinking green tea linked to fewer white matter lesions in brains of older adults

Credit: Unsplash/CC0 Public Domain

Research led by the Kanazawa University Graduate School of Medical Sciences has reported a significant connection between higher green tea consumption and fewer cerebral white matter lesions in older adults without dementia. Findings suggest that drinking three or more glasses of green tea daily may help protect brain health, while coffee consumption showed no significant effect.

Green tea and coffee are both known for their neuroprotective compounds and are the most widely consumed beverages globally after water. Prior research suggests that tea and coffee intake is linked to cognitive benefits, yet few studies have examined their direct association with brain structural changes in older adults.

Cerebral white matter lesions, often indicative of small vessel disease, have been associated with cognitive decline, vascular dementia, and Alzheimer's disease (AD). The current study aimed to evaluate the impact of green tea and coffee consumption on white matter lesion volume, hippocampal volume, and total brain volume using magnetic resonance imaging (MRI) data.

The study, "Green tea consumption and cerebral white matter lesions in community-dwelling older adults without dementia," published in *npj Science of Food*, was conducted as part of the Japan Prospective Studies Collaboration for Aging and Dementia, a large-scale, multisite observational study involving eight research centers in Japan.

Data collection occurred between 2016 and 2018, including dietary assessments, MRI scans, and cognitive evaluations of 8,766 participants aged 65 and older. A Food Frequency Questionnaire was used to measure daily green tea and coffee intake, categorized into four levels: 0–200 ml, 201–400 ml, 401–600 ml, and ≥601 ml.

Brain MRI scans provided data on the volume of white matter lesions (WML), hippocampal volume (HV), and total brain volume (TBV). Advanced statistical models were applied to adjust for confounding factors, including demographics, health conditions, lifestyle habits, and genetic risk factors for Alzheimer's disease.

The analysis excluded participants with mild cognitive impairment (MCI), dementia, or incomplete data, narrowing the final cohort to 8,766 individuals.

After adjusting for confounding factors, higher green tea consumption was significantly associated with lower WML volumes. Participants consuming 600 ml of green tea daily had WML volumes that were 3% lower than those consuming 200 ml or less, and those consuming 1,500 ml daily had WML volumes that were 6% lower than those in the reference group.

No significant associations were observed between green tea intake and hippocampal or total brain volumes. Coffee consumption did not significantly affect WML volume, HV, or TBV.

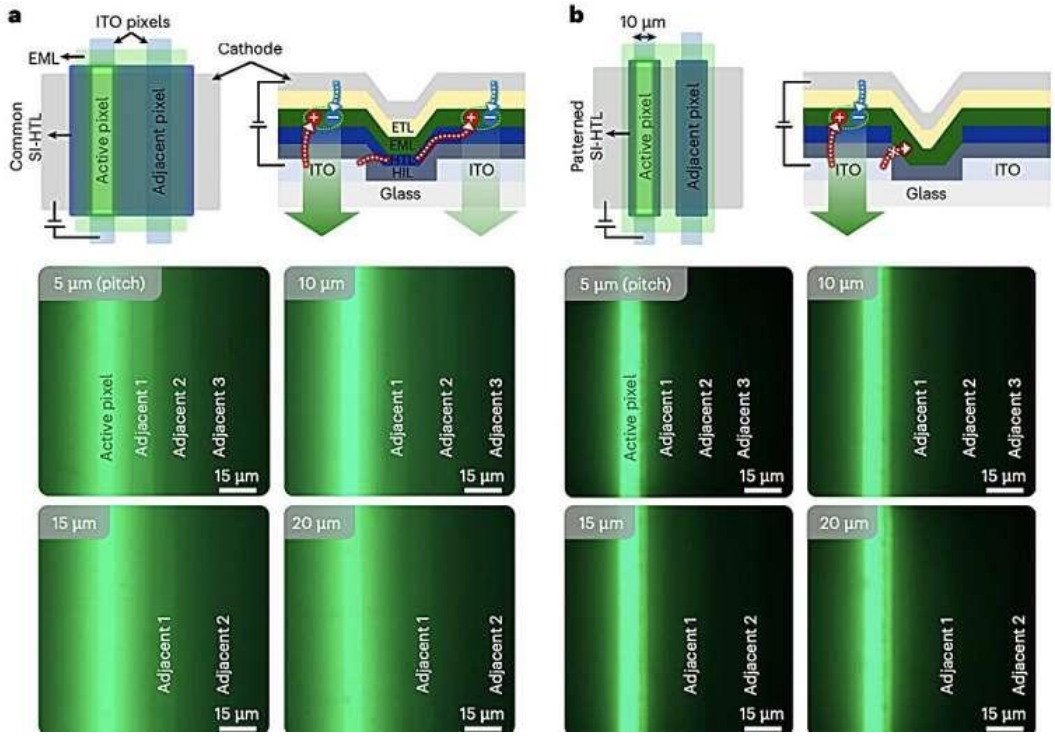
The study also examined subgroups based on depression status and the presence of the ApoE ε4 allele. Significant reductions in WML volumes with increased green tea consumption were observed only in individuals without depression or the ApoE ε4 allele.

Findings suggest that the antioxidant and anti-inflammatory properties of green tea catechins, such as epigallocatechin gallate, may mitigate vascular damage and promote brain health, though specific components were not experimentally validated as causal.

More information: Shutaro Shibata et al, Green tea consumption and cerebral white matter lesions in community-dwelling older adults without dementia, *npj Science of Food* (2025). DOI: 10.1038/s41538-024-00364-w

FEBRUARY 7, 2025

High-definition organic LED microdisplays with reduced electrical crosstalk could enhance VR and AR experiences



Evaluation of electrical pixel crosstalk in OLEDs with micro-patterned SI-HTL. Credit: *Nature Electronics* (2025). DOI: 10.1038/s41928-024-01327-5

The rapid advancement of the electronics industry is opening new possibilities for the development of increasingly advanced device components, including displays. Many of the most widely used and highly performing displays developed to date are based on organic light-emitting diodes (OLED), devices based on organic materials that emit light when an electric current is applied to them.

Compared to conventional displays based on liquid crystals, OLED-based displays do not require a backlight and can thus consume significantly less power. Despite their energy-efficiency, the performance of OLEDs, in terms of image quality and color rendition, has been found to decline as the density of pixels increases, due to undesired interactions between adjacent pixels referred to as electrical crosstalk.

Electronics engineers have devised various strategies to overcome this limitation, most of which entail increasing the thickness of an OLED component known as the hole transport layer (HTL), which facilitates the movement of holes in the devices. Yet these strategies can compromise a display's energy-efficiency, due to increases in the devices' driving voltages.

Researchers at Hanyang University, Yonsei University and Sogang University in South Korea recently introduced an alternative approach to reduce electrical crosstalk between pixels, which could in turn boost the performance and efficiency of OLED displays.

Their proposed solution, presented in a paper published in *Nature Electronics*, involves the use of a silicon-integrated small-molecule hole transport layer (SI-HTL) patterned using microlithography, a well-established technique to precisely structure materials on a microscopic scale.

"High-density displays are required for the development of virtual and augmented reality devices," Hyukmin Kweon, Seonkwon Kim and their colleagues wrote in their paper. "However, increasing the pixel resolution can lead to higher electrical pixel crosstalk, primarily due to a shared hole transport layer. We show that a silicone-integrated small-molecule hole transport layer can be patterned at the wafer scale with microlithography to mitigate electrical pixel crosstalk."

Using microlithography, the researchers created the SI-HTL layer and integrated it in OLEDs. They then created micro-patterned OLED arrays and tested their performance in a series of tests.

Notably, they found that the hole transport layer they created exhibited an improved performance. The prototype display they created was found to enable remarkable pixel resolutions, while also retaining a good energy efficiency.

"With this approach, we create high-fidelity micro-pattern arrays with a resolution of up to 10,062 pixels per inch on a six-inch wafer," wrote Kweon, Kim and their colleagues. "The silicone-integrated small-molecule hole transport layer can effectively modulate charge balance within the emission layers, improving the luminance characteristics of organic light-emitting diodes.

"We also show that organic light-emitting diodes integrated with micro-patterned silicone-integrated small-molecule hole transport layers have a reduced electrical pixel crosstalk compared with organic light-emitting diodes with a typical hole transport layer."

This recent study by Kweon, Kim and their colleagues opens new possibilities for the development of high-definition OLED displays that also exhibit excellent energy-efficiencies. These displays could be integrated into a wide range of electronic devices, including virtual reality (VR) or augmented reality (AR) headsets, smart glasses, wearable technologies, smart phones, and many other electronics.

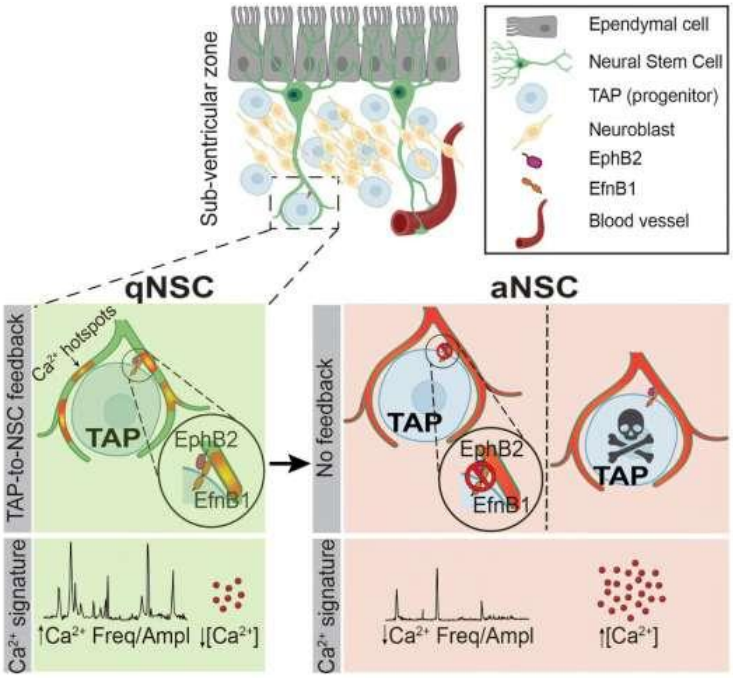
More information: Hyukmin Kweon et al, Microlithography of hole transport layers for high-resolution organic light-emitting diodes with reduced electrical crosstalk, *Nature Electronics* (2025). DOI: 10.1038/s41928-024-01327-5

Journal information: Nature Electronics

FEBRUARY 7, 2025

Study unveils new insights into how neural stem cells are activated in the adult human brain

University of Ottawa



Graphical abstract. Credit: *Cell Stem Cell* (2025). DOI: 10.1016/j.stem.2025.01.001

A University of Ottawa neuroscientist has led a Canadian research team to reveal important new insights into the activation dynamics of neural stem cells (NSCs). These are the stem cells that build our central nervous systems and self-renew.

The collaborative team led by the University of Ottawa's Dr. Armen Saghatelyan aimed to shed light on how neural stem cells integrate a multitude of signals from different cell types in the brain—and how they decode these signals.

These are big questions because how NSCs react to signals in their cellular environment controls whether they remain in their dormant, non-dividing state known as "quiescence" or if they get activated to grow and divide, generating new neurons and glia in the process.

The reported findings, published in *Cell Stem Cell*, will certainly be of deep interest to scientists studying a range of adult neurological diseases and aging. In the neural landscape, rousing NSCs from dormancy, where they conserve resources and energy, is key for neural regeneration and brain injury repair.

"These data make it possible to understand better how NSCs can be activated to generate more neurons and glia in order to counteract different neurological disorders and aging. We are currently studying NSCs' responses for some of these conditions," says Dr. Saghatelyan, Canada Research Chair in Postnatal Neurogenesis and the new publication's senior author.

Cellular 'parent-child' relationship

One avenue of new insight focuses on how stem cells wrap around progeny called "daughter" cells—genetically identical cells created after a parent cell divides.

The team discovered that neural stem cells are in fact receiving constant feedback from their chatty daughter cells. Dr. Saghatelyan likens this to a "parent-child relationship" in which the parent is closely attuned to their child's feedback.

"Many parents will relate to this, since parents like to receive news, or feedback, from their children. Based on this feedback, the parents will either stay reassured that everything is going well or take an action," he says, comparing this dynamic to the cellular state of quiescence or activation.

Revealing this hidden mechanism is a major finding because it provides an entirely new framework for how to understand this cellular relationship in the human brain.

"Until now it was thought that NSCs only generate progeny and that there is no interaction between them," Dr. Saghatelyan says.

"But our work challenged this notion and showed that there is tight structuro-functional interaction between NSCs and their progeny—and that the number of progeny or the efficiency of progeny-NSC interaction determines whether neural stem cells stay quiescent or get activated to generate neurons and glia."

In a nutshell, the research team found that a low number of daughter cells leads to activation of neural stem cells, while a large number of offspring keeps them in their typical state of quiescence in the adult brain.

Further, the new study advances our understanding of how NSCs integrate and decode a multitude of signals in space and time. Dr. Saghatelyan says the research unveils for the

first time that "calcium signaling in NSCs allows for integration and decoding of all these signals."

Informing future therapeutics

These new windows of understanding into how NSCs decode signals and how their activation is triggered offers strong potential for informing any future treatments for human neurodevelopmental disorders. Indeed, advancing this potential is the next step for the research collaborators as they explore questions suggested by this work.

"We are now exploring how interactions of NSCs with different cell types in their micro-environment is affected in different physiological and pathological conditions as well as in healthy aging," says Dr. Saghatelyan, whose Faculty of Medicine research lab focuses on generating new knowledge to help boost neuronal regeneration.

The study—which started at Université Laval where Dr. Saghatelyan's lab was located until 2022—was conducted at the uOttawa Faculty of Medicine, where a cutting-edge two-photon imaging system made it possible to assess the functional activity of neural stem cells.

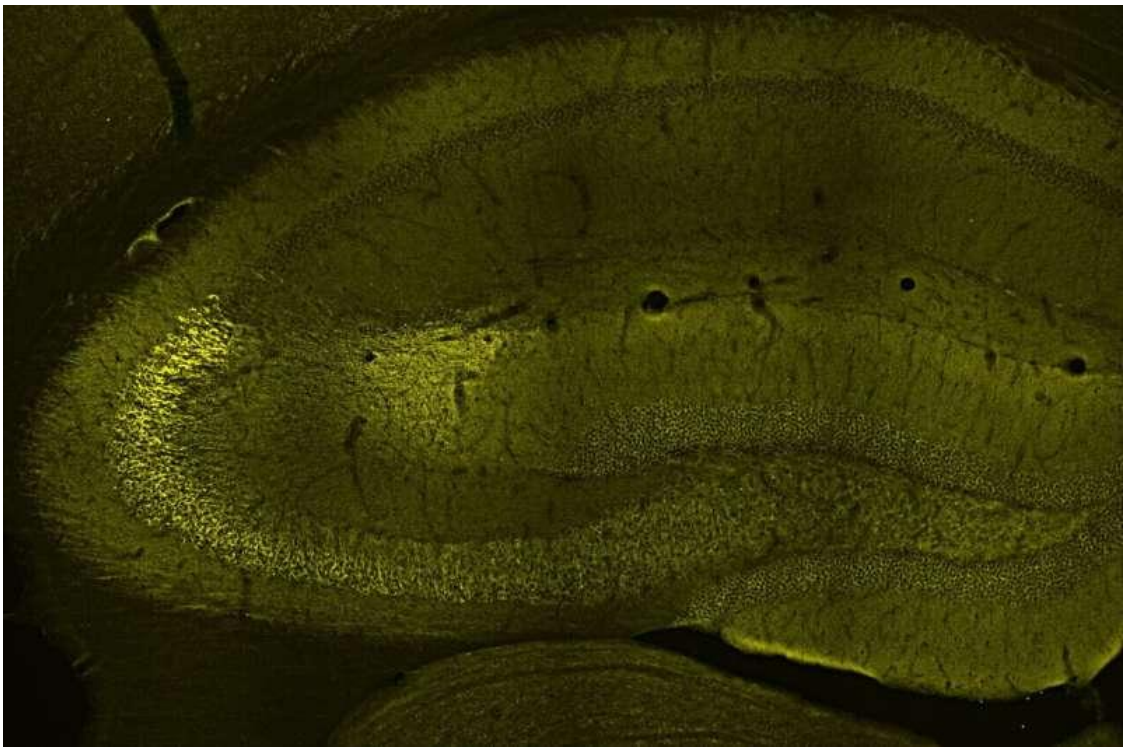
Single cell sequencing and spatial transcriptomics were performed by collaborators at University of Toronto and the University of British Columbia. Machine learning collaboration was performed at Université Laval.

More information: Alina Marymonchyk et al, Neural stem cell quiescence and activation dynamics are regulated by feedback input from their progeny under homeostatic and regenerative conditions, *Cell Stem Cell* (2025). DOI: 10.1016/j.stem.2025.01.001
Journal information: Cell Stem Cell
Provided by University of Ottawa

FEBRUARY 7, 2025

Scientists discover mitochondria's role in shaping memory circuits

by Virginia Tech



Research led by Shannon Farris, an assistant professor at the Fralin Biomedical Research Institute at VTC, found a mitochondrial mechanism that helps explain how CA2 neurons, like those highlighted here, function in mice. The research has implications in better understanding memory and social recognition. Credit: Shannon Farris/Virginia Tech

Virginia Tech neuroscientists have uncovered a mitochondrial process that supports the brain cells critical for learning, memory, and social recognition.

Led by Shannon Farris, assistant professor at the Fralin Biomedical Research Institute at VTC, the research in mouse models examines the hippocampal CA2 region, a specialized area in the brain's memory center essential for social recognition memory.

Published this week in *Scientific Reports*, the study reveals the critical role of the mitochondrial calcium uniporter (MCU), a protein that regulates calcium flow into mitochondria, in enabling neurons to strengthen connections. This process, known as synaptic plasticity, is fundamental to cognitive function and adaptive learning.

"Our findings highlight a distinct mitochondrial mechanism that helps explain how CA2 neurons function, which may contribute to its role in social cognition and its vulnerability in certain neurological disorders," Farris said.

A unique role for the CA2 region in social memory

The hippocampal CA2 region is a small but critical hub for social recognition—the ability to remember and distinguish individuals. Unlike neighboring hippocampal regions, CA2 neurons resist certain forms of synaptic plasticity, raising intriguing questions about their specialized function.

Farris and her team discovered that mitochondria in CA2 neurons are not uniform. Instead, their structure and function vary depending on their location within the neuron. Mitochondria in the farthest reaches of the dendrites of neurons—at the outermost synaptic input connections—are highly specialized and depend heavily on MCU to control their activity.

To explore this, the researchers deleted the MCU gene in CA2 neurons of genetically engineered mice. This caused a disruption in plasticity at the outermost synapses, while those closer to the cell body were unaffected.

"This suggests that mitochondrial diversity isn't just a biological quirk," said Farris. "It's a fundamental feature that allows different parts of the same neuron to function in distinct ways."

Potential implications for Alzheimer's, autism spectrum disorder

Mitochondrial dysfunction is increasingly recognized as a major contributor to neurological disorders such as Alzheimer's disease, autism, schizophrenia, and depression.

Synapses need a lot of energy to stay connected and process information. When mitochondria don't work properly, it can disrupt the functional capacity of these cell-cell communications channels, leading to problems with thinking and memory.

It is known that the most distal outermost synapses are among the first synaptic connections affected in Alzheimer's disease. The findings suggest that MCU's function in CA2 neurons may contribute to this initial weakness, offering potential insight into why this circuit is particularly susceptible to neurodegeneration.

Shannon Farris, assistant professor at the Fralin Biomedical Research Institute at VTC, led a team that recently published research in *Scientific Reports* examining a specialized area in the brain's memory center essential for social recognition memory. Credit: Clayton Metz/Virginia Tech

"Understanding why mitochondria in CA2 neurons are different—and how they fail—could help us design therapies to protect or restore function in specific brain regions," Farris said.

Beyond Alzheimer's, the study raises broader questions about how mitochondrial diversity might influence other neurological disorders. The ability of neurons to fine-tune mitochondrial properties could be a critical factor in understanding autism, where CA2 dysfunction could be linked to the known social deficits that occur in this spectrum.

Decoding mitochondrial function in neural circuits

This study advances understanding of mitochondrial biology and overcomes a technical hurdle in assessing mitochondria in dense and diverse brain tissues, the researchers said.

Using electron microscopy and artificial intelligence to unbiasedly identify only the dendritic mitochondria within the densely packed synaptic layer, Farris's team mapped mitochondrial structure in CA2 neuron dendrites at high spatial resolution with extreme precision over millimeter expanses of tissue. The analysis revealed that MCU-deficient mitochondria were smaller and more fragmented, a structural shift that may underlie their impaired ability to support synaptic function.

More broadly, the study challenges the long-held assumption that mitochondria work the same way throughout all parts of the neuron. Instead, neurons may actively modify mitochondrial properties to optimize function at specific synapses, a concept that could reshape our understanding of neural energy regulation and plasticity.

"These findings challenge the long-held assumption that mitochondria function uniformly within dendrites," said Katy Pannoni, a senior research associate in Farris's lab and the study's first author. "Instead, our work suggests that mitochondria are highly specialized to support the distinct needs of different neural circuits."

By applying artificial intelligence to analyze large-scale electron microscopy datasets, the research team quantified mitochondrial structure and distribution across circuits at a scale unattainable by conventional manual methods. This new approach will allow future studies to investigate mitochondrial function with greater precision and depth of analysis.

The future of mitochondrial research

This discovery opens new pathways to consider for potential therapies, particularly for neurological disorders where energy deficits weaken brain connections. By revealing how mitochondria support neural plasticity, Farris's research lays the groundwork for strategies to preserve brain function and slow neurodegeneration.

Next, her team will investigate how mitochondria in CA2 neurons develop their specialized properties and whether similar adaptations exist in other brain regions. They also aim to explore therapeutic strategies that could bolster mitochondrial health and protect neurons from disease.

"The more we understand mitochondrial diversity, the closer we get to unlocking how the brain learns, remembers, and adapts—and how we can keep it healthy," Farris said.

More information: Katy E. Pannoni et al, MCU expression in hippocampal CA2 neurons modulates dendritic mitochondrial morphology and synaptic plasticity, *Scientific Reports* (2025). DOI: 10.1038/s41598-025-85958-4
Journal information: Scientific Reports
Provided by Virginia Tech

FEBRUARY 7, 2025

Researchers confirm best approach for stroke in medium-sized blood vessels

by University of Calgary

Credit: CC0 Public Domain

University of Calgary's Hotchkiss Brain Institute researchers with the Calgary Stroke Program at Foothills Medical Centre have revolutionized treatment for stroke with the ESCAPE Trial, proving that a clot retrieval procedure known as endovascular thrombectomy (EVT) can dramatically improve patient outcomes after an acute ischemic stroke caused by a blockage in a large-sized blood vessel.

Building on that knowledge, the team launched the ESCAPE-MeVO clinical trial to assess whether ischemic stroke patients with blockages in smaller medium-sized vessels could also benefit from EVT. Ischemic strokes are the most common form of stroke. The study, published in the *New England Journal of Medicine,* found that EVT does not result in improved outcomes.

"When someone has a stroke, it's critical that doctors know what the best approach is for each situation. Brain cells die quickly when blood flow stops," says Dr. Mayank Goyal, MD, Ph.D., interventional neuroradiologist, clinical professor at the Cumming School of Medicine

(CSM) and study co-principal investigator. "The brain is fed by a network of arteries of varying size. Our findings show patients with blockages in medium-sized vessels in the brain who had endovascular treatment did not do any better and did not see any improvement compared to patients who had the standard of care."

The international study included 530 patients at 58 sites in five countries. Patients were randomly allocated into two groups; one group received usual care, the second received EVT plus usual care. Patients were assessed 90 days post-stroke. Outcomes were measured using the modified Rankin Score, a clinical tool that measures the level of disability a person experiences after a stroke, and the Barthel Index score that measures a patient's ability to do daily tasks.

"Our findings will help doctors better determine the best treatment for their patient," says Dr. Michael Hill, MD, neurologist, professor at the CSM and study co-principal investigator. "Knowing usual medical care, often with thrombolytic (clot-busting) drugs, is best for blockages in medium-sized vessels helps with resourcing and ensuring each patient is getting the right care for their situation."

Hill says the results are especially important for doctors who see stroke patients at smaller centers, and rural locations where EVT may not be available. The study will continue patient follow-up to one-year to see whether a late benefit emerges with a longer duration of evaluation.

"Ultimately, we do this research because we want to improve treatments for patients and reduce death and disability from stroke," says Goyal. "This study helps us better understand when EVT is effective and when it isn't. That knowledge is important."

Goyal and Hill presented the results at the International Stroke Conference in Los Angeles, California, US on February 5, 2024.

More information: Mayank Goyal et al, Endovascular Treatment of Stroke Due to Medium-Vessel Occlusion, *New England Journal of Medicine* (2025). DOI: 10.1056/NEJMoa2411668
Journal information: New England Journal of Medicine
Provided by University of Calgary

FEBRUARY 7, 2025

Brain stimulation did not improve impaired motor skills after stroke: Clinical trial

by American Heart Association

Credit: Rice University

Mild electrical brain stimulation did not further improve motor recovery in stroke survivors, according to late-breaking science presented at the American Stroke Association's International Stroke Conference 2025, held in Los Angeles, Feb. 5–7, 2025.

"The results are somewhat surprising to us," said study leading-principal investigator Wayne Feng, M.D., M.S., professor of neurology and biomedical engineering at Duke University School of Medicine in Durham, North Carolina. "We initially hoped that a higher dose at 4 milliamps electrical stimulation had a better effect than a lower dose as well as the sham group, but we did not see that."

In the United States, stroke is the fifth leading cause of death and a leading cause of long-term disability, according to the American Heart Association's Heart Disease and Stroke Statistics 2025 Update. Depending on the part of the brain affected, stroke may impair arm and/or leg movement and activities of daily life among survivors. Motor impairment (arm and/or leg weakness) is the most common complication after stroke.

Constraint-induced movement therapy (CIMT) restricts movement on the unaffected arm (by wearing a mitt over a hand) to force the use of the stroke-affected side. This therapy has been shown to improve motor function and quality of life in certain stroke patients with preserved hand movement.

However, it requires intensive treatment. For example, the traditional format requires six hours per day and a modified treatment format requires two hours per session in the clinic, five days per week, with additional homework after the clinical session. This can be challenging for stroke survivors, Feng said.

Researchers studied whether transcranial direct current stimulation could enhance the effects of constraint-induced movement therapy, allowing for better use of the arm affected by the stroke. In this study, a weak electrical current—up to 4 milliamps (4 one thousandth of an ampere) powered by a 9-volt battery—was delivered through the skull.

The study, Transcranial direct current stimulation for post-stroke motor recovery—a Phase II study (TRANSPORT 2), is the first funded multi-center stroke recovery study by the National Institutes of Health (NIH) StrokeNet, a network of U.S. regional centers and hospitals conducting major stroke-related clinical trials focusing on acute treatment, prevention and recovery.

Researchers assessed three aspects of arm function (impairment, function and quality of life) after 10 sessions over the two-week period using three doses of electrical stimulation—sham/placebo stimulation, low dose (2 milliamps) and higher dose (4 milliamps or mA)—on 129 stroke survivors undergoing constraint-induced movement therapy in major medical centers across the U.S. The stimulation was 30 minutes and the CIMT therapy was 120 minutes each session.

The analysis found:

- Transcranial direct current stimulation up to 4mA did not amplify the effect of constraint-induced movement therapy.
- The stroke survivors in all three groups improved after two weeks of treatment, and the effect continued at one month and three months after the intervention; however, the magnitude of improvement among the three groups was similar.
- The stimulation is safe and tolerable in stroke patients. The combined intervention was feasible to implement in the multi-center clinical trial setting.

A limitation of the study is the trend of uneven representation of women in each group, considering that women may respond differently than men to brain stimulation. Another limitation is that the study was interrupted by the COVID-19 pandemic, which slowed enrollment and scoring issues on the primary outcomes.

"In future clinical trials, we plan to enhance our approach by implementing several improvements," Feng said. "These improvements will include using a higher dose—more than 4 milliamps, ensuring men and women are equally distributed in each group and ensuring consistent administration and scoring the primary outcomes across all clinical trial sites. It may take us a few attempts before we achieve success."

Study design, background and details:

- Study participants were first-ever ischemic (clot-caused) stroke survivors who suffered a stroke one to six months earlier and had persistent arm weakness but still had slight movement of the hand.
- The study included 129 stroke survivors with an average age of 59 years. 42% were women, 53% were white adults, 41% were Black adults, 3% were Asian population and about 2% said they were multiple races. Participants were randomly assigned to one of three doses of brain stimulation.
- It was conducted between September 2019 and September 2024 in 15 U.S. medical centers in 11 U.S. states and the District of Columbia. Each person participated in the study for about four months.
- Clinical outcome was assessed using the Fugl-Myer Upper-Extremity Scale (measuring motor impairment), Wolf Motor Functional Test (measuring motor function) and the Stroke Impact Scale Hand Subscale (measuring quality of life).
- All clinical outcomes were assessed immediately after two weeks of intervention, and again one month and three months after the initial intervention.
- Researchers found the combined brain stimulation and intensive rehabilitation therapy was safe, tolerable and feasible.
- Feng led the study with co-principal investigator Gottfried Schlaug, M.D., Ph.D., FAHA., vice-chair for Research at University of Massachusetts Chan Medical School—Baystate in Springfield.

More information: American Stroke Association International Stroke Conference – Late-Breaking Science Presentation LB 16
Provided by American Heart Association

Stretchy, self-healing ‘jelly batteries’ could revolutionize medical implants

In a nutshell

- Cambridge scientists have created stretchy, self-healing “jelly batteries” that can extend to 15 times their length while maintaining electrical conductivity – a combination never achieved before in a single material
- The materials repair themselves within hours of damage and could revolutionize medical implants, as they match human tissue properties and are less likely to be rejected by the body
- Inspired by electric eels, these hydrogels can generate power like a battery (about 1/10th of a AA battery’s voltage) and maintain stable performance even when stretched 50% – five times better than previous versions

CAMBRIDGE, England — The next generation of medical devices won’t just interact with the human body, they’ll move and flex with it. University of Cambridge researchers have created remarkable “jelly batteries” that stretch, conduct electricity, and even heal themselves, potentially revolutionizing everything from brain implants to wearable health monitors.

Unlike traditional electronics, which rely on rigid metal components and wires, these new materials are primarily water-based and can stretch to more than 15 times their original length without losing their ability to conduct electricity. The breakthrough, published in *Science Advances*, overcomes a fundamental challenge in materials science.

“It’s difficult to design a material that is both highly stretchable and highly conductive since those two properties are normally at odds with one another,” explains lead author Stephen O’Neill from Cambridge’s Yusuf Hamied Department of Chemistry, in a statement. “Typically, conductivity decreases when a material is stretched.”

A research team from the University of Cambridge solved this challenge by creating special *hydrogels*, which are materials composed of 3D networks of *polymers* containing over 60% water. These hydrogels use the same principle as our own bodies to conduct electricity, carrying charges through ions rather than electrons like traditional electronics.

"Normally, hydrogels are made of polymers that have a neutral charge, but if we charge them, they can become conductive," says co-author Dr. Jade McCune. "And by changing the salt component of each gel, we can make them sticky and squish them together in multiple layers, so we can build up a larger energy potential."

The secret to these materials' remarkable properties lies in their molecular structure. The researchers developed a system using special barrel-shaped molecules called *cucurbiturils*, which act like molecular handcuffs to bind different layers of the material together. These bonds can repeatedly break and reform, allowing the material to stretch, compress, and even heal itself when damaged.

This self-healing capability is particularly impressive. When the material is cut, it can repair itself within minutes. Tests showed that after just two hours of healing time, the material recovers 90% of its original stretchability. The team demonstrated this by cutting samples in half and watching them fuse back together, tracking the healing process using fluorescent dyes under a microscope.

Taking inspiration from electric eels, which stun their prey using special cells called *electrocytes*, the researchers created a working prototype of a soft, stretchable power source. By stacking different types of their conductive gels together in layers, they built a device that generates electricity through ion concentration gradients, similar to how electric eels produce their shock.

The device produces about 115-125 *millivolts* (roughly a tenth of an AA battery's voltage), and by connecting two cells in series, they could double this to around 248 millivolts. Most importantly, it maintains stable performance even when stretched up to 50%, which is about the same amount human skin can stretch. Previous attempts at similar devices would fail at just a 10% stretch.

"We can customize the mechanical properties of the hydrogels so they match human tissue," explains Professor Scherman. "Since they contain no rigid

components such as metal, a hydrogel implant would be much less likely to be rejected by the body or cause the build-up of scar tissue."

Beyond medical applications, these materials could revolutionize soft robotics, machines designed to interact safely with humans or handle delicate objects. The combination of flexibility, conductivity, and durability could enable robots that move more naturally and adapt better to their environment.

The materials are remarkably resilient in other ways, too. They can be compressed by more than 90% without permanently losing their shape, and they bounce back within 30 seconds, though some variations show minor delays in full recovery. This level of durability, combined with their self-healing properties, suggests they could last longer than traditional electronic components in many applications.

This invention is a significant step forward in creating electronics that adapt to humans rather than forcing humans to adapt to electronics. As testing continues, they could fundamentally change our approach to everything from medical implants to wearable devices.

Paper Summary

Methodology

The researchers created these hydrogels by combining water-based polymers with specially designed molecular structures that can form reversible bonds. The key innovation was using barrel-shaped molecules called cucurbiturils as tiny molecular containers that can hold and release other molecules, creating dynamic links between polymer chains. They tested several types of charged molecules to create different versions of the hydrogel, each with unique properties. The team used multiple testing methods including mechanical stretching tests, electrical conductivity measurements, and microscopic imaging with fluorescent dyes to analyze how the materials performed.

Results

The hydrogels achieved several breakthrough properties: they could stretch to more than 15 times their original length, compress by over 90%, and conduct electricity at levels up to 0.1 Siemens per centimeter. They demonstrated rapid self-healing abilities, recovering most of their strength within hours of being damaged. When used as a power source, the materials maintained consistent voltage even when stretched to 50% – five times more than previous versions. The team also proved these materials could stick strongly to each other without separating under strain.

Limitations

While the research shows promise, several challenges remain. The materials show some trade-off between stretchability and immediate elastic recovery – meaning they don't snap back to their original shape as quickly as some applications might require. The power output, while stable, remains relatively low compared to conventional batteries. Additionally, more testing is needed to fully understand how these materials would perform in long-term use, particularly in medical applications.

Discussion and Takeaways

This research represents a significant advance in creating electronics that can better integrate with biological systems. The combination of stretchability, conductivity, and self-healing properties could enable new applications in medicine and robotics that weren't previously possible. The approach of using reversible molecular bonds provides a framework for developing other advanced materials with similar properties. The biocompatibility of these materials makes them particularly promising for medical implants and devices that need to interface directly with human tissue.

Funding and Disclosures

The research was funded by the European Research Council (ERC) grant CAM-RIG and the Engineering and Physical Sciences Research Council (EPSRC), part of UK Research and Innovation (UKRI). The authors declared no competing interests. Professor Oren Scherman, who led the research, is a Fellow of Jesus College, Cambridge.

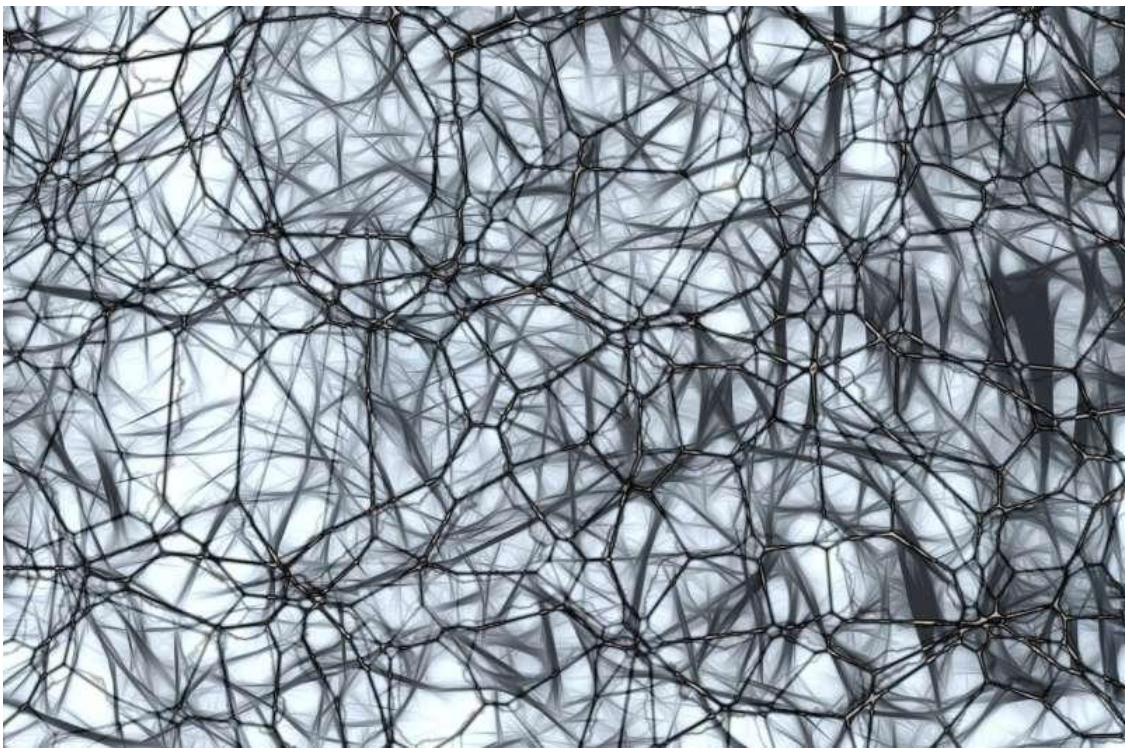
Publication Information

This research paper, “Highly stretchable dynamic hydrogels for soft multilayer electronics,” was published in *Science Advances* on July 17, 2024. The study was conducted by researchers at the University of Cambridge’s Melville Laboratory for Polymer Synthesis and the Electrical Engineering Division, in collaboration between the Yusuf Hamied Department of Chemistry and the Department of Engineering.

FEBRUARY 8, 2025

Brain cells mimic muscle signaling to enhance learning and memory

by Howard Hughes Medical Institute



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Our biceps and our brain cells may have more in common than previously thought.

New research led by the Lippincott-Schwartz Lab shows that a network of subcellular structures similar to those responsible for propagating molecular signals that make muscles contract are also responsible for transmitting signals in the brain that may facilitate learning and memory.

"Einstein said that when he uses his brain, it is like he is using a muscle, and in that respect, there is some parallel here," says Janelia Senior Group Leader Jennifer Lippincott-Schwartz. "The same machinery is operating in both cases but with different readouts."

The first clue about the possible connection between brain and muscle cells came when Janelia scientists noticed something strange about the endoplasmic reticulum, or ER—the membranous sheets and folds inside cells that are crucial for many cellular functions.

Lorena Benedetti, a research scientist in the Lippincott-Schwartz Lab, was tracking molecules at high resolution along the surface of the ER in mammalian neurons when she

saw that the molecules were tracing a repeating, ladder-like pattern along the entire length of the dendrites—the branch-like extensions on brain cells that receive incoming signals.

Around the same time, Senior Group Leader Stephan Saalfeld alerted Lippincott-Schwartz to high-resolution 3D electron microscopy images of neurons in the fly brain where the ER was also forming regularly spaced, transversal structures.

The ER normally appears like a huge, dynamic net, so as soon as Lippincott-Schwartz saw the structures, she knew her lab needed to figure out what they were for.

"In science, structure is function," says Lippincott-Schwartz, who also heads Janelia's 4D Cellular Physiology research area. "This is an unusual, beautiful structure that we are seeing throughout the whole dendrite, so we just had this feeling that it must have some important function."

The researchers, led by Benedetti, started by looking at the only other area of the body known to have similar, ladder-like ER structures: muscle tissue. In muscle cells, the ER and the plasma membrane—the outer membrane of the cell—meet at periodic contact sites, an arrangement controlled by a molecule called junctophilin.

New research details the subcellular structures in neurons that enable signals to be transmitted from where they are received at specific sites on dendrites to the decision-making cell body located hundreds of micrometers away. The new research finds that the endoplasmic reticulum and the plasma membrane form contact sites where specialized molecules control the release of calcium, which regulates the signals sent along the dendrite to the soma. This movie shows 3D renderings of these structures in high-resolution 3D electron microscopy images of fruit fly neurons. The endoplasmic reticulum (green), plasma membrane (blue), mitochondria (pink), microtubules (tan), and ER-plasma membrane contacts (magenta) are segmented from FIB-SEM datasets of a Drosophila melanogaster MBON1 neuron. Credit: Benedetti et al.
Using high-resolution imaging, the researchers discovered that dendrites also contain a form of junctophilin that controls contact sites between their ER and plasma membrane. Further, the team found that the same molecular machinery controlling calcium release at muscle cells' contact sites—where calcium drives muscle contraction—was also present at dendrite contact sites—where calcium regulates neuronal signaling.

Because of these clues, the researchers had a hunch that the molecular machinery at the dendritic contact sites must also be important for transmitting calcium signals, which cells use to communicate. They suspected that the contact sites along the dendrites might act like a repeater on a telegraph machine: receiving, amplifying, and propagating signals over long distances. In neurons, this could explain how signals received at specific sites on dendrites are relayed to the cell body hundreds of micrometers away.

"How that information travels over long distances and how the calcium signal gets specifically amplified was not known," says Benedetti. "We thought that ER could play that role, and that these regularly distributed contact sites are spatially and temporally localized

amplifiers: they can receive this calcium signal, locally amplify this calcium signal, and relay this calcium signal over a distance."

The researchers found that this process is triggered when a neuronal signal causes calcium to enter the dendrite through voltage-gated ion channel proteins, which are positioned at the contact sites. Although this initial calcium signal dissipates quickly, it triggers the release of additional calcium from the ER at the contact site.

This influx of calcium at the contact site attracts and activates a kinase called CaMKII, a protein known to be important in memory. CaMKII alters the plasma membrane's biochemical properties, changing the strength of the signal that is passed down the plasma membrane.

This process continues from contact site to contact site all along the dendrite to the cell body, where the neuron decides how it will communicate with other neurons.

The new research reveals a novel mechanism for signal transmission in brain cells and helps answer an open question in neuroscience about how intracellular signals travel over long distances in neurons, enabling information received at specific sites on dendrites to be processed in the brain.

It also sheds light on the molecular mechanisms underlying synaptic plasticity—the strengthening or weakening of neuronal connections that enables learning and memory. Figuring out this process at the molecular level could increase understanding of how the brain works normally and in diseases where these processes go awry, like Alzheimer's.

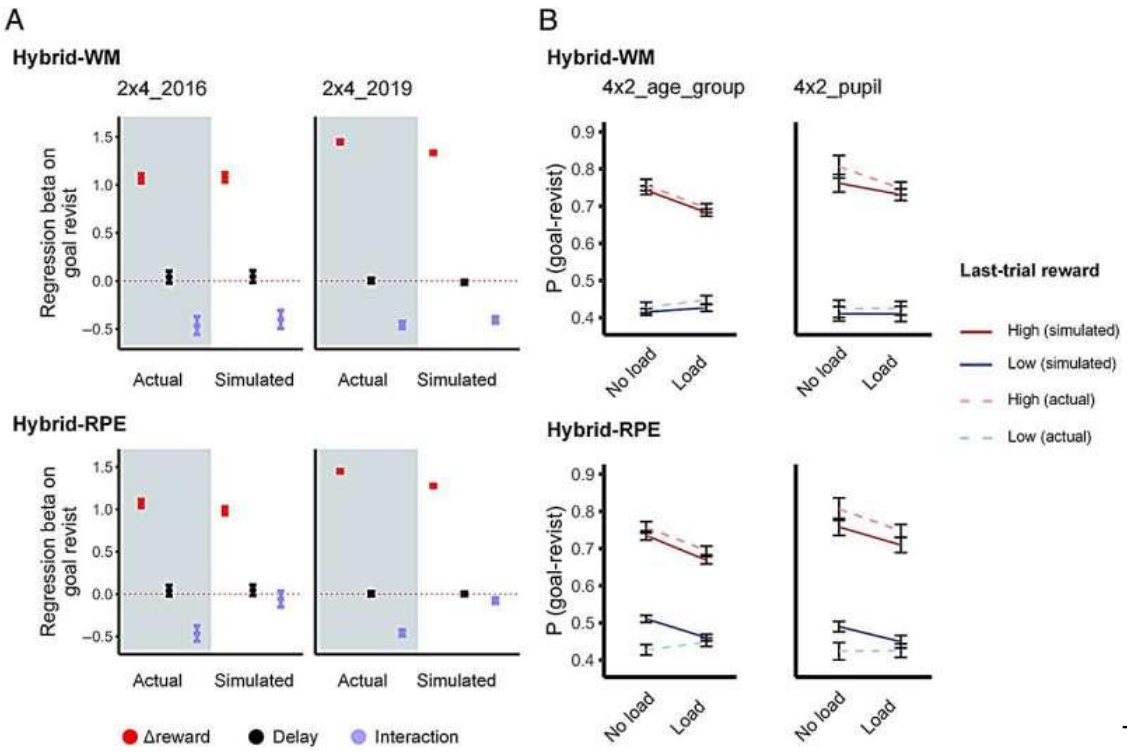
"We are showing that a structure—a beautiful structure—operating at a level of subcellular organization is having a huge effect on the way the entire neuronal system is operating vis-à-vis calcium signaling," Lippincott-Schwartz says. "This is a great example of how, in doing science, if you see a beautiful structure, it can take you into a whole new world."

More information: Lorena Benedetti et al, Periodic ER-plasma membrane junctions support long-range Ca2+ signal integration in dendrites, *Cell* (2024). DOI: 10.1016/j.cell.2024.11.029
Journal information: Cell
Provided by Howard Hughes Medical Institute

FEBRUARY 10, 2025

Unlocking the mind's decision-making engine: How working memory shapes our choices

by Zhang Nannan, Chinese Academy of Sciences



The simulation results demonstrate the superiority of the Hybrid-WM model over the classical Hybrid-PRE model. Credit: Yang Lizhuang

A study led by Prof. Li Hai from the Hefei Institutes of Physical Science of the Chinese Academy of Sciences has revealed that the balance between habitual and goal-directed decision-making strategies is influenced by the availability of working memory resources.

The findings, published in the *Journal of Cognitive Neuroscience*, provide a new framework for understanding how sequential decisions are made.

Everyday decisions often involve a series of choices aimed at reaching a goal-whether selecting a restaurant or deciding on the route. People vary in how they make decisions: some rely on habits, while others adjust based on new information and changing goals.

The key question, however, is what determines the balance between these two strategies. This challenge, known as meta-control, has long puzzled cognitive neuroscience.

To address this, the researchers combined behavioral experiments with computational modeling, demonstrating that working memory limitations play a crucial role in decision-making. They introduced the Hybrid-WM reinforcement learning model, which integrates working memory constraints into the decision-making process.

"Unlike older models, this new framework takes into account the brain's memory limits," said Prof. Li Hai. "By accounting for the brain's memory limits, it offers a more accurate representation of how we make decisions under various conditions—such as stress, distractions, or mental fatigue."

This research quantifies the role of working memory constraints in meta-control and offers new insights into sequential decision-making processes. "The findings hold promise for applications in human-computer interaction," said Prof. Li.

More information: Zhaoyu Zuo et al, Working Memory Guides Action Valuation in Model-based Decision-making Strategy, *Journal of Cognitive Neuroscience* (2024). DOI: 10.1162/jocn_a_02237
Journal information: Journal of Cognitive Neuroscience
Provided by Chinese Academy of Sciences

FEBRUARY 10, 2025

How the brain can miraculously switch off pain

By The Conversation

In the second world war, the physician Henry Beecher observed that some of his soldier patients, despite being injured on the battlefield, required no strong painkillers to manage their pain. In some cases, the injury was as severe as losing part of a limb.

A truly remarkable phenomenon had come into play—the effects of fear, stress and emotion on the brain had switched off their pain. But how does this work—and how can we use it to our advantage?

We all struggle with pain at times. The burning of indigestion, the wince of a scald from the kettle. The sharp stabbing of a sliced finger.

But despite its unpleasantness, pain has a critically important purpose, designed to protect the body rather than harm it. A fundamental concept to first understand is that you do not detect pain—it is a sensation. A sensation that your brain has created—from information it receives from the countless neurons (nerve cells) which supply your skin.

These specialized neurons are called nociceptors—they detect stimuli which are noxious, or potentially damaging to the body. This stimulation might range from a mechanical cut or crush injury, to extreme hot or cold temperatures.

So, if you touch a hot iron, or stand on a sharp nail, the correct reaction is to move your hand or foot away from it. The brain responds to pain by initiating muscle contractions in your arm or leg. In doing so, any further damage is averted.

The course of information, rushing along one neuron to another in a relay, is carried as electrical currents called action potentials. These begin at the skin, travel along nerve highways and into the spinal cord. When the information reaches the uppermost level of the brain—the cerebral cortex—a sensation of pain is generated.

Blocking pain signals

Many different factors can interfere with this transmission of information—we don't perceive pain if the route to the cortex is blocked. Take the use of anesthetics, for instance.

Local anesthetics are injected directly into the skin to deactivate nociceptors (like lidocaine)—perhaps in A+E to perform stitches. Other agents induce a loss of consciousness—these are general anesthetics, for more extensive surgical operations.

Pain is also a very variable experience. Commonly, we ask patients to quantify their pain by giving a value along a scale of nought to ten. What one person would consider a five out of ten pain, another might consider a seven—and another a two.

Some patients are born without the ability to sense pain—this rare condition is called congenital analgesia. You might think this confers an advantage, but the truth is quite the opposite. These individuals will be unaware of circumstances where their bodies are being damaged, and can end up sustaining more profound injuries, or missing them entirely and suffering the consequences.

How to trick your brain

What is more extraordinary is that we all possess an innate ability to control our pain levels. In fact, a natural painkiller is found deep within the nervous system itself.

The secret lies in a structure located in the very middle of your brain: the periaqueductal grey (PAG). This small, heart-shaped region contains neurons whose role is to alter incoming pain signals reaching the cerebral cortex. In doing so, it is able to dampen down any pain that would otherwise be experienced.

Let's consider this in practice using the extreme example of the battlefield. This is an instance where sensing pain might actually prove more of a hindrance than of help. It might hamper a soldier's ability to run, or assist comrades. In temporarily numbing the pain, the soldier becomes able to escape the dangerous environment and seek refuge.

But we encounter many examples of this ability coming into action in our everyday routines. Ever picked something in the kitchen that you suddenly realize is extremely hot? Sometimes that casserole dish or saucepan descends to the floor, but sometimes we are able to hold on just long enough to transfer it to the stove-top. This action may be underpinned by the PAG shutting off the sensation of clasping something too hot to handle, just long enough to prevent dropping it.

The substances which generate this effect are called enkephalins. They are produced in many different areas of the brain (including the PAG) and spinal cord, and may have similar actions to strong analgesics such as morphine. It has also been suggested that long term or chronic pain—which is persistent and not useful to the body—might arise as a result of abnormalities within this natural analgesic system.

This begs the question: how might you go about hacking your own nervous system to produce an analgesic effect?

There is growing evidence to suggest that the release of painkilling enkephalins can be enhanced in a variety of different ways. Exercise is one example—one of the reasons why prescribed exercise might be able to work wonders for aches and pains (backache for instance) instead of popping paracetamols.

Besides this, stressful situations, feeding and sex might also affect the activity of enkephalins and other related compounds.

So, how could we go about it? Take up strength or endurance training? Alleviate our stress? Good food? Good sex? While more work is needed to clarify a role for these options in pain management, their reward might be greater than we thought.

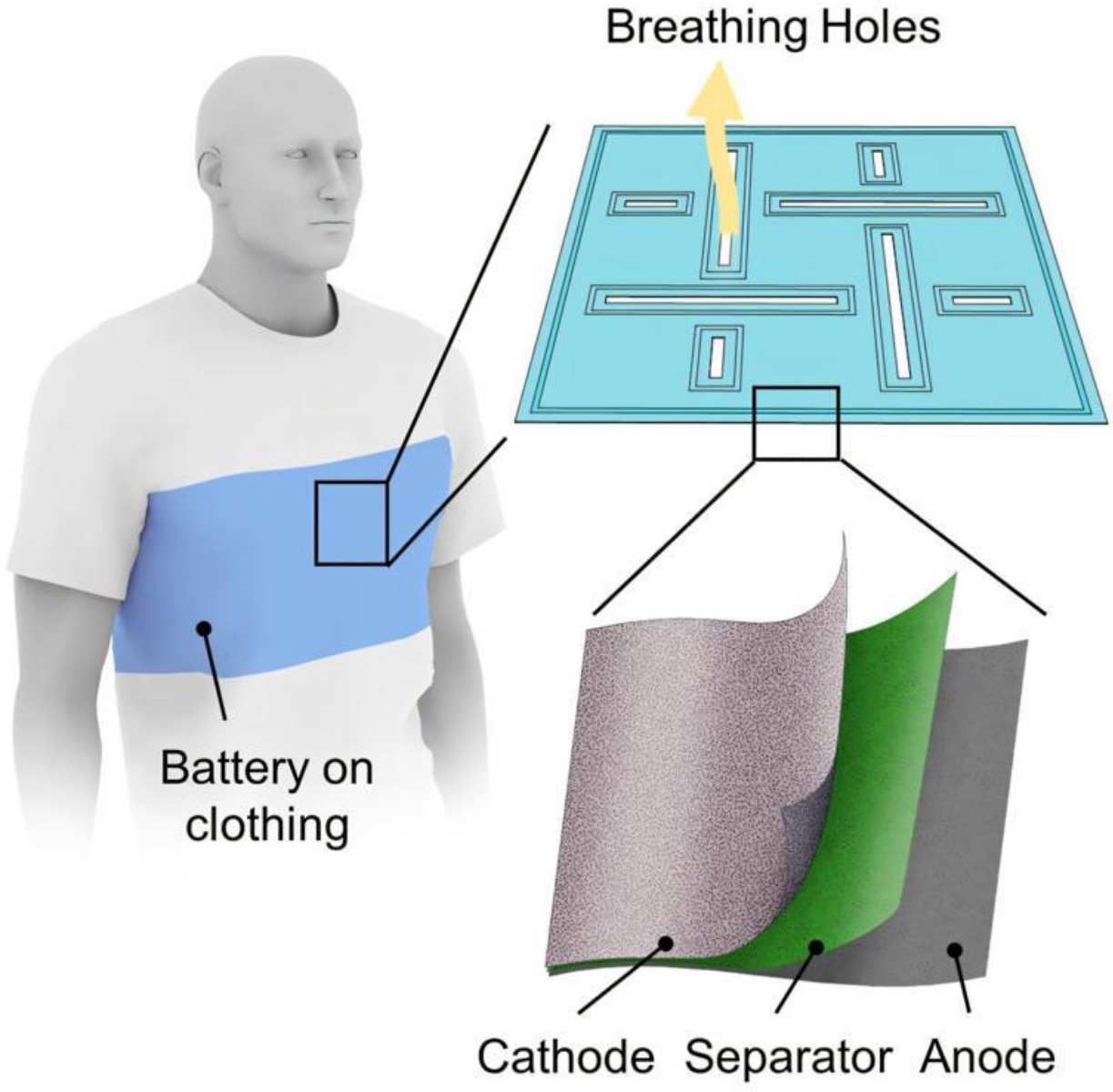
Pain remains a complex, poorly understood experience, but the future is bright. Only last month, the FDA approved the use of a new medication Journavx for managing acute pain.

It works by switching off nociceptors in the peripheral nervous system, and therefore preventing pain signals getting to the brain. This represents a potential new breakthrough in a world which has become dependent on addictive opioid medications, such as morphine and fentanyl.

Developing new painkilling treatments relies on the work of pain researchers to help unravel the intricate neuronal circuitry and function. There is no denying that this is going to be difficult task. But in considering the neuroscience of how our bodies generate and suppress pain, we can hope to understand how they can act as their own healers.

Provided by The Conversation

Unique hole type and placement makes a wearable battery more bendable and breathable



Graphical abstract. Credit: Matter (2025). DOI: 10.1016/j.matt.2025.101959

A team of engineers and materials scientists from the U.S. has found that holes of a certain size and shape placed in certain locations can turn a slightly flexible and stretchy battery pouch into one that can be stretched significantly or folded 180 degrees. In their paper published in *Matter*, the group describes how they came

up with the design and explain how it makes a battery that is barely stretchy into one that can be folded.

Over the past couple of decades, as electronics have become smaller and more resilient, textile makers have been looking for ways to add them and their batteries to clothes. Advances in small devices and displays have led to the development of clothes that can display electronic messages or allow them to change colors and patterns; the tricky part has been in powering them. Some small devices that can be added to clothes consume so little energy that they can be powered by a wearer's movement. Unfortunately, most others still need a battery.

The difficulties of adding batteries to clothes include size, weight and stiffness. There have also been fears of batteries setting clothes on fire. In this new effort, the research team has developed a battery that is both bendable and has a built-in cooling mechanism to prevent overheating.

The battery made by the team is essentially the same as other battery pouches, except for one major difference—it has holes cut in it. Pouch batteries are typically just a little bit flexible. To make them more flexible, other researchers have tried cutting square or round holes in them in various places.

In this new effort, the researchers studied how putting holes in such a material increases stretchiness, and worked to find a design that would provide the most stretchiness without sacrificing battery capacity.

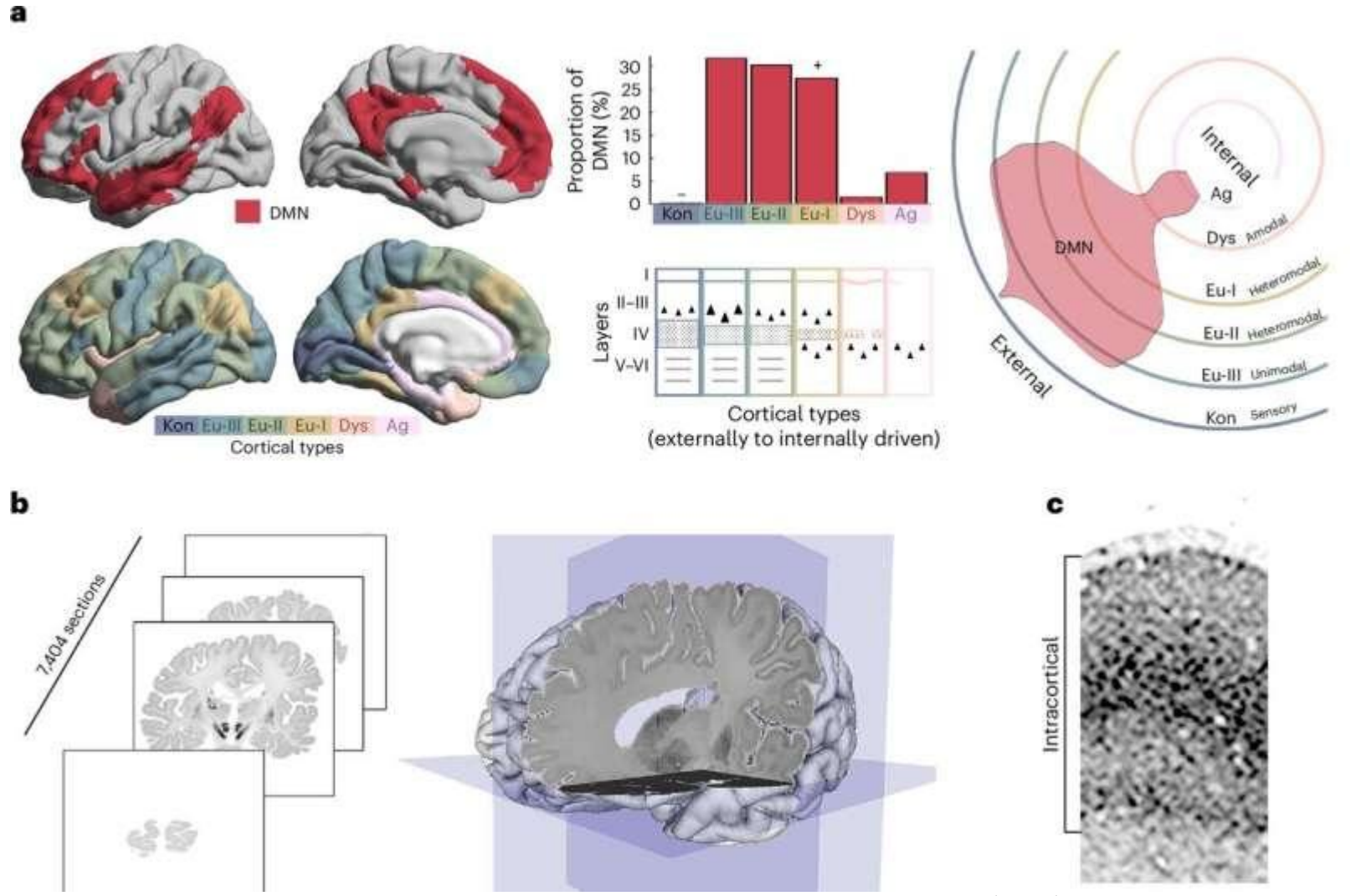
The resulting battery has longer and shorter rectangular holes of the right size and placement. Testing showed it was capable of holding a charge when folded 180 degrees, and could be stretched by as much as 10% of its length. The researchers also found that it held up without fail after 100 folds/unfolds, was twice as breathable as cotton, and that the holes served to dissipate heat.

More information: Lin Xu et al, Stretchable, breathable, wearable batteries using a holey design, *Matter* (2025). DOI: 10.1016/j.matt.2025.101959

FEBRUARY 12, 2025

Mapping the human brain's default mode network: Anatomical study suggests it has widespread influence

by Ingrid Fadelli , Medical Xpress



Cytoarchitectural heterogeneity of the DMN. Credit: *Nature Neuroscience* (2025). DOI: 10.1038/s41593-024-01868-0

The default mode network (DMN) is a set of interconnected brain regions known to be most active when humans are awake but not engaged in physical activities, such as relaxing, resting or daydreaming. This brain network has been found to support a variety of mental functions, including introspection, memories of past experiences and the ability to understand others (i.e., social cognitions).

The DMN includes four main brain regions: the medial prefrontal cortex (mPFC), the posterior cingulate cortex (PCC), the angular gyrus and the hippocampus. While several studies have explored the function of this network, its anatomical structure and contribution to information processing are not fully understood.

Researchers at McGill University, Forschungszentrum Jülich and other institutes recently carried out a study aimed at better understanding the anatomy of the DMN, specifically examining the organization of neurons in the tissue of its connected brain regions, which is known as cytoarchitecture. Their findings, published in *Nature Neuroscience*, offer new indications that the DMN has a widespread influence on the human brain and its associated cognitive (i.e., mental) functions.

"The default mode network (DMN) is implicated in many aspects of complex thought and behavior," Casey Paquola, Margaret Garber and their colleagues wrote in their paper. "We leverage postmortem histology and in vivo neuroimaging to characterize the anatomy of the DMN to better understand its role in information processing and cortical communication."

To closely examine the anatomy of the DMN, Paquola, Garber and their colleagues used two main experimental approaches, known as post-mortem histology and in vivo neuroimaging. The first of these approaches entails the microscopic examination of brain tissue preserved from deceased patients, while the second involves scanning the brains of living individuals.

"Our results show that the DMN is cytoarchitecturally heterogenous, containing cytoarchitectural types that are variably specialized for unimodal, heteromodal and memory-related processing," wrote Paquola, Garber and their colleagues. "Studying diffusion-based structural connectivity in combination with cytoarchitecture, we found the DMN contains regions receptive to sensory cortex input and a core relatively insulated from environmental input."

By mapping white matter pathways in the human brain, the researchers learned more about the organization and structure of the DMN. Specifically, they found that this network is made up of brain regions that receive sensory inputs and a "core" that is relatively "shielded" from the outside world (i.e., does not receive many external inputs).

"Finally, analysis of signal flow with effective connectivity models showed that the DMN is unique among cortical networks in balancing its output across the levels of sensory hierarchies," wrote Paquola, Garber and their colleagues. "Together, our study establishes an anatomical foundation from which accounts of the broad role the DMN plays in human brain function and cognition can be developed."

This recent study by Paquola, Garber and their colleagues could significantly advance the present understanding of the DMN, offering valuable insight about its cytoarchitecture, the connections between its underlying brain structures, and how it contributes to mental functions. The researchers' findings and the anatomical framework they introduced could inspire further research into this crucial brain network, which could shed new light on its contribution to healthy cognitive function, and specific mental health disorders.

More information: Casey Paquola et al, The architecture of the human default mode network explored through cytoarchitecture, wiring and signal flow, *Nature Neuroscience* (2025). DOI: 10.1038/s41593-024-01868-0.
Journal information: Nature Neuroscience

FEBRUARY 18, 2025

The Brain Science of Elusive 'Aha! Moments'

What happens in your mind when insight strikes?

BY JOHN KOUNIOS & YVETTE KOUNIOS EDITED BY MADHUSREE MUKERJEE

March 2025 Issue
Neuroscience

One evening in 1951 astronomer William Wilson Morgan was strolling home from Yerkes Observatory in Wisconsin when he looked up at the night sky and had a "flash inspiration ... a creative intuitional burst." It solved one of the great mysteries of astronomy.

The observable universe contains billions, possibly even trillions, of galaxies. With a modest telescope, their varied forms are discernible—spirals, ellipsoids and others with irregular structures. But what about our own galaxy, the Milky Way?

Morgan had been calculating the distances from Earth of groups of big, hot, bright stars, nowadays called OB associations. He knew that in spiral galaxies these clusters reside in the trailing arms. Gazing at the sky while walking home, he located the familiar dots of the OB associations. But this time the flat image of the night sky merged in his mind with the star distances that he had calculated and committed to memory, and it sprang to three-dimensional life. Morgan's vision: the stars of the OB association are arranged in a long strand—an arm of our spiral galaxy.

An "aha! moment," such as Morgan's marvelous insight that the Milky Way is a spiral, is a new idea or perspective that arrives abruptly, often bursting into an ongoing stream of thought. It may pop up while someone is actively trying to solve a problem, but it can also arrive spontaneously. "When I write songs, it's never a conscious decision—it's an idea that floats down in front of me at four in the morning or in the middle of a conversation or on a tour bus or in the mall or in an airport bathroom," singer-songwriter Taylor Swift related to an interviewer. "I never know when I'm gonna get an idea and I never know what it's gonna be."

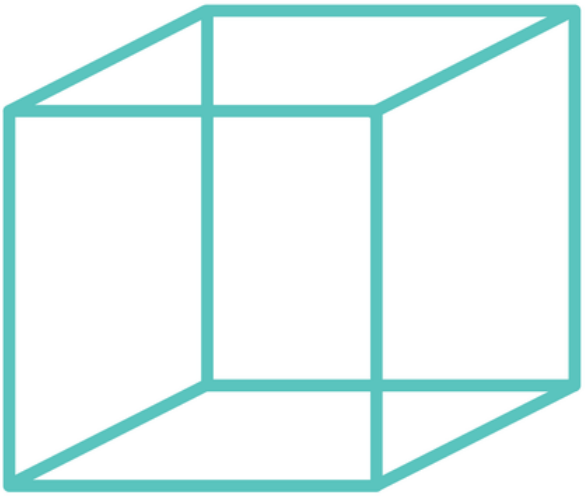
These revelations feel pleasing, even thrilling, and they can be portals to a scientific breakthrough, an innovative business proposal, a hit song or the plot of a best-selling novel. Or they may provide a life-changing perspective on a personal dilemma. People can overcome many challenges by analyzing them step by arduous step, but leaps of insight are more often associated with out-of-the-box ideas. And though often obvious in hindsight, the revelation can be astounding when it arrives.

Scholars have sought to capture the elusive essence of the aha! moment for more than a century, and it is finally within our grasp. We now know where it happens in the brain and when it's more likely to happen. And we're discovering some surprising benefits of insight, including elevated mood, memory and, oddly, the ability to distinguish fake news from real.

Psychologists of the Gestalt school, based in Germany in the 1910s, were the first to systematically study insight. The term "aha! moment" was popularized by media magnate Oprah Winfrey. Defined by *Merriam-Webster* as a "sudden realization, insight, recognition or comprehension," the aha! moment is also known as the Eureka! moment, as Archimedes is said to have exclaimed the Greek word *eureka* when he realized an object displaces a volume of water equal to its own. The Gestalt psychologists, who were interested in how the mind interprets patterns or forms, used visual illusions to argue that a problem could have features that mislead one's brain into misinterpreting it. The correct interpretation emerges when a shift of attention enables a person to restructure their understanding and see the problem in a new light.

Necker Cube Illusion

This illustration can be viewed in two ways, with the left square to the front or back, but not in both ways at the same time.



Jen Christiansen

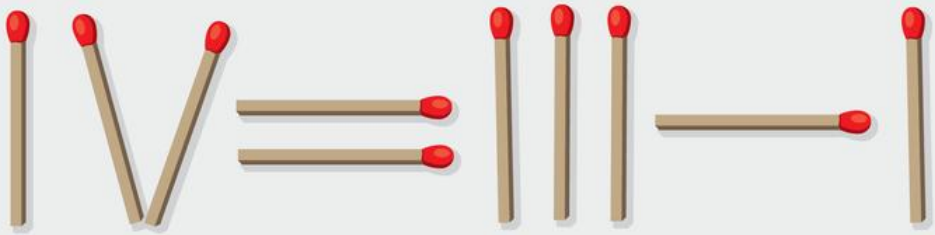
These pioneering psychologists tasked people with complex brainteasers designed to reveal how and when humans are likely to have revelatory insights. They were the first to demonstrate that insight is driven by unconscious processes. Later, during the 1980s and 1990s, cognitive psychologists applied more powerful experimental methods that tracked progress toward solving a problem. Janet Metcalfe of Columbia University showed that "warmth," a person's feeling of being close to a solution, increases gradually while they work on a problem that requires step-by-step, analytical thinking, such as one involving algebra, but more sharply just before they solve a brainteaser through insight. Jonathan Schooler of the University of California, Santa Barbara, discovered that requiring participants to describe their thought processes while they solve problems suppresses insight but not analysis.

Brainteasers

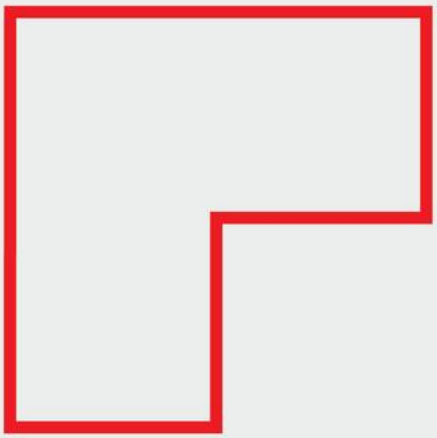
Insight studies make use of puzzles like these in their experimental setups. *See the end of the article for solutions.*

Demonstrate how you can move three of the circles so that the triangle points to the bottom of the page.

Move only one matchstick to make this equation true.



Show how you can divide this figure into four equal parts that are the same size and shape.



Given a candle, a book of matches and a box of push pins, how would you mount the candle to a wall?

Jen Christiansen; Sources: “Intuition in Insight and Noninsight Problem Solving,” by Janet Metcalfe and David Wiebe, in *Memory & Cognition*, Vol. 15; May 1987 (*triangle and polygon reference*); “Restructuring Processes and Aha! Experiences in Insight Problem Solving,” by Jennifer Wiley and Amory H. Danek, in *Nature Reviews Psychology*, Vol. 3; January 2024 (*candle problem reference*)

The 1990s saw rapid developments in neuroimaging. By the early 2000s cognitive neuroscientist Mark Beeman and one of us (John), both then at the University of Pennsylvania, concluded that imaging technologies were advanced enough for us to try to see what happens in the brain when a person has an insight. We used two complementary methods: electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). EEG measures the electrical activity of the brain with electrodes placed on a person’s scalp. It provides very precise information about when something is happening in the brain. In contrast, fMRI measures slower changes in blood flow (when a region of the brain is working harder, it draws more blood) and provides very detailed maps of where things are happening. By using EEG and fMRI in parallel experiments with different people solving the same puzzles, we were able to isolate the brain’s aha! moments in both space and time.

FEBRUARY 20, 2025

Eating walnuts for breakfast may boost your brain function

by University of Reading

Credit: Pixabay/CC0 Public Domain

Eating walnuts for breakfast could improve brain function throughout the day for young adults, a new study has shown.

Researchers at the University of Reading found that eating 50 g of walnuts (a generous handful) mixed into muesli and yogurt led to faster reaction times throughout the day and better memory performance later in the day when compared to eating an equivalent calorie-matched breakfast without nuts.

The research, published this month in *Food & Function*, involved 32 healthy young adults aged 18–30 who consumed both a walnut-rich breakfast and a matched breakfast on separate occasions. Participants completed various cognitive tests while their brain activity was monitored in the six hours after eating each breakfast.

Professor Claire Williams, who led the research from the University of Reading, said, "This study helps strengthen the case for walnuts as brain food. A handful of walnuts with

breakfast could give young adults a mental edge when they need to perform at the top of their game. It's particularly exciting that such a simple dietary addition could make a measurable difference to cognitive performance."

More work to be done

The findings build on previous research showing the cognitive impacts of regular nut consumption, including walnuts. This is the first study to examine the immediate effects of walnuts on brain function in young adults throughout a single day.

Brain activity recordings revealed changes in neural activity that suggest walnuts may help the brain work more efficiently during challenging mental tasks, while blood samples revealed positive changes in glucose and fatty acid levels—both factors that could influence brain function.

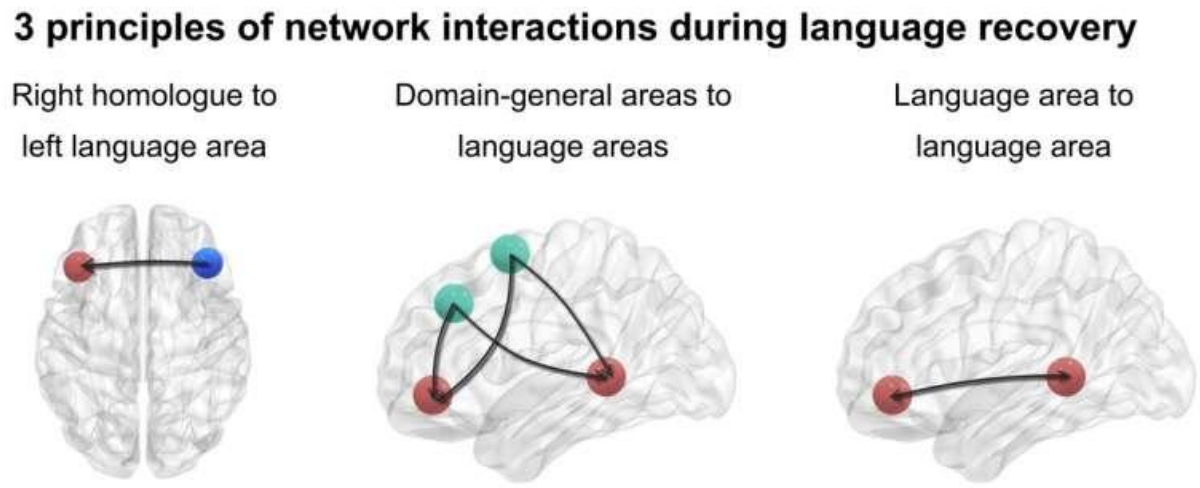
The researchers suggest that walnuts' mix of nutrients—including omega-3 alpha linolenic fatty acids, protein, and plant compounds called polyphenols—may enhance cognitive performance. However, they note that more research is needed to fully understand how walnuts produce these beneficial effects on the brain.

More information: L. Bell et al, The impact of a walnut-rich breakfast on cognitive performance and brain activity throughout the day in healthy young adults: a crossover intervention trial, *Food & Function* (2025). DOI: 10.1039/D4FO04832F
Journal information: Food & Function
Provided by University of Reading

FEBRUARY 20, 2025

How the brain rewires itself for language recovery after a stroke

by Birgit Pfeiffer, Leipzig University



Credit: Dr. Philipp Kuhnke

A new study shows how the brain reorganizes itself in the first few months after a stroke to improve the ability to speak again. The findings will help researchers understand how functional networks work in the brain. They also have the potential to be used in the future for personalized treatment of stroke patients.

The researchers from the Wilhelm Wundt Institute of Psychology at Leipzig University, the Max Planck Institute for Human Cognitive and Brain Sciences, the University of Leipzig Medical Center and the University of Cambridge have published these results in the journal *Brain*.

It would be a nightmare for anyone: suffering a stroke and losing the ability to communicate properly. In many cases, speech will recover to some extent in the days and weeks that follow. This is because the brain, stimulated by its own efforts and speech therapy, tries to restore speech as far as possible on its own. Until now, it was not known exactly what processes were involved in language recovery.

"In our study, we examined stroke patients at the university hospital at three stages: immediately after their stroke, then two weeks and six months later," says author Professor Gesa Hartwigsen from the Wilhelm Wundt Institute of Psychology at Leipzig University and the Max Planck Institute for Cognitive and Brain Sciences.

While previous studies have focused on the activity of classical language centers in the brain, the authors of this study went a step further: For the first time, they investigated the interactions between different areas of the brain at network level.

"This is because language involves many areas of the brain that form functional networks," says the scientist. "But it was still unclear exactly how these areas of the brain work together and influence each other during language recovery.

Quick help from other network areas

The authors of the study identified three principles: "Firstly, language-specific network areas of the left hemisphere of the brain that are affected by the stroke very quickly receive functional reinforcement from other network areas," says Hartwigsen. "These 'domain-general' areas are present in both sides of the brain and perform cognitive support functions here."

Secondly, the scientists found that "the mirror-image areas of the right side of the brain, which are normally less involved in language processing than those on the left side damaged by the stroke, step in," says Dr. Philipp Kuhnke. These mirror-image areas are also called homologues.

"And thirdly, we saw that network communication between the language areas in the left hemisphere of the brain also intensifies during language recovery," says the scientist.

Adaptation processes themselves are flexible

Patients' functional adaptation processes for regaining lost language skills changed over several months, in some cases significantly. How this happened depended, among other things, on whether the tissue damaged by the stroke was in the front or back of the patient's left brain hemisphere.

Because the distribution of language-specific areas differs between right-handed and left-handed people, the researchers only looked at right-handed people who had suffered a stroke in the left hemisphere.

A total of 51 participants—34 patients and 17 healthy controls—were examined at the Department of Neurology at the University of Leipzig Medical Center, led by Professor Dorothee Saur. Their brain activity was measured using functional MRI while they performed language tasks.

The researchers then analyzed the data using a modeling method that takes causal relationships into account. This method makes it possible to determine the direction of network communication between different areas of the brain.

"Our method allowed us to determine not only which areas are activated at the same time, but also which part influences which other part in which recovery phase," says Dr. Kuhnke.

"The findings hold the potential for personalized treatment of patients in the future, for example with targeted neurostimulation," says Professor Hartwigsen. Until then, she adds, more research is needed, with more subjects and more extensive and more detailed analyses.

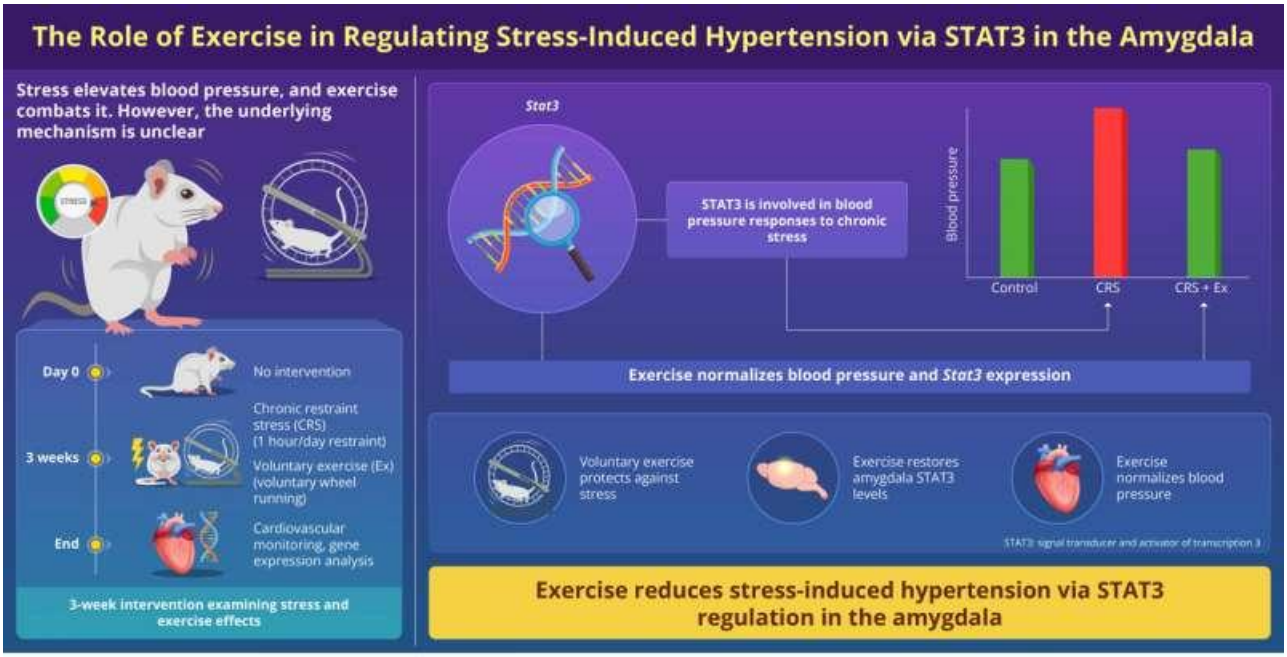
At the same time, the scientists are working to identify key factors that can be used to predict good speech recovery shortly after a stroke.

More information: Zhizhao Jiang et al, Dynamic reorganization of task-related network interactions in post-stroke aphasia recovery, *Brain* (2025). DOI: 10.1093/brain/awaf036
Journal information: Brain
Provided by Leipzig University

FEBRUARY 20, 2025

Exercise can restore STAT3 levels in the amygdala, preventing stress-induced high blood pressure

by Juntendo University Research Promotion Center



Potential role of signal transducer and activator of transcription 3 in the amygdala in mitigating stress-induced high blood pressure via exercise in rats
Tomita *et al.* (2025) | *Acta Physiologica* | DOI: 10.1111/apha.14274

Juntendo University

Exercise reduces stress-induced hypertension via STAT3 regulation in the amygdala. Credit: Prof. Hidefumi Waki, from Juntendo University

Hypertension (high blood pressure) is a debilitating condition and a major cause of premature death worldwide. Chronic stress plays a significant role, but the underlying mechanism involving biochemical pathways by which stress leads to hypertension has not been well understood. Understanding these pathways could lead to the development of therapeutic agents to combat hypertension.

Now, a new study from Juntendo University, Japan, led by Professor Hidefumi Waki, Dr. Keisuke Tomita, and Dr. Ko Yamanaka, published online in the journal *Acta Physiologica* on January 13, 2025, has shown that voluntary exercise prevents stress-induced hypertension through restoration of amygdala signal transducer and activator of transcription 3 (Stat3), a gene that is crucial to the normal function of the amygdala, an almond-shaped part of the brain involved with the experiencing of emotions.

"In the amygdala, the gene Stat3 is involved in the regulation of blood pressure and possibly plays a role in blood pressure elevation in response to chronic stress. It might also be

involved in the improvement of stress by voluntary exercise," explains Prof. Waki while elaborating on the role of STAT3.

The amygdala is a key player in the body's cardiovascular response. When exposed to prolonged stress, this region triggers an increase in blood pressure, heightening the risk of heart disease. To understand how exercise influences this process, researchers subjected rats to three weeks of chronic stress, with one group engaging in voluntary wheel running. Subsequently, they analyzed blood pressure levels and the levels of various genes using gene expression analysis in the amygdala to identify changes at the molecular level.

The study found that chronic stress led to a marked increase in blood pressure. Moreover, gene expression analysis revealed decreased Stat3 gene expression in the amygdala. However, when stressed rats underwent daily exercise, their blood pressure was normal, and STAT3 levels rebounded.

Subsequent experiments demonstrated that Stat3 expression blockade in the amygdala, in the absence of stress, produced an increase in blood pressure, underlining its important function in cardiovascular control.

"The improvement of cardiovascular dynamics after exercise is attributed to the rescue of Stat3 expression possibly because of mechanisms such as neuroprotection and anti-inflammation," explains Prof. Waki while elaborating on the underlying mechanism.

The findings of the study highlight a previously unknown brain-based mechanism behind exercise's ability to combat high blood pressure. While regular physical activity is already recommended for heart health, this study suggests it may also serve as a non-drug therapy for stress-induced hypertension and related conditions like anxiety. However, researchers caution that more studies are needed to confirm these findings in humans and to explore whether therapies targeting STAT3 could offer new treatments for hypertension.

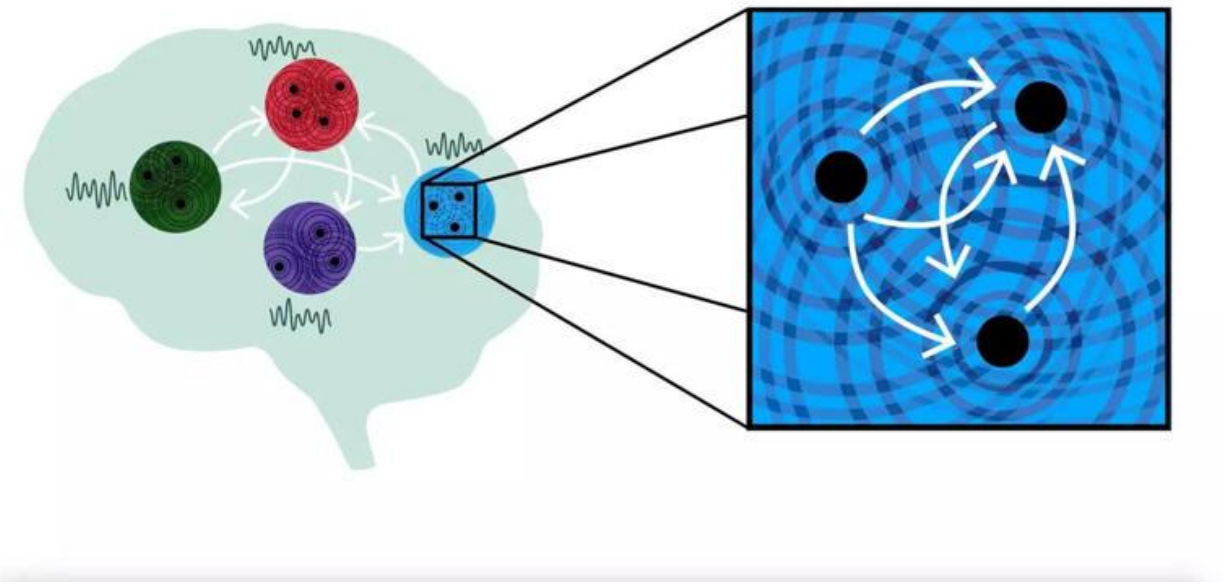
"STAT3 plays a potential role in arterial pressure elevation in response to chronic stress and its improvement through exercise, both of which need to be clarified in future studies," concludes Prof. Waki.

Next, the team plans to explore whether specific types of exercise—or even pharmacological approaches—can enhance STAT3 activity in the amygdala to offer protection against hypertension.

Overall, their research reinforces a simple yet powerful message: exercise is not just for your body—it's for your brain too.

More information: Keisuke Tomita et al, Potential role of signal transducer and activator of transcription 3 in the amygdala in mitigating stress-induced high blood pressure via exercise in rats, *Acta Physiologica* (2025). DOI: 10.1111/apha.14274
Provided by Juntendo University Research Promotion Center

Neural waves study provides evidence that brain's rhythmic patterns play key role in information processing



Schematic representation of the "Harmonic Oscillator Recurrent Network Model" (HORN). Credit: ESI

Researchers at the Ernst Strüngmann Institute in Frankfurt am Main, Germany, led by Wolf Singer, have made a new discovery in understanding fundamental brain processes. For the first time, the team has provided compelling evidence that the brain's characteristic rhythmic patterns play a crucial role in information processing. While these oscillatory dynamics have long been observed in the brain, their purpose has remained mostly elusive until now.

The study has the potential to transform our understanding of brain activity. Using computer simulations, the researchers show that recurrent networks with oscillating nodes demonstrate better performance compared to non-oscillating networks and replicate many experimentally observed phenomena.

These findings indicate that oscillatory dynamics are not just an epiphenomenon but are essential for efficient computation in the brain. The work is published in the journal *Proceedings of the National Academy of Sciences*.

Furthermore, the study demonstrates that incorporating heterogeneity in network parameters, such as introducing different oscillation frequencies and conduction delays, further enhances network performance. This suggests that the heterogeneity observed in biological networks is not just a result of nature's imprecision but a signature of a computational substrate optimized for efficient computation of stimuli with highly varying properties.

"Our findings challenge the traditional view of brain dynamics, which often assumes rather localized information processing," said Felix Effenberger, first author of the study. "Instead, we propose that the brain uses waves to perform computations in a highly distributed and parallelized manner. The interference patterns produced by such wave-based responses facilitate a holistic representation and highly distributed encoding of both spatial and temporal relationships among stimulus features".

Networks serve as a medium for generating waves

The researchers propose a novel interpretation of neuronal dynamics in which networks serve as a medium for generating and propagating waves rather than functioning as a complicated circuit board with well-defined and directed signal flows, as assumed by current theories in neurobiology and as is also the case in conventional digital computers.

The authors of the study suggest that the brain uses the superposition and interference patterns of waves to represent and process information in a highly distributed way, exploiting the unique properties of coupled oscillator networks such as resonance and synchronization.

"This is a major step forward in our understanding of how the brain computes," said Singer, senior author of the study. "The computational strategy proposed is ideally suited for cognitive functions requiring the simultaneous evaluation of large numbers of nested relations between spatial and temporal stimulus features.

"Such tasks need to be solved to comprehend visual scenes and language. Furthermore, the proposed computational strategy provides a mechanism for

solving the 'Binding Problem,' confirming the hypothesis that feature binding—the joint evaluation of features belonging to an object—can be achieved by synchronizing oscillatory responses."

Beyond its significant contributions to neuroscience, the findings pave the way for the development of novel, energy-efficient chips for artificial intelligence—for example, in the development of new, significantly more energy-efficient technical components. The authors propose a departure from conventional digital designs, advocating for analog chips inspired by the dynamic processes of the brain.

They also suggest that their findings could guide the development of a new generation of AI systems that are more robust, energy-efficient, and better equipped to learn on smaller datasets. This study greatly enhances our understanding of how the brain processes information and paves the way for new research opportunities in neuroscience and artificial intelligence.

More information: Felix Effenberger et al, The functional role of oscillatory dynamics in neocortical circuits: A computational perspective, *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2412830122

Provided by Max Planck Society

Editing Bad Memories Is No Longer Science Fiction (And May Be The Future Of Mental Healthcare)

Concept of using an eraser on an MRI image of a brain© Gso Images/Getty Images

Research shows that repetitively recalling bad memories can have negative effects on mental health, such as leading to anxiety or depression because they're sources of psychological stress. In the search for more successful treatment options for mental disorders with bad memories as an underlying cause, scientists have discovered that it's possible to weaken those memories by strengthening positive ones.

Published in the Proceedings of the National Academy of Sciences in July 2024, the study of 37 individuals underwent a multi-day experiment. It involved an evening of training the brain to associate nonsense words with negative images. The following day, after sleeping to consolidate the memories, the participants underwent more brain training to associate half of the nonsense words with positive images in an attempt to reprogram the associations and create positive memories that interfere with the negative ones. During the non-rapid eye movement (NREM) phase of the next night of sleep, the researchers played a

recording of the words being spoken while monitoring brain activity with electroencephalography, which is used to detect even the slowest delta waves in sleep studies.

For several days after the night of memory reactivation, the participants completed questionnaires and tasks to assess their ability to recall the positive and negative memories. Ultimately, they were more likely to have positive associations with the nonsense words that were mixed up with the negative associations. The researchers noted in the paper that, although this research is in its early stages and involved a tightly controlled experiment, "our findings may offer new insights relevant for the treatment of pathological or trauma-related remembering."

Read more: The Truth About Gut Feelings And When You Should Trust Them

Sleep Has A Major Role In How We Remember And Forget

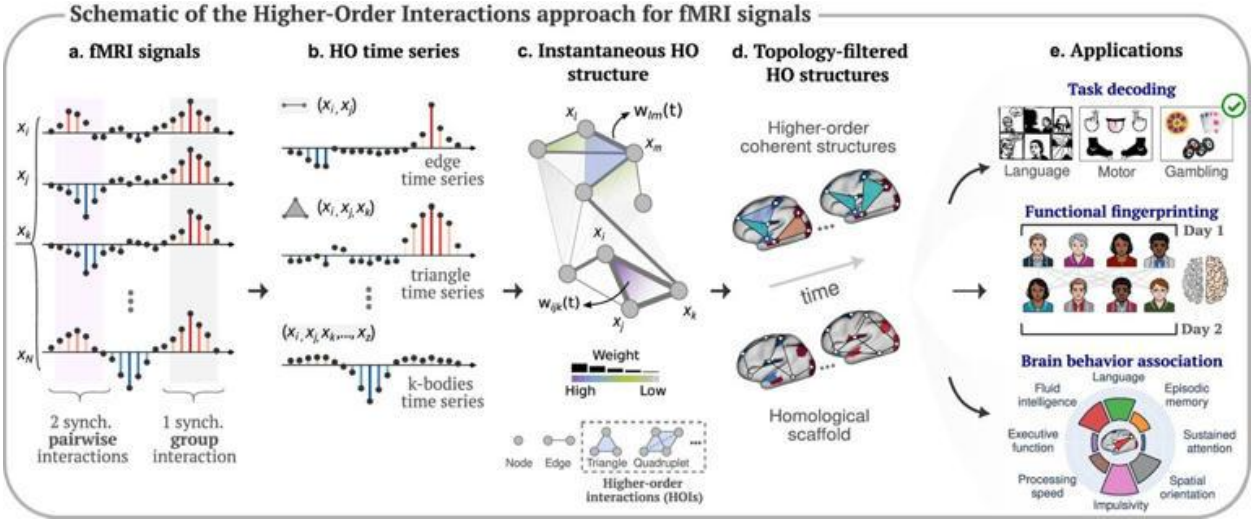
Scientists have long known that one of the purposes of the temporal lobe is to control memory encoding and storage in the brain. In regards to memory specifically, the function of the left temporal lobe is to remember verbal information, while the right temporal lobe does the same for non-verbal information. And, although the research continues, more than 100 years of study shows that sleep has a huge impact on the brain's ability to carry out those functions.

During the two light stages of NREM sleep, the brain sorts through the previous day of memories, saving what it deems as important ones and deleting everything else. The preserved memories are consolidated during the third, deep NREM phase. This process continues through the REM (dream) stage, during which the brain processes information from the memories, some of which can end up in dreams. Studies suggest that information may be deleted during REM sleep, too, which is why so many dreams are forgotten.

Additionally, the brain prepares for learning new information after waking during the NREM stages. That's why researchers have seemingly found a correlation between lack of sleep and cognitive decline. There is also evidence that sleep

deprivation hinders the brain's ability to restrict the recollection of negative memories

Brain mapping technique reveals insights into brain's higher functions



Higher-order brain mapping: schematic of the approach and applications. Credit: Nature Communications (2024). DOI: 10.1038/s41467-024-54472-y

A new way of mapping activity and connections between different regions of the brain has revealed fresh insights into how higher order functions like language, thought and attention, are organized.

Traditional models of human brain activity represent interactions in pairs between two different brain regions. This is because modeling methods have not developed sufficiently to describe more complex interactions between multiple regions.

A new approach, developed by researchers at the University of Birmingham is capable of taking signals measured through neuroimaging, and creating accurate models from these to show how different brain regions are contributing to specific functions and behaviors. The results are published in *Nature Communications*.

Lead researcher, Dr. Enrico Amico, said, "Complex systems like the brain depend on interactions between groups of regions, not just between pairs of regions.

Although we know—in theory—that this is the case, until now we have not had the processing power required to model this."

In the study, the group used data from fMRI scans recorded as part of the Human Connectome Project. This large-scale research consortium was set up to map the human brain, connecting its structure to function and behavior.

These scans, however, can provide only "noisy" estimates of neural activity, so statistical methods are needed to clean up the data and compile accurate estimates of interactions from the neuroimaging signals.

Taking 100 unrelated subjects from the projects' databank, the team produced detailed models of higher-order interactions. They tested these in three key areas, designed to test how useful the approach is.

In the first, they were able to show it was possible to identify what task the individual might have been doing while in the fMRI scanner. In the second area of research, the team showed it was possible to identify a specific individual from their brain signals—using the signals as a sort of unique brain fingerprint for the individual. And in the third area, the researchers demonstrated how higher order brain signals of an individual could be separated out from the lower order signals, and how they can be associated with the behavioral features of each individual.

Dr. Andrea Santoro, of the CENTAI Institute in Italy, is the first author of the paper. He said, "Our approach, validated using data from healthy individuals, demonstrates the substantial advantages that this method can offer to neuroscience research. In the future, this method could also be used to help model interactions in individuals with neurodegenerative diseases, such as Alzheimer's, where they could give valuable insights into how brain function is changing over time, or even to identify pre-clinical symptoms of these conditions."

More information: Andrea Santoro et al, Higher-order connectomics of human brain function reveals local topological signatures of task decoding, individual identification, and behavior, *Nature Communications* (2024). DOI: 10.1038/s41467-024-54472-y

Provided by University of Birmingham

As the world moves toward sustainability, the demand for efficient alternatives across industries continues to grow. Ammonia, a key chemical used in fertilizers, explosives, and various other products, is primarily synthesized through the energy-intensive Haber-Bosch process.

This process requires extremely high temperatures and pressures, contributing to global carbon dioxide emissions. Conventional catalysts, such as iron and ruthenium, rely on these harsh conditions to drive the reaction.

However, a study by researchers from the Institute of Science Tokyo, the National Institute for Materials Science, and Tohoku University, Japan, led by Professor Masaaki Kitano, explores $Ba_3SiO_{5-x}N_yH_z$ catalyst as a sustainable alternative to traditional catalysts, potentially revolutionizing ammonia synthesis.

Vacancies, especially anion vacancies within the three-dimensional structure of catalysts, function as active sites. These active sites are energetically involved in the process of catalysis. However, anion vacancies alone are not effective without the presence of transition metal sites. This limitation inspired researchers to develop a transition metal-free catalyst.

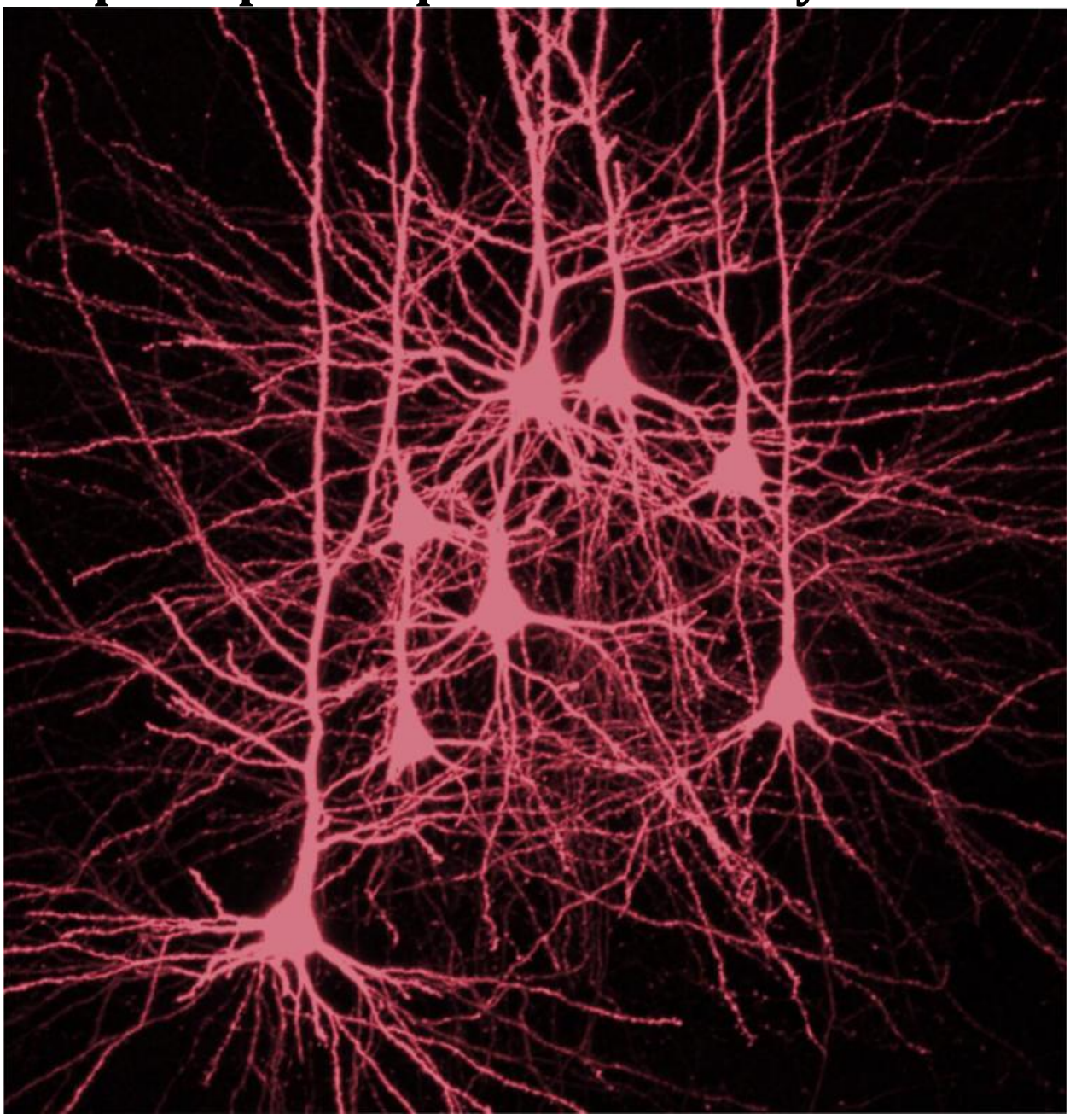
Published online in *Nature Chemistry* on 17 February 2025, the study aims to develop more efficient, sustainable ammonia synthesis methods.

Kitano explains, "We have focused on tribarium silicate (Ba_3SiO_5) for the synthesis of our novel catalyst due to its unique crystal structure and chemical properties, offering the potential to lower energy requirements and reduce operating conditions."

To address the environmental and energy challenges posed by conventional synthesis methods, the research team developed and tested various mixed-anion materials.

The study progressed through several stages. First, the researchers synthesized a novel Ba-Si oxynitride-hydride, $Ba_3SiO_{5-x}N_yH_z$, through a low-temperature (400–700 °C) solid-state reaction of barium amide with silicon dioxide. The resulting chemical composition was determined to be $Ba_3SiO_{2.87}N_{0.80}H_{1.86}$.

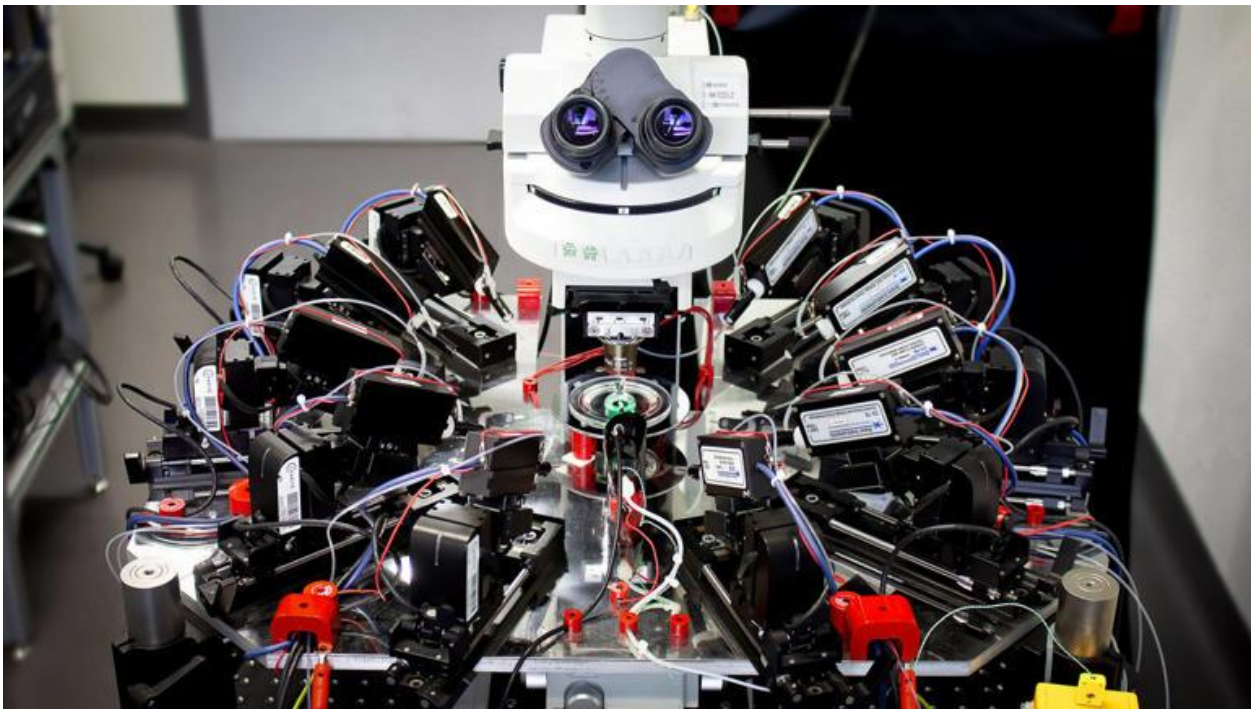
Slow brain waves and the neocortex: Why deep sleep is helpful for memory



Neurons in the neocortex: Slow-wave sleep strengthens the connections between them, supporting memory formation. Credit: Charité | Sabine Grosser

It has been known for nearly 20 years that slow, synchronous electrical waves in the brain during deep sleep support the formation of memories. Why that is, was previously unknown.

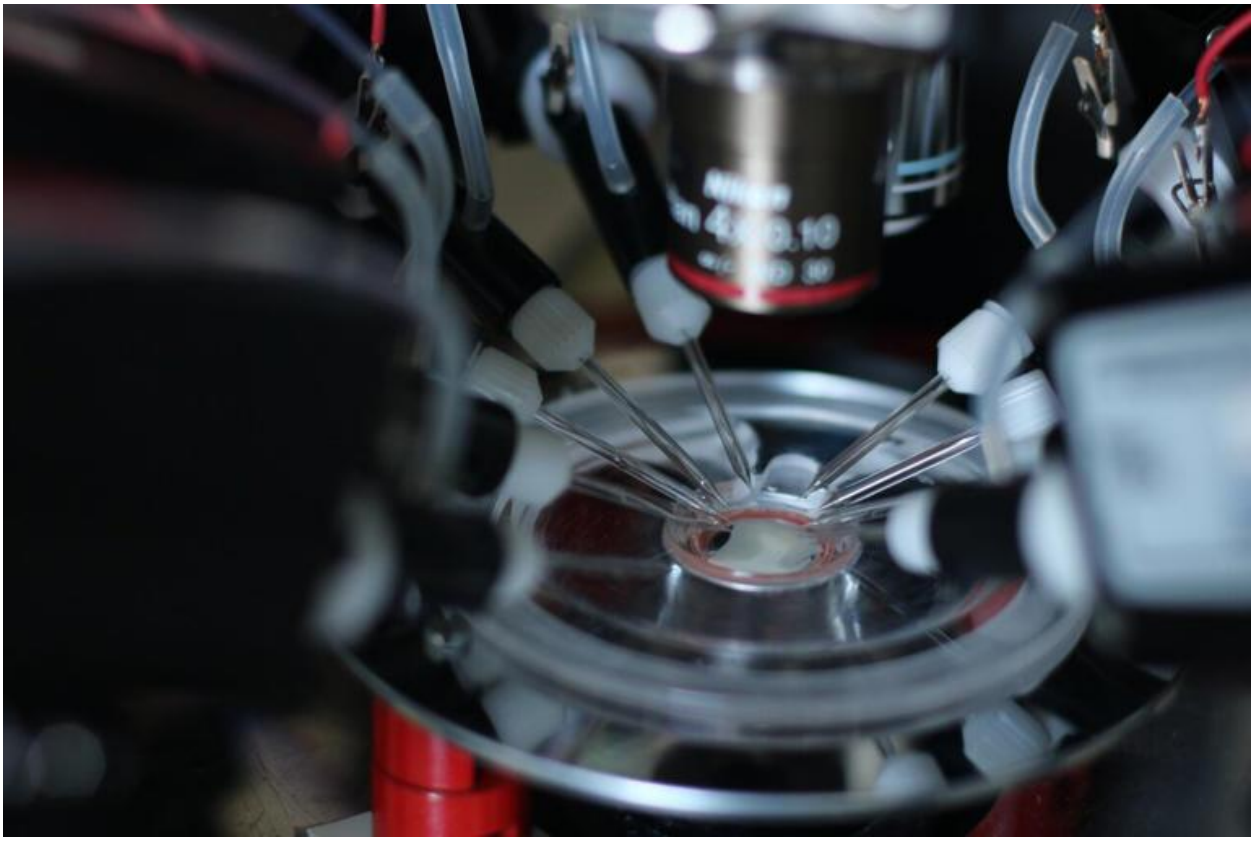
Now, writing in the journal *Nature Communications*, a team of researchers from Charité—Universitätsmedizin Berlin posits an explanation. According to the study, the slow waves make the neocortex, the location of long-term memory, especially receptive to information. The findings could help to optimize the treatment approaches that are intended to support memory formation from outside.



Ten "feelers" to track deep sleep: This friendly-looking microscope was instrumental in decoding the effects of the slow waves typical of sleep. Equipped with ten glass pipettes that can be controlled precisely down to the nanometer using robot arms, it can stimulate and read the electrical activity of just as many nerve cells in the connected tissue. Credit: Charité | Franz Xaver Mittermaier

How do permanent memories form? Experts believe that while we sleep, our brains replay the events of the day, moving information from the location of short-term memory, the hippocampus, to the long-term memory located in the neocortex.

"Slow waves" are especially key to this process: slow, synchronous oscillations of electrical voltage in the cortex that occur during the deep sleep phase. They can be measured using an electroencephalogram (EEG). The waves originate when the electrical voltage in many neurons rises and falls simultaneously once per second.



Ten "pipette feelers" in use. Credit: Charité | Yangfan Peng

"We've known for many years that these voltage fluctuations contribute to the formation of memory," explains Prof. Jörg Geiger, director of the Institute of Neurophysiology at Charité and the head of the newly published study.

"When slow-wave sleep is artificially augmented from outside, memory improves. But what we didn't know until now was what exactly is happening inside the brain when this occurs, because it is extremely difficult to study the flows of information inside the human brain."

Slow waves strengthen synapses

He and his team have now used intact human brain tissue, which is extremely rare, to clarify the processes that are very likely to underlie the formation of memory during deep sleep. According to their findings, the slow electrical waves influence the strength of synaptic connections between the neurons in the neocortex—and thus their receptivity.

For their study, the team of researchers studied intact neocortical tissue samples taken from 45 patients who had undergone neurosurgery to treat epilepsy or a brain tumor at Charité, the Evangelisches Klinikum Bethel (EvKB) hospital, or the University Medical Center Hamburg-Eppendorf (UKE).

The researchers simulated the voltage fluctuations typical of slow brain waves during deep sleep in the tissue and then measured the nerve cells' response.

To achieve this, they used glass micropipettes positioned precisely down to the nanometer. To "listen in" on the communications among multiple nerve cells connected through the tissue, they used up to 10 "pipette feelers" at once—an extra large number for this method, which is known as the multipatch technique.

Perfect timing contributes to memory formation

The team of researchers discovered that the synaptic connections between neurons in the neocortex are maximally enhanced at a very specific point in time during the voltage fluctuations.

"The synapses work most efficiently immediately after the voltage rises from low to high," explains Franz Xaver Mittermaier, a researcher at the Institute of Neurophysiology at Charité and the first author of the study.

"During that brief time window, the cortex can be thought of as having been placed in a state of elevated readiness. If the brain plays back a memory at exactly this time, it is transferred to long-term memory especially effectively. So, slow-wave sleep evidently supports memory formation by making the neocortex particularly receptive for many short periods of time."

This knowledge could be used to improve memory, for example in mild cognitive impairment in the elderly. Research groups around the world are working on methods of using subtle electrical impulses—transcranial electrostimulation—or acoustic signals to influence slow waves during sleep.

"Right now, though, these stimulation approaches are being optimized through trial and error, which is a laborious and time-consuming process," Geiger says.

"Our findings about the perfect timing could help with this. Now, for the first time, they allow for targeted development of methods of stimulation to boost memory formation."

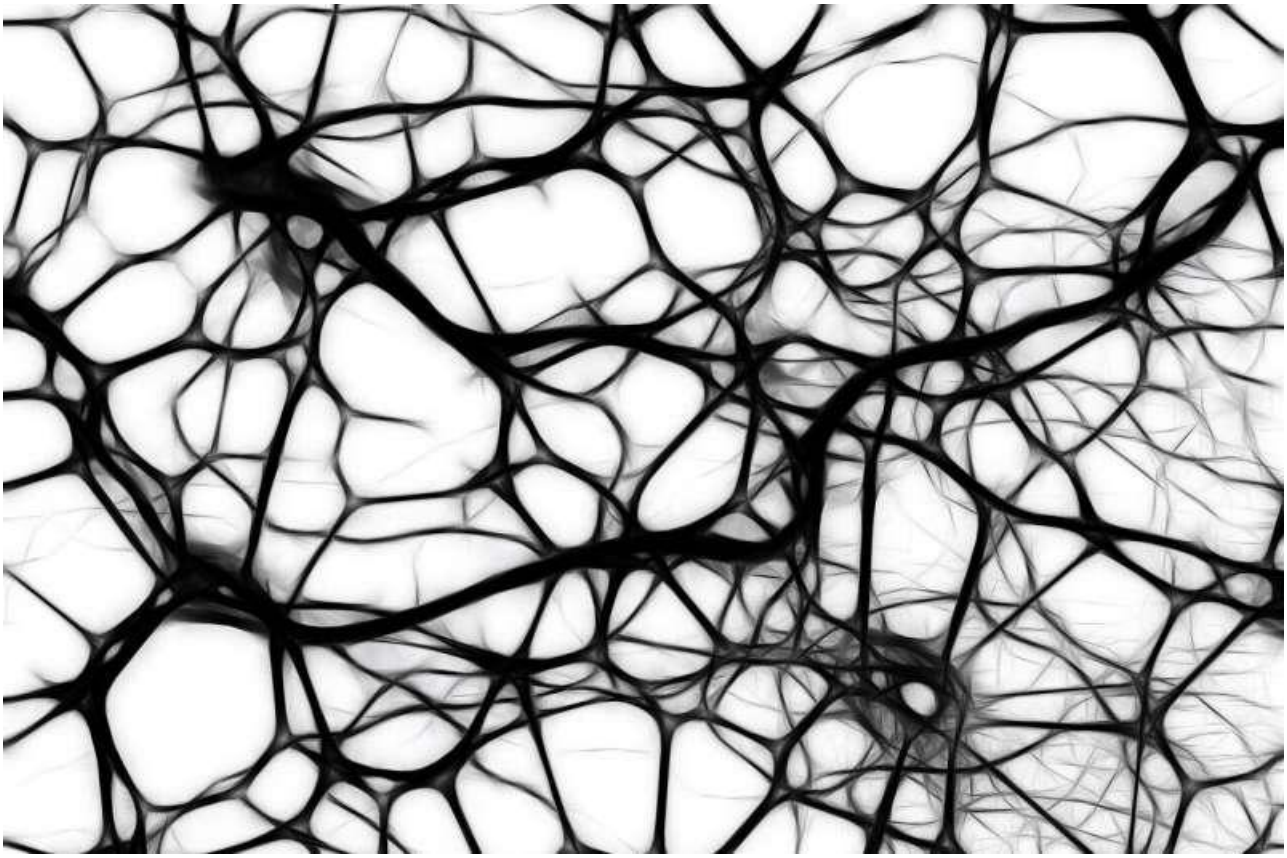
More information: Franz X. Mittermaier et al, Membrane potential states gate synaptic consolidation in human neocortical tissue, *Nature Communications* (2024). DOI: 10.1038/s41467-024-53901-2

Provided by Charité - Universitätsmedizin Berlin

FEBRUARY 24, 2025

The brain's map of space: A new discovery about how our brains represent information

by Hebrew University of Jerusalem



Credit: Pixabay/CC0 Public Domain

A new study led by Prof. Yoram Burak of the Edmond and Lily Safra Center for Brain Sciences and the Racah Institute of Physics at the Hebrew University of Jerusalem unveils a unifying mathematical framework to explain how "place cells" in the hippocampus encode spatial information across diverse species and environments.

The study is published in the journal *Neuron*.

Place cells are specialized neurons in the hippocampus that help animals navigate by creating firing patterns that encode locations within the animals' surroundings. Traditionally, these cells were thought to fire in single, compact regions of space with a stereotypical symmetric shape.

However, recent research has revealed that in larger environments, these cells display much more complex and irregular patterns of activity, firing in multiple locations with varied shapes and sizes.

Prof. Burak's team has found that a remarkably simple yet powerful mathematical model explains the irregular firing patterns of place cells in large environments. The model is based on the concept of "Gaussian Processes", a class of random functions that play an important role in diverse natural phenomena ranging from cosmology to oceanography.

In the model, firing regions of place cells emerge by marking regions of space in which a random Gaussian process crosses a certain threshold. Using this simple model, the researchers showed that the activity of place cells in bats and rodents across 1D, 2D, and 3D spaces follows universal principles.

Field arrangements of place fields in 2d and 3d spaces are explained by the thresholded Gaussian process model. Credit: Nischal Mainali
These findings imply that these patterns arise from largely random inputs to the hippocampus, challenging the idea that the brain relies on precise organization for its spatial map.

"Our findings suggest that randomness, rather than specific design, governs the synaptic organization of inputs to CA1 neurons in the hippocampus," explains Nischal Mainali, a student at the Hebrew University and one of the authors of the study.

This perspective challenges long-held assumptions about the structure of neural circuits and opens new avenues for understanding spatial cognition.

The model also makes precise testable predictions about the arrangements of place cell firing fields, and their geometry, which were verified by re-examining recordings of place cell activity, collected in previous experiments from bats, mice, and rats that navigated in diverse environments.

These insights not only shed light on the neural mechanisms of spatial navigation but also provide a foundation for exploring how the brain encodes information.

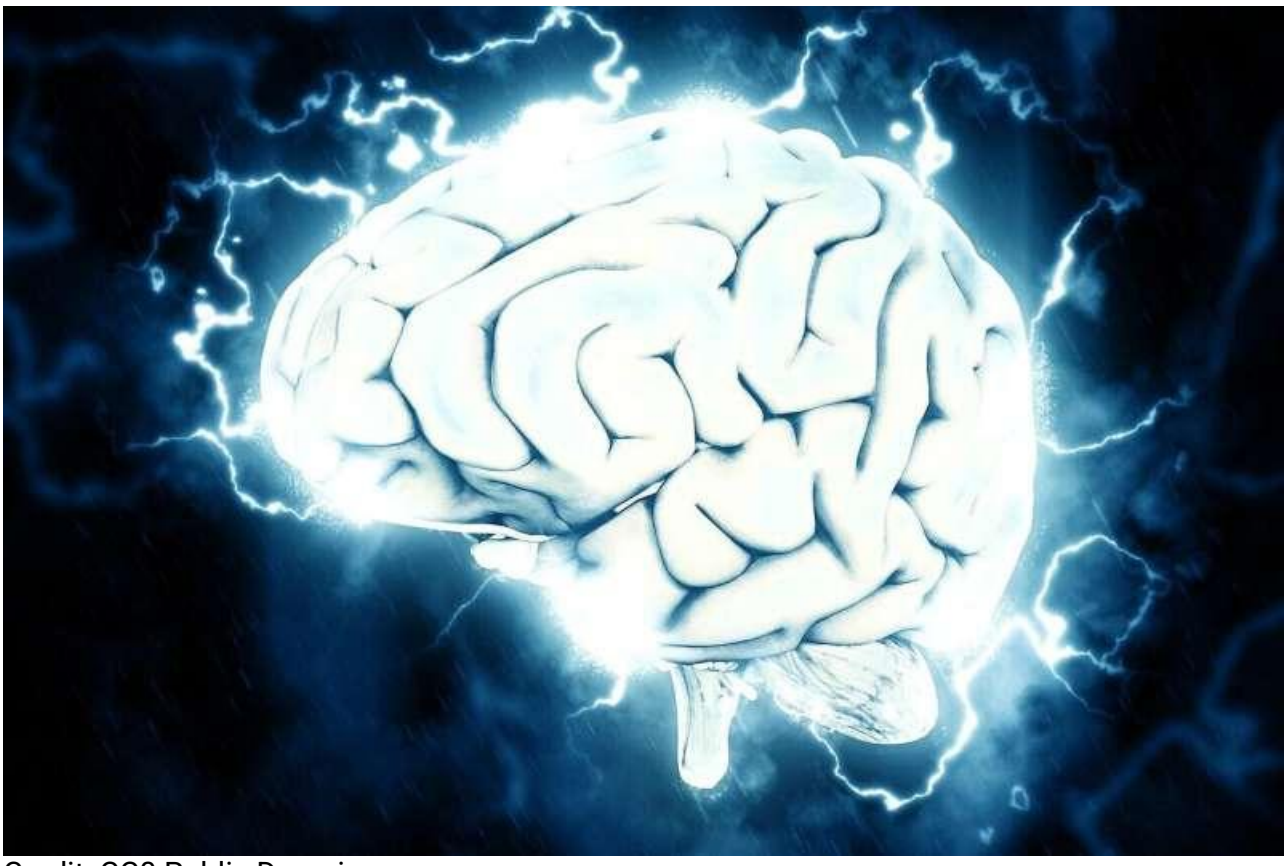
Prof. Burak explains, "The seemingly random firing patterns of place cells in large environments form 'codewords' that are uniquely assigned to different positions in space. We believe that the brain tunes the statistics of these random codewords to create a very efficient representation of positions in large environments".

More information: Nischal Mainali et al, Universal statistics of hippocampal place fields across species and dimensionalities, *Neuron* (2025). DOI: 10.1016/j.neuron.2025.01.017. www.cell.com/neuron/fulltext/S0896-6273(25)00043-1
Journal information: Neuron
Provided by Hebrew University of Jerusalem

FEBRUARY 24, 2025

AI-powered tool detects invisible brain abnormalities in children with epilepsy

by King's College London



Credit: CC0 Public Domain

Scientists have developed an AI-powered tool that detects 64% of brain abnormalities linked to epilepsy that human radiologists miss.

MELD Graph is an AI tool that could drastically change the care for 30,000 patients in the UK and 4 million worldwide with one cause of epilepsy, researchers say.

The study, published in *JAMA Neurology* by a team at King's College London and University College London (UCL), shows how the tool significantly improves the detection of focal cortical dysplasias (FCDs), which is a leading cause of epilepsy.

Researchers say the tool will speed up diagnosis times, get patients the surgical treatment they need quicker, and reduce costs to the NHS by up to £55,000 per patient.

In the UK, one in 100 people are affected by epilepsy. One in five people with epilepsy have seizures caused by a structural abnormality ("lesion") in the brain. FCDs are a common structural cause of epilepsy and in people with this type of epilepsy, seizures are usually not able to be controlled with medications. Surgery to remove the lesion can be an effective and safe way to stop the seizures.

However, the challenge is that FCDs can be subtle and difficult to see with the human eye and up to half of these lesions are missed by radiologists. Delays to diagnosis and surgery mean more seizures, more visits to A&E, and more disruption to school, work and home life.

In the study, the researchers pooled MRI data from 1,185 participants—including 703 people with FCD and 482 controls—from 23 epilepsy centers around the world in the Multicenter Epilepsy Lesion Detection project (MELD). Half of the dataset is from children. They then trained the artificial intelligence tool, MELD Graph, to detect these subtle brain abnormalities that might otherwise go undetected.

Project lead-author, Dr. Konrad Wagstyl, from King's College London, said, "Radiologists are currently inundated with images they have to review. Using an AI-powered tool like MELD Graph can support them with their decisions, making the NHS more efficient, speeding time to treatment for patients and relieving them of unnecessary and costly tests and procedures."

Co-author Dr. Luca Palma, from Bambino Gesù Children's Hospital, Italy, said, "MELD Graph identified a subtle lesion missed by many radiologists in a 12-year-old boy who had daily seizures and had tried nine anti-seizure medications with no improvement to his condition.

"This tool could identify patients with surgically operable epilepsy and help with surgical planning—reducing risks, saving money, and improving outcomes."

While the tool is not yet clinically available, the research team have released the AI-tool as an open-source software. They are running workshops to train clinicians and researchers around the world, including Great Ormond Street Hospital and the Cleveland Clinic, in how to use it.

First author, Dr. Mathilde Ripart from UCL, said "One of the highlights for me is hearing from doctors around the world, including the UK, Chile, India and France have been able to use our tools to help their own patients."

Co-author Professor Helen Cross, Prince of Wales's Chair of Childhood Epilepsy, President of the International League Against Epilepsy, Consultant Epileptologist at Great Ormond Street Hospital, and Director of the UCL Great Ormond Street Institute of Child Health, OBE said, "Many of the children I see have experienced years of seizures and investigations before we find a lesion.

"The epilepsy community is searching for ways to speed up diagnosis and treatment. Initiatives such as MELD have the potential to rapidly identify abnormalities that can be removed and potentially cure the epilepsy."

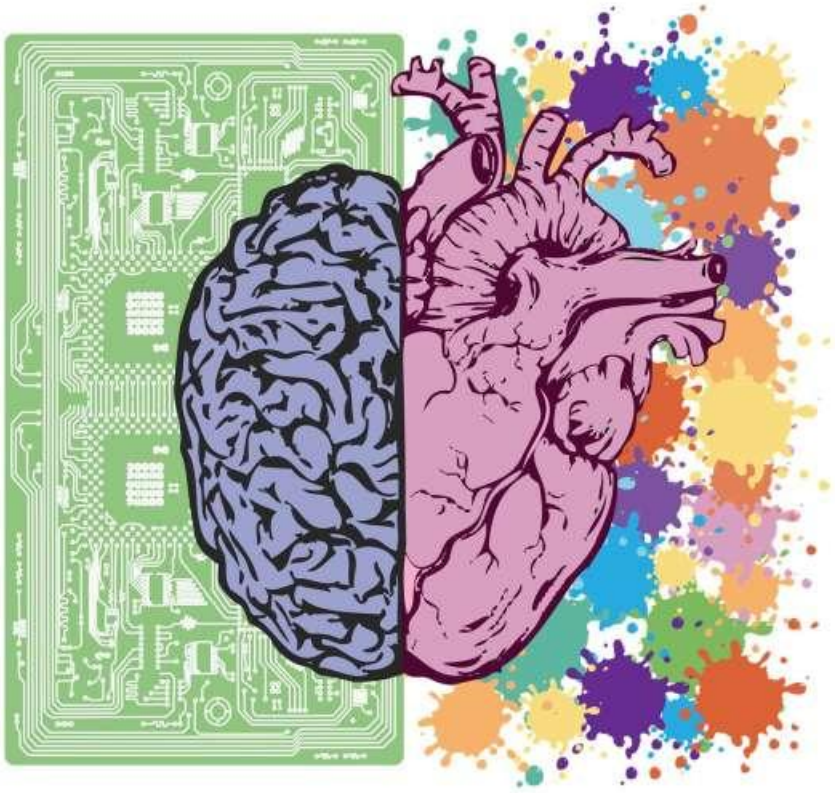
Co-lead Dr. Sophie Adler from UCL said, "This type of research is only possible with international collaboration. We were privileged to work with 75 researchers and clinicians towards this common goal of 'no missed epilepsy lesions worldwide'".

More information: *JAMA Neurology* (2025). DOI: 10.1001/jamaneurol.2024.5406
Journal information: Archives of Neurology
Provided by King's College London

FEBRUARY 24, 202

New research unpacks the complex brain–heart relationship

by University of Melbourne



Credit: Pixabay/CC0 Public Domain

New research led by the University of Melbourne is helping to shed light on the aging process of the heart and how age-related changes in the cardiovascular system impact brain networks.

While it is commonly understood that the brain and heart are interconnected and both are affected by aging, this study uniquely mapped age-related changes using advanced imaging techniques to uncover how these systems interact over a lifespan.

The study involved data from almost 3,000 healthy adults aged between 46 and 80.

Diseases often impact both the brain and heart simultaneously, as the brain regulates heart activity, while the heart supplies the brain with blood and oxygen. But it is not yet known why cardiovascular disease and neurodegeneration co-occur.

The research, published in the *Journal of Neuroscience*, offers new insights into this relationship and highlights poor cardiovascular health as a risk factor for brain-related diseases.

"The inference of our research to the everyday person suggests that cardiovascular exercise may reduce both the risk of heart disease and neurodegenerative diseases, which include dementia, Parkinson's, motor neuron diseases, and other less common diseases that can often overlap," Professor Andrew Zalesky, Department of Psychiatry in the Faculty of Medicine, Dentistry and Health Sciences and the Department of Biomedical Engineering, Faculty of Engineering and Information Technology, said.

Using multiorgan imaging technology and advanced analyses, the team has identified which specific areas of the brain are affected as the cardiovascular system ages.

These areas are involved in specific brain networks, namely the salience, default mode, and somatomotor networks, which play key roles in regulating the autonomic nervous system and heart function.

It is hoped this research could inform clinical interventions and treatments in the future.

"Our findings suggest more effective strategies to predict, manage, and prevent both cardiovascular and brain-related diseases in the aging process," Ph.D. candidate Yalda Amirmoezzi said.

More information: Yalda Amirmoezzi et al, Characterizing Brain–Cardiovascular Aging Using Multiorgan Imaging and Machine Learning, *The Journal of Neuroscience* (2024). DOI: 10.1523/JNEUROSCI.1440-24.2024 , www.jneurosci.org/content/45/8/e1440242024
Journal information: Journal of Neuroscience
Provided by University of Melbourne

FEBRUARY 24, 2025

'Empathic disequilibrium' concept helps explain social characteristics of neurological conditions

by Ben-Gurion University of the Negev

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Ben-Gurion University of the Negev's psychology researcher Prof. Florina Uzefovsky has developed a new concept she terms empathic disequilibrium, which she finds better explains social characteristics in a range of clinical conditions such as autism, schizophrenia and more.

Empathic disequilibrium is the imbalance between cognitive and emotional aspects of empathy. Cognitive empathy (CE) is the ability to understand the emotions of others, whereas emotional empathy (EE) is the tendency to resonate with and respond to the emotional experience of others with matching and appropriate emotions.

While the concepts of cognitive and emotional empathy are not new, Uzefovsky found that they failed to explain symptoms as effectively as an imbalance in the two did.

Prof. Uzefovsky has successfully applied empathic disequilibrium to aspects of autism, anxiety, psychopathic traits, and, most recently, to schizophrenia.

Her findings about schizophrenia were published in the *Journal of Psychiatric Research*.

Her findings about autism have also been published in the journals *Molecular Autism*, *Autism Research*, and *Autism in Adulthood*.

Empathic disequilibrium predicted schizophrenia better than empathy alone, she and her fellow researchers from Harvard and Yale Universities found.

"I invite and encourage my fellow researchers and practitioners to utilize empathic disequilibrium in their work as a powerful diagnostic and potential treatment tool," says Prof. Uzefovsky.

More information: Ido Shalev et al, Empathic disequilibrium in schizophrenia: An individual participant data meta-analysis, *Journal of Psychiatric Research* (2024). DOI: 10.1016/j.jpsychires.2024.11.045
Journal information: Molecular Autism , Journal of Psychiatric Research , Autism Research
Provided by Ben-Gurion University of the Negev

FEBRUARY 27, 2025

Scientists discover key protein in resilience to stress

by Laval University

When faced with chronic stress, why do some people develop anxiety and depressive symptoms while others show resilience? A protein that acts as a cannabinoid receptor and is present in the structure controlling exchanges between the bloodstream and the brain could be part of the answer, according to a study published in *Nature Neuroscience*.

"The protein, called cannabinoid receptor type 1 (CB1), is part of the blood-brain barrier, the dynamic structure that protects the brain by regulating the passage of molecules between the bloodstream and the brain," explains study leader Caroline Ménard, a professor at Université Laval's Faculty of Medicine and researcher at the CERVO Brain Research Center.

"In the context of chronic social stress, the integrity of this barrier is altered, inflammatory molecules make their way into the brain, and anxiety and depressive symptoms appear."

CB1 receptors are abundant in neurons, but they're also found in astrocytes, star-shaped cells allowing communication between the brain's blood vessels and neurons.

"Astrocytes are an essential component of the barrier," explains Prof. Ménard. "We noticed that mice resilient to stress had more CB1 receptors in the barrier than mice with depressive-like behavior or mice not exposed to stress. That gave us the idea to investigate the role of astrocytic CB1 receptors in the response to chronic stress."

The research team first induced an increase in CB1 receptor abundance in mouse astrocytes by developing a viral vector that contained the genetic material coding for the CB1 receptor as well as a mechanism that limited its expression only to astrocytes. When injected, this virus increased the levels of CB1 receptors in the mice's astrocytes but not in their neurons.

These mice were then subjected to chronic social stress. "Each day, for five minutes, they were brought into direct contact with a dominant male. The rest of the time, a transparent divider was placed in the cage. The mice could see their bully without any physical interaction, so it was essentially a psychosocial stress," says Ménard.

Three weeks after the injections, the level of CB1 receptors had more than doubled in the astrocytes of mice in the experimental group.

"In these mice, baseline anxiety levels—those observed in the absence of stress—were reduced, as were symptoms of anxiety and depression-like behaviors induced by social stress. Overexpression of CB1 receptors leads to resilience by promoting vascular health in the brain," summarizes the researcher.

Other experiments carried out by her team showed that mice that had access to an exercise wheel or those given antidepressants also had higher levels of CB1 receptors in their astrocytes.

In addition, examination of human brains from the Douglas-Bell Canada Brain Bank in Montreal confirmed the association between CB1 receptors and depressive symptoms.

"We found that the level of CB1 receptors in astrocytes was lower in people with major depression at the time of death than in people without depression or those treated with antidepressants," says Ménard.

These results suggest the possibility of using molecules capable of activating CB1 receptors in astrocytes to reduce anxiety and depressive symptoms, and to increase resilience in the face of stress, the researcher suggests.

"The challenge, however, is to limit their effects to astrocytes, because strong and prolonged activation of the same receptors in neurons can have side effects, notably on alertness, anxiety and appetite. Until we find a molecule that acts specifically on CB1 receptors in astrocytes, we can mitigate the negative repercussions of stress by taking advantage of the protective effect of physical activity."

More information: Astrocytic cannabinoid receptor 1 promotes resilience by dampening stress-induced blood–brain barrier alterations, *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01891-9
Journal information: Nature Neuroscience
Provided by Laval University

FEBRUARY 27, 2025

Why does music evoke emotions?

by Katrina McFerran, The Conversation

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Imagine a scene from the movie Jaws, with the great white shark closing in on another helpless victim. The iconic semi-tone pattern builds and your heartbeat rises with it; the suspense pulls you further to the edge of your seat.

Now picture that scene without the score. Much of the tension evaporates.

Maybe it's a heartfelt pop ballad or a suspenseful soundtrack. If you are my age, it might be the Friends theme song, forever associated with the (largely unfulfilled) hope for sharing apartments with mates and growing old together in a blissful acceptance of one another's limitations. Music is a powerful force to induce and pre-empt all kinds of emotions in us.

But how do so many different combinations of rhythm, harmony and melody trigger such profound reactions?

The categorical approach

Swedish music psychology researcher Patrik Juslin proposed the most popular explanation of music's ability to trigger emotion.

He identified eight key mechanisms under the acronym BRECVEMA. The categories begin with more fundamental connections:

Brain stem reflexes—maybe a movie jumpscare moment or another sudden, frightening sound triggering a pre-conscious response. Evolution programmed these reactions into the brain over thousands of years in order to influence arousal levels and initiate the necessary emotional response.

Rhythmic entrainment, like the tendency to tap your foot to the beat; the benefits of moving in time together have been critical to human survival and evolution.

Then, the listings become increasingly complex:

Evaluative conditioning in the fashion of Pavlov's dog. After years of watching and cultural references, we hear the Jaws music and automatically feel tense.

The **contagion effect**, wherein we feel the emotions we perceive in the music. Lyrics aren't necessary; the Peanuts cartoon's signature tune, for example, strongly conveys childhood wonder and freedom without any words.

The **visual imagery** many people experience when listening to music, imagery which is often tied to some deep emotion.

Episodic memories, when hearing certain music brings up recollections of a past event. Music therapists can monitor the emotional reactions people have when unexpectedly reminded of particular situations, be they positive, negative or both. The therapists then use their expertise to support people in processing these resulting emotions.

From there, Juslin's model gets more technical and music theory-based:

Musical expectancy, when we anticipate the resolution of a chord or phrase. This is something you might feel rather than consciously notice. Take "My Heart Will Go On": a delicate tension builds through the chorus, before finally resolving as Celine Dion sings the final line of the section and listeners are put to ease.

Aesthetic judgements, closely related to the ways we experience pleasure, are our personal emotional responses to how beautiful (or not) we consider a piece of music.

It makes sense that a theory using the brain to explain otherwise indescribable relationships would be popular. It provides a level of objectivity to what is, in essence, a purely subjective and non-generalisable experience.

Is it just about neurological pathways?

Evolutionary theories suggest music and emotions are connected because of the inherent musicality we are each born with, essential to our ability to develop relationships and flourish.

Parent-infant interactions often have musical aspects to them, described as:

- **pulse**, a shared tempo, where infant and caregiver move in time together and synchronize to one underlying beat
- **quality**, the character and melodic interplay of voices and movements, mirroring one another in dynamics and timbre
- **narrative**, the tendency for the same phrases, gestures and movements to be repeated on the same pitch and pace over time.

When responding to musical sounds, babies are also able to recognize musical phrases even when they start on a different note.

Subsequently, however, other learning and our limited brain capacity mean this ability is buried deep, so it rarely translates to perfect pitch or other forms of music theory knowledge that underpin Mozart-like genius.

This baby-talk theory may be the most intimate and emotion-based explanation for why music affects us so strongly—it was designed to enhance our emotional bonds with others. When adults coo and dance with babies, they are being musical, meaning emotional reactions to music are implicit in human nature.

Cognitive developmental theorists like Steven Pinker have opinions firmly in contrast to this. Pinker calls music "evolutionary cheesecake," functioning only to tickle the senses and serving no evolutionary purpose.

Pleasure for purpose

Cultures across the world have long acknowledged the healing power of music.

Sound healing practitioners in India and China, for example, point to ancient traditions of healing and draw correlations between recovery from illness and certain tones, scales and chants. Some suggest the vibrations of different tones can serve specific purposes.

In the West, the idea of emotional differences between major and minor scales still has public traction even though its academic credibility hasn't really extended in the past 100 years.

None of these concepts have been used in the modern practice of music therapy, but they do reflect assumptions many people hold about how music works.

Instead, a fundamental principle of music therapy is based on how each person's unique connections with music shapes their emotional reactions. What moves your sibling to tears might leave you cold, for example. It always depends on a range of conditions—historical, cultural and personal.

Cultural upbringing, simple song-like phrases from infancy and our own unique musical preferences and behaviors all shape these connections. They're powerful, but they sure ain't simple.

Provided by The Conversation
FEBRUARY 27, 2025

What's the difference between burnout and depression?

by Gordon Parker, The Conversation

If your summer holiday already feels like a distant memory, you're not alone. Burnout—a state of emotional, physical and mental exhaustion following prolonged stress—has been described in workplaces since a 5th century monastery in Egypt.

Burnout and depression can look similar and are relatively common conditions. It's estimated that 30% of the Australian workforce is feeling some level of burnout, while almost 20% of Australians are diagnosed with depression at some point in their lives.

So what's the difference between burnout and depression?

Depression is marked by helplessness and burnout by hopelessness. They can have different causes and should also be managed differently.

What is burnout?

The World Health Organization defines burnout as an "occupational phenomenon" resulting from excessively demanding workload pressures. While it is typically associated with the workplace, caregivers of children or elderly parents with demanding needs are also at risk.

Our research created a set of burnout symptoms we captured in the Sydney Burnout Measure to assist self-diagnosis and clinicians undertaking assessments. They include:

- exhaustion as the primary symptom
- brain fog (poor concentration and memory)
- difficulty finding pleasure in anything
- social withdrawal
- an unsettled mood (feeling anxious and irritable)
- impaired work performance (this may be result of other symptoms such as fatigue).

People can develop a "burning out" phase after intense work demands over only a week or two. A "burnout" stage usually follows years of unrelenting work pressure.

What is depression?

A depressive episode involves a drop in self-worth, increase in self-criticism and feelings of wanting to give up. Not everyone with these symptoms will have clinical depression, which requires a diagnosis and has an additional set of symptoms.

Clinically diagnosed depression can vary by mood, how long it lasts and whether it comes back. There are two types of clinical depression:

1. melancholic depression has genetic causes, with episodes largely coming "out of the blue"
2. non-melancholic depression is caused by environmental factors, often triggered by significant life events which cause a drop in self-worth.

When we created our burnout measure, we compared burnout symptoms with these two types of depression.

Burnout shares some features with melancholic depression, but they tend to be general symptoms, such as feeling a loss of pleasure, energy and concentration skills.

We found there were more similarities between burnout and non-melancholic (environmental) depression. This included a lack of motivation and difficulties sleeping or being cheered up, perhaps reflecting the fact both have environmental causes.

Looking for the root cause

The differences between burnout and depression become clearer when we look at why they happen.

Personality comes into play. Our work suggests a trait like perfectionism puts people at a much higher risk of burnout. But they may be less likely to become depressed as they tend to avoid stressful events and keep things under control.

Those with burnout generally feel overwhelmed by demands or deadlines they can't meet, creating a sense of helplessness.

On the other hand, those with depression report lowered self-esteem. So, rather than helpless, they feel that they and their future are hopeless.

However, it is not uncommon for someone to experience both burnout and depression at once. For example, a boss may place excessive work demands on an employee, putting them at risk of burnout. At the same time, the employer may also humiliate that employee and contribute to an episode of non-melancholic depression.

What can you do?

A principal strategy in managing burnout is identifying the contributing stressors. For many people, this is the workplace. Taking a break, even a short one, or scheduling some time off can help.

Australians now have the right to disconnect, meaning they don't have to answer work phone calls or emails after hours. Setting boundaries can help separate home and work life.

Burnout can also be caused by compromised work roles, work insecurity or inequity. More broadly, a dictatorial organizational structure can make employees feel devalued. In the workplace, environmental factors, such as excessive noise, can be a contributor. Addressing these factors can help prevent burnout.

As for managing symptoms, the monks had the right idea. Strenuous exercise, meditation and mindfulness are effective ways to deal with everyday stress.

Deeper contributing factors, including traits such as perfectionism, should be managed by a skilled clinical psychologist.

For melancholic depression, clinicians will often recommend antidepressant medication.

For non-melancholic depression, clinicians will help address and manage triggers that are the root cause. Others will benefit from antidepressants or formal psychotherapy.

While misdiagnosis between depression and burnout can occur, burnout can mimic other medical conditions such as anemia or hypothyroidism.

For the right diagnosis, it's best to speak to your doctor or clinician, who should seek to obtain a sense of "the whole picture." Only then, once a burnout diagnosis has been affirmed and other possible causes ruled out, should effective support strategies be put in place.

Provided by The Conversation

FEBRUARY 27, 2025

Study finds pursuit of happiness drains self-control, increases unhappiness

by University of Toronto

Credit: Unsplash/CC0 Public Domain
Researchers have a new explanation for why we experience the "happiness paradox"—a phenomenon wherein trying to make ourselves happier actually makes us less happy.

Studies have documented the paradox for more than a decade, yet few have dug into what causes it. It turns out, according to new U of T Scarborough research published in the journal *Applied Psychology: Health and Well-Being*, trying to be happier is mentally exhausting in a way that drains our ability to use self-control and willpower. As a result, we're more susceptible to temptation, and to making the kind of self-destructive decisions that make us less happy.

"The pursuit of happiness is a bit like a snowball effect. You decide to try making yourself feel happier, but then that effort depletes your ability to do the kinds of things that make you happier," says study co-author Sam Maglio, professor of marketing in the Department of Management at U of T Scarborough and the Rotman School of Management.

Maglio likens the fallout of constantly trying to be happier to coming home after a long day at work—the more mentally rundown we are, the more tempted we'll be to skip cleaning the house and instead scroll social media, for example. Maglio and study co-author Aekyoung Kim, lecturer in the Business School at the University of Sydney, also tackled the paradox in a 2018 study that found people who try to be happier tend to feel like they're short on time, the stress of which makes them unhappier.

"The story here is that the pursuit of happiness costs mental resources. Instead of just going with the flow, you are trying to make yourself feel differently," says Maglio.

Manually regulating our thoughts, emotions and behaviors is particularly exhausting, the researchers note, and in the multi-million-dollar self-help industry, there's a lot of pressure and responsibility placed on the self. Happiness is particularly exhausting when people view it in the same vein as money, as though it's inherently something we can and should gather and hoard as much as we can.

Pursuit of happiness puts unique strain on mental resources

Researchers surveyed hundreds of people and found the more they habitually tried to be happier, the less they reported using self-control in their daily lives. Maglio and Kim figured this was because happiness-seeking and self-control must be competing for the same finite source of mental energy.

So, they concluded their next round of surveys by having participants rank lists of objects, since making choices—and completing any mundane task—requires mental resources and self-regulation. As suspected, the more people reported happiness-seeking, the less time they spent on the task.

One experiment used ads with the word "happiness" in them to trigger a phenomenon whereby people try to be happier just by seeing the word. The participants were then given a big bowl of chocolates, told they could eat as many as they like, and asked to rank the taste. Researchers rationalized the more self-control a participant had, the fewer chocolates they'd eat, and found those shown the "happiness prime" ad ate more than their counterparts.

But, Maglio and Kim wondered, had they eaten more because happiness-seeking is ultra exhausting, or would chasing any goal tire them out just as much? For the final study, participants were presented pairs of everyday items; one group was asked to choose the option that would improve their happiness, while the other was told to choose based on their personal preferences. Both groups were then given a mental task that gauged their self-control abilities. The happiness group quit earlier, indicating they had fewer mental resources left after a bout of happiness-seeking.

The pursuit of happiness isn't inherently futile, Maglio clarifies. He recommends we think of happiness more like sand at the beach. You can cling to a fistful of sand and try to control it, but the harder you hold, the more your hand will cramp. Eventually, you'll have to let go.

"Just chill. Don't try to be super happy all the time," says Maglio, whose work is supported by a grant from the Social Sciences and Humanities Research Council of Canada. "Instead of trying to get more stuff you want, look at what you already have and just accept it as something that gives you happiness."

More information: Aekyoung Kim et al, Happiness depletes me: Seeking happiness impairs limited resources and self-regulation, *Applied Psychology: Health and Well-Being* (2025). DOI: 10.1111/aphw.70000
Provided by University of Toronto

FEBRUARY 27, 2025

Going against gut feelings heightens self-blame, research shows

by Holly Hartigan, Cornell University

Credit: Pixabay/CC0 Public Domain

Kaitlin Woolley '12 was leaning toward taking snow pants to an outdoor event, but her husband suggested she leave them home. As she shivered later, she kicked herself—but did not blame her husband. "I felt like I was living out our research," she said.

In a series of experiments, Woolley, professor of marketing and management communications in the Cornell SC Johnson College of Business, and Dr. Sunita Sah, associate professor of management and organizations in the SC Johnson College and faculty fellow at the Cornell Health Policy Center, found that when people go along with opinions that go against their better judgment, they feel more culpable for the decision if things go wrong than if they hadn't received another opinion.

"If you have another person in the decision process, you would think that's going to help spread the responsibility," Woolley said. "And yet not only do people not blame the adviser more, they're blaming themselves more."

Woolley and Sah published their findings in "Kicking Yourself: Going Against Your Inclinations Leads to Greater Feelings of Control and Culpability," which was published in *Personality and Social Psychology Bulletin*.

In a set of five studies, participants chose between two lotteries, one with clearly superior prizes. Some subjects were offered input from an adviser who had no more knowledge about the choices. The adviser recommended the lesser lottery, and in 4 of the 5 studies, participants received the lowest possible prize: 10 cents.

The research included a 200-subject, in-person experiment with physical prizes in the lobby of the Samuel Curtis Johnson Graduate School of Management, and four online studies, with up to 1,200 participants per experiment.

Across all studies, they found that participants' feelings of culpability and the perception that they had control over the situation were greater in the group that received input than in the group that made an independent decision.

The effect may seem counterintuitive, but going against one's better judgment increases thoughts about better decisions that could have been made, which amplify feelings of control over the situation. Participants think about how they could have ignored the advice and enjoyed the better prize—or been warm in the snow pants they left at home.

"This effect could extend beyond small decisions. It can apply to major life choices, like wondering, "What if I had chosen a different career?'" Sah said.

In previous research, Sah, a physician turned organizational psychologist, found that people often followed obviously bad advice. This new research explored the downstream effects of regret, responsibility and blame after following bad advice—at least from an adviser who is not an expert.

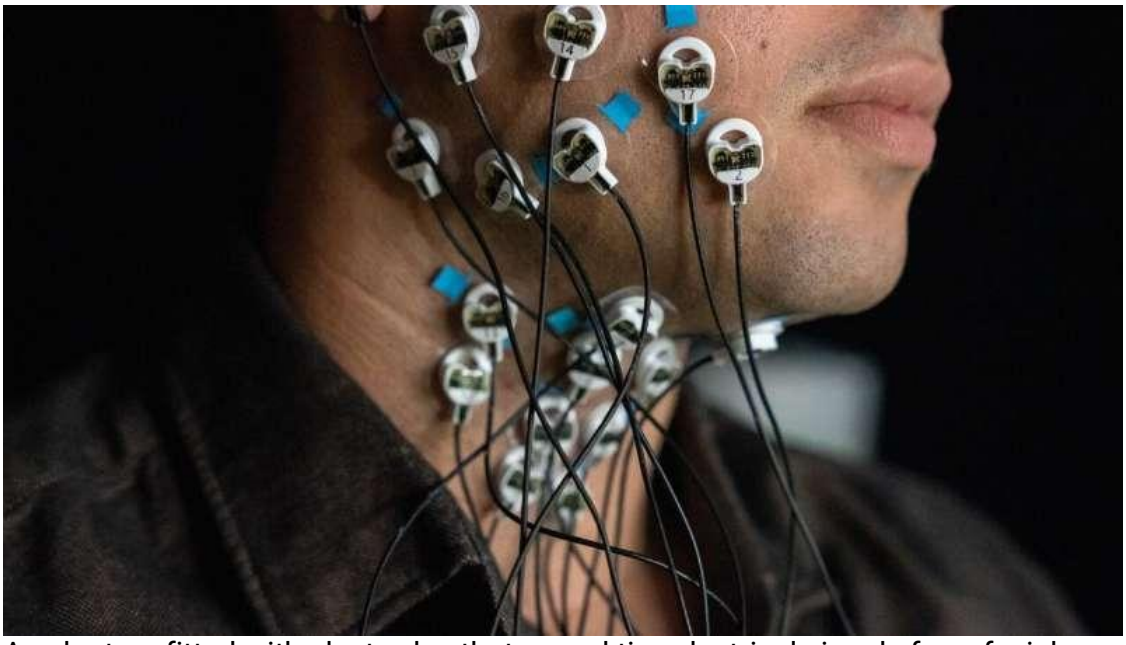
"Our research highlights the importance of rejecting suggestions that go against our better judgments," Sah said. "People often assume that following someone else's suggestion will shield them from responsibility or regret. But in reality, the opposite happens. You end up feeling worse when you ignored what you knew was the better choice."

More information: Kaitlin Woolley et al, Kicking Yourself: Going Against Your Inclinations Leads to Greater Feelings of Control and Culpability, *Personality and Social Psychology Bulletin* (2025). DOI: 10.1177/01461672251319380
Journal information: Personality and Social Psychology Bulletin
Provided by Cornell University

FEBRUARY 27, 2025

Neuroengineering decodes facial and muscle signals, restoring voices and identity

by Douglas Fox, UC Davis



A volunteer fitted with electrodes that record tiny electrical signals from facial muscles during speech. By measuring these signals and comparing them to the sound of someone's voice, Lee Miller and colleagues hope to reconstruct a person's natural speech after they have lost their ability to speak normally. Credit: Sasha Bakhter, UC Davis College of Biological Sciences

Lee Miller vividly recalls the day in 2021 when he met a woman who had lost the function of her vocal cords. In hoarse, whispering tones, she explained how her voice had been instrumental to her vocation. Losing it, she said, undercut her life's purpose. Her words were faint, but the lesson was powerful.

"Our voice is so important to our sense of identity and empowerment," said Miller, a professor of neurobiology, physiology and behavior in the University of California, Davis College of Biological Sciences, a professor of otolaryngology and head and neck surgery at the UC Davis School of Medicine and technical director of the Center for Mind and Brain.

Now, Miller is working to restore original voices to those who have lost them—based partly on adapting technology for interpreting gestures and controlling robotic limbs.

Every year, nearly 1 million people worldwide are diagnosed with head and neck cancer. Many of them lose their ability to speak intelligibly due to surgical removal of—or radiation damage to—the larynx, mouth and tongue. These people can learn to speak again using devices that emit artificial sounds, which they can shape into words. But their new voices are often weak, mechanical or distressingly unfamiliar.

Miller and his collaborators are developing a system that could one day restore a person's unique, original voice.

Decoding the mind

Miller is working on a project to record electromyographic (EMG) signals on a person's skin, generated by the muscle contractions created by reaching out or clenching a fist, and decode them into digital instructions that can be used to control a robotic arm. Doing this might one day allow astronauts to repair equipment outside a space station without undertaking a potentially risky spacewalk.

In a 2024 study published in the *Journal of Neural Engineering*, Miller worked with the company Meta to use EMG signals to recognize and interpret a person's gestures so they can interact with computers using natural body language—rather than a mouse and keyboard.

The difficulty is that EMG signals often vary from person to person, depending on their age, skin characteristics, body weight and other factors. These biological signals also produce mountains of data per second—which computers will need to be able to quickly process.

"We have only a limited amount of time," said Miller, "perhaps only 50 milliseconds, before the computer causes a delay, which would make real-time interpretations impossible."

Miller and graduate student Harsha Gowda (in the Electrical and Computer Engineering Graduate Group), solved this by using only tiny bits of the incoming signals while ignoring everything else. Rather than tracing the chaotic ups and downs of each EMG electrode on a person's arm, Gowda employed a strategy that simply measures signal relationships among various pairs of electrodes.

These simplified signal representations turn out to be "very well-behaved," and don't vary from one person to another, Miller said. "So now we have a gesture decoder that works for everybody."

Miller became interested in applying these lessons to speech during a visit in 2021 with Peter Belafsky, professor of otolaryngology at the School of Medicine and director of the UC Davis Center for Voice and Swallowing. It was at Belafsky's clinic that he met the woman whose voice had been part of her vocation and others who had lost their voices. Hearing their stories "was profoundly motivating," said Miller.

Miller embarked on the Silent Speech project in 2022, collaborating with Belafsky, Sergey Stavisky, assistant professor of neurological surgery, and David Brandman, a professor of neurosurgery at the School of Medicine.

Miller and Gowda began the project by working with healthy volunteers, using EMG electrodes to record the movements of their mouth and face muscles during speech. Then, they used the simplified EMG signals with simultaneously recorded speech to train a computer to match different EMG patterns with different speech sounds for each person. The result is tailored, computer-generated speech that is created using the unique tones of the person's voice.

"We don't need that much data to clone the person's voice," said Miller. In his experience, it requires only about five minutes of speech combined with that person's EMG signals.

Miller and colleagues are now trying to use this system to restore the voices of people who no longer have functional larynxes. For those individuals, it is no longer possible to record natural voices, so Miller and his colleagues try to stitch together meaningful samples from other sources like family videos. One patient had recorded an audio diary to capture a record of his voice in the weeks before his larynx was surgically removed.

"It was a very personal choice that he made, preserving a memento of his voice that he knew he was about to lose," said Miller. "It was very special that he shared those recordings with us." They turned out to be a perfect trove of raw material for digitally recreating his voice.

Miller's team is now pairing those recordings with EMG and video of the man's face, which they recorded as he spoke the same words silently, without his larynx. Here is an example of restored "silent speech" from an individual who no longer has a voice due to laryngectomy.

Miller envisions that this system might one day run on a smartphone. The person would move their mouth to speak silently into their phone as though doing a video call. The phone would simultaneously record EMG signals and video of their face—combining these with a sample of the person's voice to create natural-sounding speech.

Engineering this system so that it works outside of the laboratory for a wide array of people could take several years, said Miller. Even so, "Ultimately, we want this to work easily for anybody."

More information: Harshavardhana T Gowda et al, Topology of surface electromyogram signals: hand gesture decoding on Riemannian manifolds, *Journal of Neural Engineering* (2024). DOI: 10.1088/1741-2552/ad5107
Journal information: Journal of Neural Engineering
Provided by UC Davis

MARCH 3, 2025

Wearable tech has far to go before challenging smartphones

by Mona GUICHARD

Ray-Ban and Meta's connected glasses saw success in 2024.

Wearable gadgets like smart watches and glasses are growing more capable every year, but experts say smartphones will remain ubiquitous for the foreseeable future—not least thanks to artificial intelligence features.

A slew of wearable products and prototypes were on show at the Mobile World Congress in Barcelona Monday, even as smartphone makers and network operators played up AI integration as making handsets more useful.

Such "new product ranges allow manufacturers to diversify the hopes until now placed in phones" said Cesar Corcoles, an IT and telecoms professor at the Open University of Catalonia.

The trade show in Barcelona will see "prototypes and demonstrations of smart glasses that place a small, very limited screen in front of our eyes."

Smart glasses have seemed on the horizon for more than a decade, with Google's Glass headset and camera released in 2013—although it has since been discontinued.

Meta has encountered more success recently with its frames developed alongside Ray-Ban, offering features including a built-in camera, music playback and voice interactions with the company's AI.

Yann LeCun, star AI researcher at the company which owns Facebook and Instagram, is often seen showing off the glasses at public appearances.

Worldwide, the market for smart glasses appears to be surging in terms of unit sales, with a 210-percent year-on-year increase in 2024 according to specialist research firm Counterpoint—far faster than the seven-percent growth in smartphone shipments calculated by analysts Canalys.

'Cool gimmick' for now

But comparing the number of devices rather than growth rates, last year's roughly two million pairs of smart glasses barely register compared to the 1.2 billion smartphones sold.

Counterpoint predicts the glasses market will grow further in the coming years as more producers—from social media giants to smartphone makers—look to claim a piece of the action.

Other wearable categories may need longer to take off, with the recent shutdown of "AI Pin" maker Humane a sign some wearable tech is not yet mature.

Designed to be worn at chest level like a brooch, the would-be smartphone replacement incorporating a camera and mini projector was designed to be used via AI-powered voice interactions but received poor reviews.

Humane has now been sold to HP after the device failed to make the hoped-for impact.

The "AI Pin" was "just not that useful yet", Canalys expert Jack Leathem said.

Voice-controlled devices are "a cool gimmick, but humans have become very, very used to text-based interactions on touchscreens," he added—habits it would take a powerful sales pitch to change.

"The most challenging thing is getting people to change their behavior," agreed Shen Ye of smartphone maker HTC's Vive wearables arm.

"We still use a QWERTY keyboard because it's what we're used to... even though there are probably much better ways of typing," he added.

AI on your phone

Beyond consumer inertia, wearable tech is still up against engineering challenges stemming from its bid to squeeze smartphone-like functionality into a smaller package.

"There are limits around the computing power currently and battery performance," Leathem said. "You can't make them that compact."

That's one reason why smart watches able to make calls and send messages largely remain tethered to wearers' smartphones for now.

"Every smart watch that comes out now is there to interact with a smartphone, not to replace it. It's an accessory," Leathem said.

What's more, manufacturers are incentivized to get consumers buying a wider range of gadgets rather than simply swapping one for another.

And even as wearables become more useful, AI is expected to pump more value into smartphones themselves.

The latest offerings from Apple, Samsung or China's Xiaomi have bet on offering users integrated "AI assistant" features.

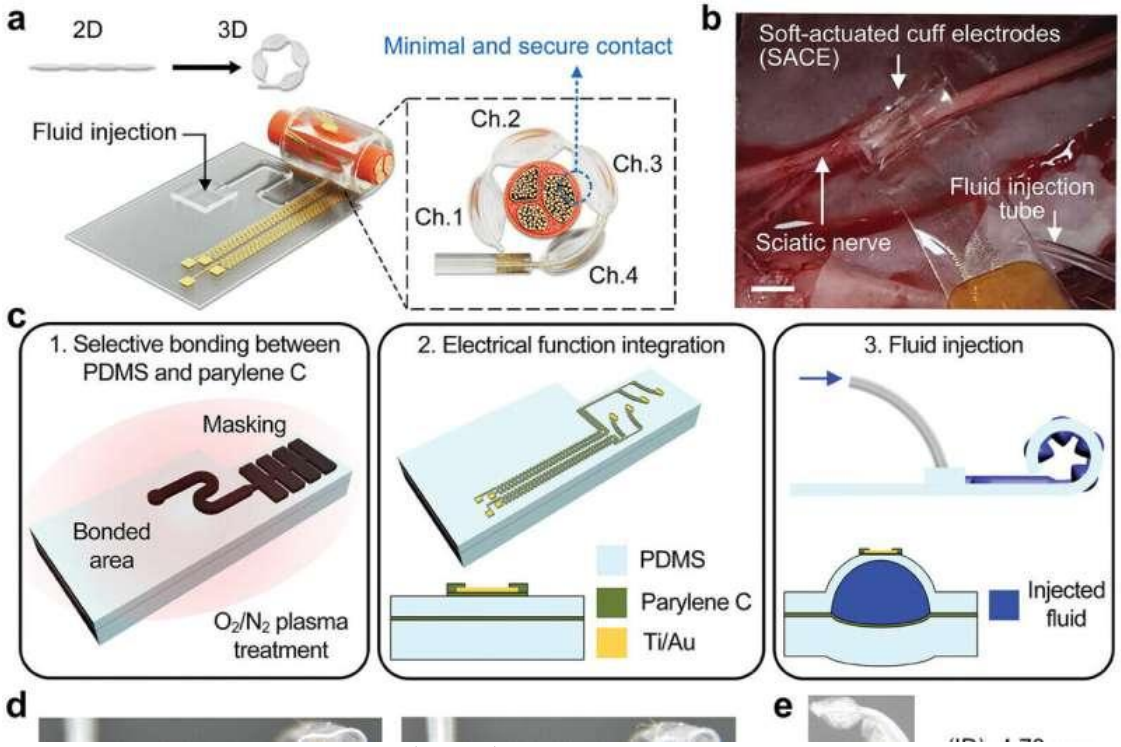
"All the money is going into AI... their vision of the future is keeping the same smartphone form factor, but making it way more useful," Leathem said.

Canalys predicts that the share of smartphones sold worldwide with AI features will leap from 16 percent at present to more than half by 2028.

MARCH 3, 2025

3D smart neural electrode uses soft actuation technology to avoid nerve damage

by Daegu Gyeongbuk Institute of Science and Technology



Soft-actuated cuff electrodes (SACE) to communicate with nerves. Credit: *Advanced Materials* (2024). DOI: 10.1002/adma.202409942

A research team has developed an electrode capable of safely encasing nerves without causing damage. The newly developed electrode features soft actuation technology that allows it to transform from a flat two-dimensional shape into a three-dimensional structure. This advance is expected to enable the emergence of various next-generation soft bioelectronic devices, including electroceuticals suitable for peripheral nerve treatment. The team was led by Professor Sohee Kim of the Department of Robotics and Mechatronics Engineering.

The paper is published in the journal *Advanced Materials*.

Neural electrodes are devices that measure the electrical signals traveling through nerves. Alternatively, they stimulate nerves by transmitting small electrical currents. These

electrodes are used to assist patients with nerve damage in regaining movement. They can also stimulate specific nerves to alleviate pain. However, without adequate contact between the nerve and the electrode, accurately measuring neural signals and effectively delivering the intended stimulation becomes difficult.

Conventional cuff electrodes wrap around the nerve securely. However, because nerves are smooth, wire-like structures, cuff electrodes tend to slip or rotate. To prevent this, the electrodes must be tightly fastened, which can compress the nerve, reducing blood flow and potentially causing nerve damage.

Due to these challenges, traditional methods struggle to securely encircle and affix on nerves. Consequently, in the absence of excessive compression, there is no way to maintain contact with the electrode. This impediment necessitated a new approach to ensure that electrodes would adhere stably without damaging the nerve.

To address these challenges, the research team developed a soft-actuated cuff electrode that allows the electrode to bend autonomously and wrap around the nerve. The novel electrode softly conforms to the nerve, allowing it to be securely fixed without the need for sutures.

Unlike conventional electrodes, this design maintains firm adhesion without requiring excessive tightening around nerves, which makes it safer for long-term use. Noteworthily, the research team incorporated a three-dimensional convex structure that reduces the direct contact area with the nerve while enhancing adhesion, thereby enabling clearer neural signal detection without the risk of nerve damage.

The research team conducted long-term experiments to test the performance of this electrode when used on peripheral nerves and confirmed that it allows accurate neural signal measurement without causing damage. Furthermore, the electrode can selectively stimulate targeted nerves. Additionally, the three-dimensional structure plays a key role in ensuring strong adhesion while minimizing pressure, thereby preventing any harm to the nerve tissue or its function.

Professor Kim stated, "This study introduces a new concept of cuff-shaped electrodes that wrap around nerves, including peripheral and vagus nerves. With its ability to provide high-quality neural signal monitoring over the long term and enable minimal-current stimulation, this technology is expected to be widely utilized in various bioelectronic devices, such as implantable electroceuticals."

Professor Kim is the corresponding author of the article reporting the results of this study, and Dr. Hyunmin Moon, a postdoctoral researcher at the Massachusetts Institute of Technology, is the first author. Additional contributions were made by Namsun Chou, a senior researcher at the Korea Brain Research Institute, and Professor Ki-Su Park of the Department of Neurosurgery at Kyungpook National University Hospital.

More information: Hyunmin Moon et al, Soft-Actuated Cuff Electrodes with Minimal Contact for Bidirectional Peripheral Interfaces, *Advanced Materials* (2024). DOI: 10.1002/adma.202409942
Journal information: Advanced Materials
Provided by Daegu Gyeongbuk Institute of Science and Technology

MARCH 3, 2025

Alcohol use leads to earlier brain aging and impaired behavioral flexibility, even in early adulthood

by Research Society on Alcoholism

\Alcohol use leads to earlier brain aging and impaired behavioral flexibility, with those effects detectable even among adults in their 20s and 30s, according to an innovative study.

Hazardous drinking is known to be linked to cognitive-behavioral impairments, including difficulty adapting to changing circumstances. This helps explain, for example, why people with alcohol-use disorder (AUD) continue to drink despite negative consequences. Evidence is growing that heavy alcohol use accelerates brain aging. It is not known, however, whether this aging effect explains the link between alcohol use and certain cognitive deficits typical of older brains.

For the study published in *Alcohol: Clinical and Experimental Research*, investigators explored whether hazardous drinking predicted brain aging as measured by a machine learning tool and whether brain aging explained the association between alcohol use and behavioral inflexibility.

Researchers from the University of North Carolina at Chapel Hill worked with 58 people aged 22–40 (35 were women), many of whom had started drinking in adolescence. The participants filled out questionnaires on their alcohol use. They also underwent task training that required them to adjust their responses as the task evolved. All participants had an MRI scan, and a machine-learning program was used to evaluate 3D structural brain images to estimate their brain age.

Researchers calculated the difference between estimated brain age and actual chronological age ("brain-PAD"). They used statistical analysis to explore the associations

between alcohol use, brain-PAD, and perseverative errors on the task test and to assess the role of brain aging on behavioral inflexibility linked to drinking.

The participants mostly reported light to moderate alcohol use and minimal use of other substances. Their brain aging results ranged from somewhat delayed to substantially accelerated, with some acceleration on average. Higher alcohol use scores predicted more accelerated brain aging. While the alcohol use scores did not directly affect perseverative errors on the behavioral inflexibility test, increases in accelerated brain aging scores did.

The findings showed that increasingly hazardous drinking strongly predicted more accelerated brain aging and implied that this mechanism accounted for at least part of the reduction in behavioral flexibility. This is the first study to show machine learning-predicted measures of brain aging linked to a task-based measure of behavioral inflexibility, with evidence that brain aging may be a causal mechanism between alcohol use and those cognitive deficits.

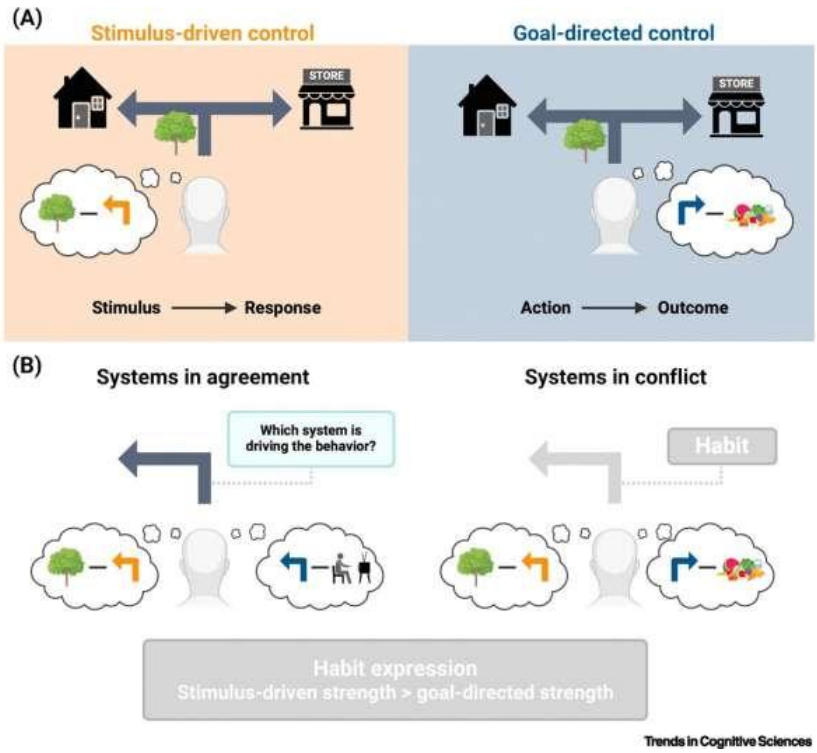
The results suggest that even a small amount of alcohol may age the brain, with effects detectable in early-to-middle adulthood, earlier than had been presumed. Further research is needed using larger samples and to explore the effects of early drinking, education, and other factors that influence cognitive decline.

More information: Jillian T. Battista et al, Greater alcohol intake predicts accelerated brain aging in humans, which mediates the relationship between alcohol intake and behavioral inflexibility, *Alcohol, Clinical and Experimental Research* (2025). DOI: 10.1111/acer.15534
Provided by Research Society on Alcoholism

MARCH 3, 2025

Five essential strategies to master your habits

by Eike Buabang, The Conversation



Credit: *Trends in Cognitive Sciences* (2024). DOI: 10.1016/j.tics.2024.10.006

We often set ambitious goals, such as going to the gym, adopting healthier eating habits, or reducing our social media use. However, despite our best intentions, staying committed can often feel like an uphill battle.

A review of evidence published in 2024 highlights why. While understanding the benefits of behavior change and believing in its value are important, these play only minor roles. The strongest determinant of our ability to shift how we act everyday is our habits.

As the 19th- and 20th-century philosopher William James put it, we are essentially "bundles of habits." He believed that these habits could hold people back from achieving their full potential. If he were around today, he would probably be concerned at the way some people mindlessly check their phones every five minutes.

In a recent academic review, my colleagues and I at Trinity College Dublin illustrated that habits are governed by a delicate balance between two distinct brain systems. One system drives automatic responses to familiar cues in the environment, while the other enables the control of behavior directed towards goals.

This interplay helps explain why we might mindlessly scroll through social media when bored, yet still retain the ability to deliberately put our phones away to focus on work. We reviewed decades of research from laboratory studies and real world settings for the study. Here, we share five practical strategies to help you build positive habits and break negative ones.

1. Forget the 21-day myth

Forget the 21-day rule—there is no magic number. This rule refers to a popular perception that it takes 21 days to form a new habit. Habit formation is different for every person.

In one study, habit formation such as having a piece of fruit with lunch was estimated to take 66 days on average, but it varied widely between individuals, from 18 days to 254 days.

It also depends on the specific habit itself. A study demonstrated this using a subset of AI called machine learning. The study analyzed more than 12 million gym visits and 40 million instances of hospital handwashing to understand how habits form.

The research found that forming a gym habit typically takes months, while hospital staff can develop a handwashing habit in just weeks. No matter how long it takes, the key is sticking with it, even if you miss a day here and there.

2. Make rewards your ally

Your brain learns to repeat behavior that is rewarding. One study examining people's intake of water throughout the day found that it was more of a habit for people who perceived it as more rewarding.

The habit loop can also be reinforced through external rewards, such as treating yourself to something enjoyable after completing a workout.

Rewards are also important for breaking habits. If scrolling through social media becomes a way to unwind, try replacing it with an alternative activity that provides a similar sense of relaxation and enjoyment.

By substituting a positive behavior, you not only avoid feeling deprived but also create a competing response to the old habit, making it easier to break the cycle.

3. Stack your habits

The brain has a natural tendency to combine different actions and respond to contextual cues—the kind that help people understand their surroundings. A strategy called habit stacking takes advantage of this by linking a desired behavior to something you already do.

For example, research on flossing found that people who flossed immediately after brushing their teeth were more likely to establish a lasting habit. The existing cue—brushing your teeth—serves as a reminder, making the new habit—flossing—feel like a natural part of your routine.

So, if you want to start meditating, pair it with your morning coffee. Sip your coffee, then meditate for five minutes. Over time, the two types of behavior become intertwined, making it easier to stick with your goals.

4. Watch out for stress

When life gets overwhelming, many of us find ourselves falling back into old habits, even ones we thought we had moved past. Acute and chronic stress can shift the balance away from controlled goal-directed behavior towards the automatic response system in the brain.

A functional magnetic resonance imaging (fMRI) study revealed that prolonged stress in humans leads to an over-reliance on the brain's circuits that drive habits, while suppressing the prefrontal cortex, which governs deliberate decision-making.

The good news? These effects are reversible. After a six-week stress-free period, participants returned to goal-directed behavior, and their brain activity normalized.

5. Plan for weak moments

We like to set new ambitious goals when we feel motivated. Motivational changes are often initiated based around time, such as the start of a new year, a phenomenon known as the "fresh start effect." But it is important to be strategic and prepare for situations when motivation is low and we still want to work towards our goals.

A powerful strategy for overcoming these weak moments is to plan ahead for specific situations by saying, "If I find myself reaching for a snack when I'm stressed, then I will take a five-minute walk instead." This strategy is generally referred to as "if-then" plans.

This approach helps to preemptively trigger a healthier response in those moments when bad habits might otherwise take over.

So, while it might seem difficult, if you're looking to rid yourself of a bad habit or replace it with a good one, our research suggests it's possible to change your behavior using strategies based on scientific evidence. Trends in Cognitive Sciences

Future wearable devices could draw power through your body using background 6G cellphone signals

published December 3, 2024

Excess energy from wireless 6G networks could be harvested by a copper coil and the human body.

(Image credit: Oscar Wong via Getty Images)

Your body could become a battery for wearable devices, thanks to a breakthrough in harvesting waste energy from 6G wireless communication.

Researchers from the University of Massachusetts Amherst found that waste radio frequency (RF) energy given off by visible light communication (VLC), if used to deliver 6G, can be harvested with small, inexpensive copper coils and transmitted to power other devices via the human body. 6G is a future wireless communication technology that is currently in development and is set to be deployed before the end of the decade.
As outlined in a 2022 research paper, the crux of this mechanism lies with VLC — which transmits data through extremely fast flashes of visible light from sources such as LEDs. VLC is one method through which 6G signals might hypothetically be transmitted in the future. But LEDs also emit side-channel RF signals, as a form of leaked energy. The researchers found that this could be harvested by a coiled copper wire, whose energy recycling efficiency is boosted when touching human skin.

According to the study, skin contact boosted efficiency by up to 10 times compared to using the coil on its own. The human body also proved to be better at amplifying the coil's ability to collect leaked radio energy than wood, plastic, cardboard or steel.

Body batteries

From this, the researchers created "Bracelet+" — a simple copper wire coil that could be worn as a bracket on the upper forearm. The design can also be adapted to be worn as a

necklace, anklet, belt or ring, although the scientists found the bracelet occupied a happy medium between power harvesting and wearability.

"The design is cheap — less than fifty cents," said the authors of the study in a statement. “But Bracelet+ can reach up to micro-watts, enough to support many sensors such as on-body health monitoring sensors that require little power to work owing to their low sampling frequency and long sleep-mode duration."

With this in mind, such technology could solve the issue of limited battery life on wearable devices. Even highly rated smartwatches, like the Apple Watch, tend to need charging on a near-daily basis, which can mitigate how useful they are unless charging is part of one’s daily routine. And now that smart rings are growing in popularity, there are even more devices that require regular power top-ups.

The energy harvesting technology that the Bracelet+ facilitates could, therefore, become a form of in-situ charger for next-generation wearable devices, providing of course that such devices come with a way of taking power from the bracelet.

Of course, this relies on 6G networks that use VLC, which are currently far away from deployment, let alone widespread adoption and integration into consumer or industrial devices.

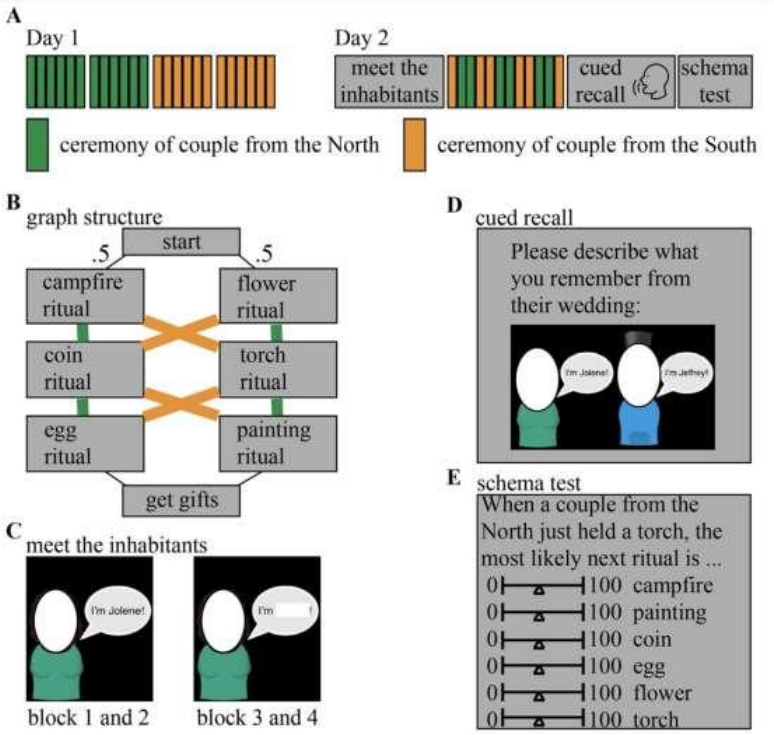
But this could be the advent of turning the human body into a form of battery to power technology, only in a more harmonious fashion than the future envisioned by "The Matrix."

"Ultimately," said lead author of the study Jie Xiong, professor of information and computer sciences at UMass Amherst, in a statement, "we want to be able to harvest waste energy from all sorts of sources in order to power future technology."

MARCH 4, 2025

Encoding study reveals how the brain uses past experiences to predict the unfolding of similar events over time

by Ingrid Fadelli , Medical Xpress



Task design. A Overview of the experiment (images generated with Unity, https://unity3d.com/), consisting of two days. B Graph structure that indicates how the ritual sequences unfold in the North graph vs the South graph. The critical sections of this graph structure for analyses are stages 2 (campfire, flower), 3 (coin, torch) and 4 (egg, painting). C Screenshots of the pretraining task in which participants were introduced to the characters before viewing the actual wedding videos. Pictures of faces omitted in the figure for privacy reasons. D Screenshot of the (self-paced) cued recall task that participants performed on day 2 of the experiment. Pictures of faces omitted in the figure for privacy reasons. E Screenshot of the schema test. Credit: Collin et al. (*Communications Psychology*, 2025)

The human brain continuously processes the wide range of information it acquires from the outside world. Over time, this information is organized into mental representations, referred to as "schema," which help us to understand what is happening at a given time and make predictions about what will happen next.

Temporal schemas are mental representations that specifically outline the order in which specific events occur. For instance, when attending a wedding, temporal schemas could allow us to anticipate the order in which different parts of the ritual (e.g., the arrival of the bride, the exchange of vows, etc.) will take place.

Researchers at Tilburg University and Princeton University recently carried out a study aimed at further exploring how the brain represents these structured sequences of events.

Their findings, published in *Communications Psychology*, suggest that the brain simultaneously encodes context-dependent temporal sequences in different ways, creating different representations for different general contexts, as well as for specific past and current events in a sequence.

"The inspiration for this project is the notion that people are generally very good in building up expectations as to which events to expect to happen in the near future in any specific context they have experience with," Silvy H. P. Collin, first author of the paper, told Medical Xpress.

"We wanted to investigate how the brain uses past, related events and experiences to build such expectations of future events."

Collin and her colleagues carried out a two-day experiment involving 40 participants, who were asked to watch videos of wedding rituals originating from two fictional cultures, dubbed North and South. While the rituals for these two cultures were similar, the sequence in which events unfolded differed.

While the participants were viewing these videos, the team recorded their brain activity using functional magnetic resonance imaging (fMRI). This is a widely used imaging technique that maps brain activity by detecting changes in blood flow.

"We ran an fMRI experiment and used so-called multivariate pattern analysis to investigate various ways as to how the brain represents a narrative, at a generic level (i.e., schema) and at various more fine-grained levels, like a specific sequence of events or distinct events," explained Collin.

"All these levels are relevant to give someone a coherent understanding and memory of a certain experience, but in particular, the generic schema level of representing a narrative turned out to be relevant to remembering the narrative in a detailed way."

Overall, the data collected by Collin and her colleagues suggests that the human brain encodes temporal event sequences by creating overlapping mental representations, which discern between cultural differences (i.e., North and South in the experiment) and what has already happened or is yet to take place. In addition, the researchers found that the strength of temporal schemas is linked to people's episodic memory.

In other words, participants who had created clearer neural representations of how weddings unfolded for the experiments' fictional cultures also performed better (on average) when completing episodic memory tasks than those who created weaker representations. This suggests that temporal schemas serve as a general structure for memories, helping people to better remember their past experiences.

"Our study showed that a generic level of representation of a narrative, which can probably be viewed as a way of representing the general context of a narrative, is in a way used by the brain as a 'skeleton' onto which relevant details are attached," said Collin.

"However, at the same time, the brain also represents the same narrative at more specific and fine-grained levels, each of these levels in different brain regions."

This study by Collin and her colleagues contributes to the understanding of how the brain represents temporal sequences of events. The new insight it provides could serve as a basis for future research focusing on schemas, their contribution to memory and how they are encoded by the brain.

"In our next studies, we hope to better understand how such schema representations in the brain are used when people are recalling events and experiences, as so far we have mostly focused on the part at which people encode events and experiences," added Collin.

More information: Silvy H. P. Collin et al, Neural codes track prior events in a narrative and predict subsequent memory for details, *Communications Psychology* (2025). DOI: 10.1038/s44271-025-00211-y.
Journal information: Communications Psychology

Smart contact lenses

Dubai-based startup Xpanceo is aiming to fit smart features including an "extended reality" display, health monitoring and wireless power reception into a flexible contact lens.

Demonstrator models at their stand show off proofs of concept for each of the capabilities that co-founder Roman Axelrod says they want to pack into a single prototype device "by the end of 2026".

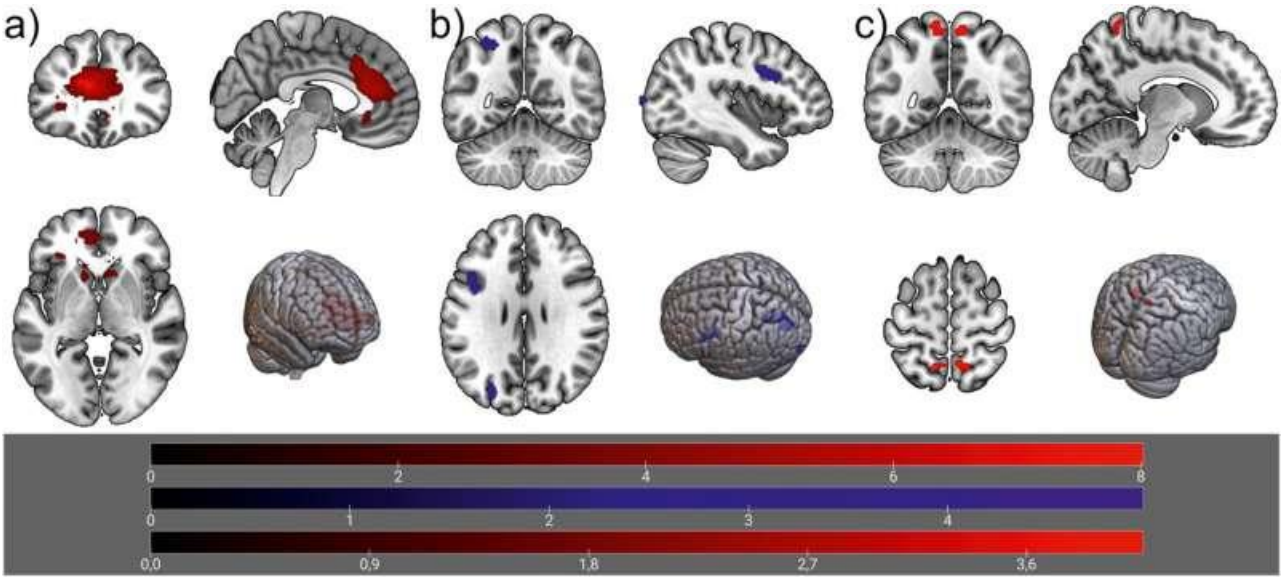
For now the devices are relatively clunky, with a large metal coil needed to receive the wireless power to light up a single pixel on one demonstration lens.

Those components would be miniaturized using "two-dimensional materials... only one atom thick," Axelrod said.

"That is the scientific know-how that differentiates us".

Scientists observe that smartphone restriction for three days can alter brain activity

by Sanjukta Mondal , Medical Xpress



CR-related brain activity over time. a) PHONE > NEU T2 – T1 (red) at p < 0.001, k = 7. b) ON > OFF T1 – T2 (blue) at p < 0.001, k = 9. c) Time-group interaction T2 > T1 and ESU > non-ESU of ON > OFF (red) at p < 0.001, k = 9. Color bars depict T-values of the respective contrasts, top: a), middle: b), bottom c). This figure was created using GIMP and MRIcroGL (https://www.nitrc.org/projects/mricrogl; last visited 01/21/2024).
Credit: *Computers in Human Behavior* (2025). DOI: 10.1016/j.chb.2025.108610

A smartphone's glow is often the first and last thing we see as we wake up in the morning and go to sleep at the end of the day. It is increasingly becoming an extension of our body that we struggle to part with. In a recent study in *Computers in Human Behavior*, scientists observed that staying away from smartphones can even change one's brain chemistry.

The researchers recruited young adults for a 72-hour smartphone restriction diet where they were asked to limit smartphone use to essential tasks such as work, daily activities, and communication with their family or significant others.

During these three days, the researchers conducted psychological tests and did brain scans using functional magnetic resonance imaging (fMRI) to examine the effects of restricting phone usage. Brain scans showed significant activity shifts in reward and craving regions of the brain, resembling patterns seen in substance or alcohol addiction.

There is an ongoing debate about the term "smartphone addiction" (SPA) making an appearance in many psychological tests, as experts believe that this term might create an inaccurate image of the complex emotional, mental and social aspects associated with

smartphone overuse. Nevertheless, neuroscience has seen a growing focus on excessive smartphone use (ESU) due to its association with negative physical and mental health effects, and its links to addictive behaviors.

For this study, 25 young adults aged 18 to 30 who regularly used smartphones were selected. Before the 72-hour restriction period, participants were screened for the severity of physical, psychological, and social issues related to smartphone use and computer gaming, as well as to ensure they did not have any existing mental health conditions.

To assess their mood, smartphone habits, and cravings, participants completed two questionnaires before their first brain scan. They were then instructed to limit phone use for the next 72 hours.

After the three-day restriction period, participants underwent fMRI scans while being shown different sets of images: neutral scenes (such as landscapes and boats), smartphones turned on, and smartphones turned off.

The scans revealed that limiting smartphones led to brain activity changes in areas associated with dopamine and serotonin—neurotransmitters that regulate mood, emotions and also addiction.

The researchers noted that smartphone restriction can resemble withdrawal from addictive substances or even food cravings in some ways, which was noticeable in both heavy (ESU) and regular smartphone (non-ESU) participants.

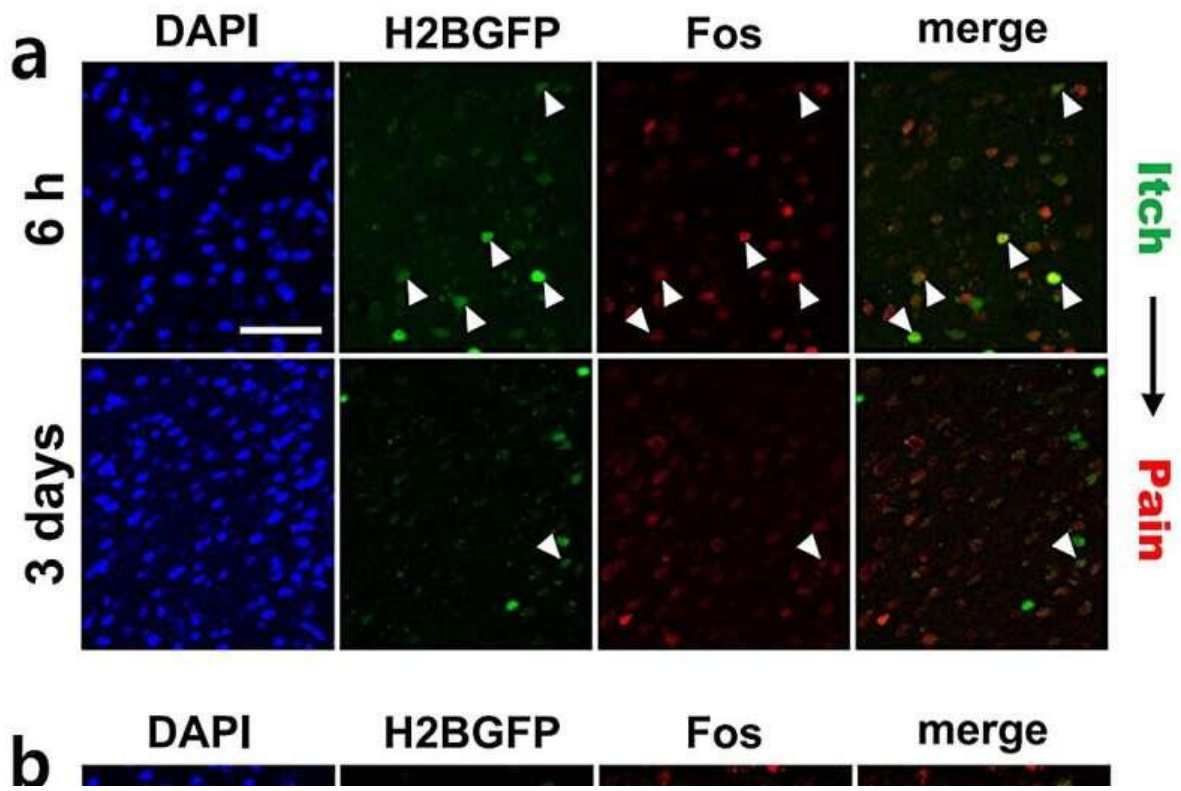
As technology advances, recognizing how our smartphone usage habits affect our brains is crucial for building healthier digital routines.

More information: Mike M. Schmitgen et al, Effects of smartphone restriction on cue-related neural activity, *Computers in Human Behavior* (2025). DOI: 10.1016/j.chb.2025.108610
Journal information: Computers in Human Behavior

MARCH 4, 2025

How the brain distinguishes between pain and itch

by Institute for Basic Science



Visualization of neurons activated by pain- and itch-inducing stimuli. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-57041-z. https://www.nature.com/articles/s41467-025-57041-z

A research team led by Kaang Bong-Kiun, director of the Center for Cognition and Sociality within the Institute for Basic Science (IBS), and Ko Hyoung-Gon, professor at Kyung Hee University College of Dentistry, have uncovered the neural mechanisms underlying the processing of pain and itch in the anterior cingulate cortex (ACC).

This study, published in *Nature Communications*, provides new insights into how the brain distinguishes between these two distinct sensory experiences.

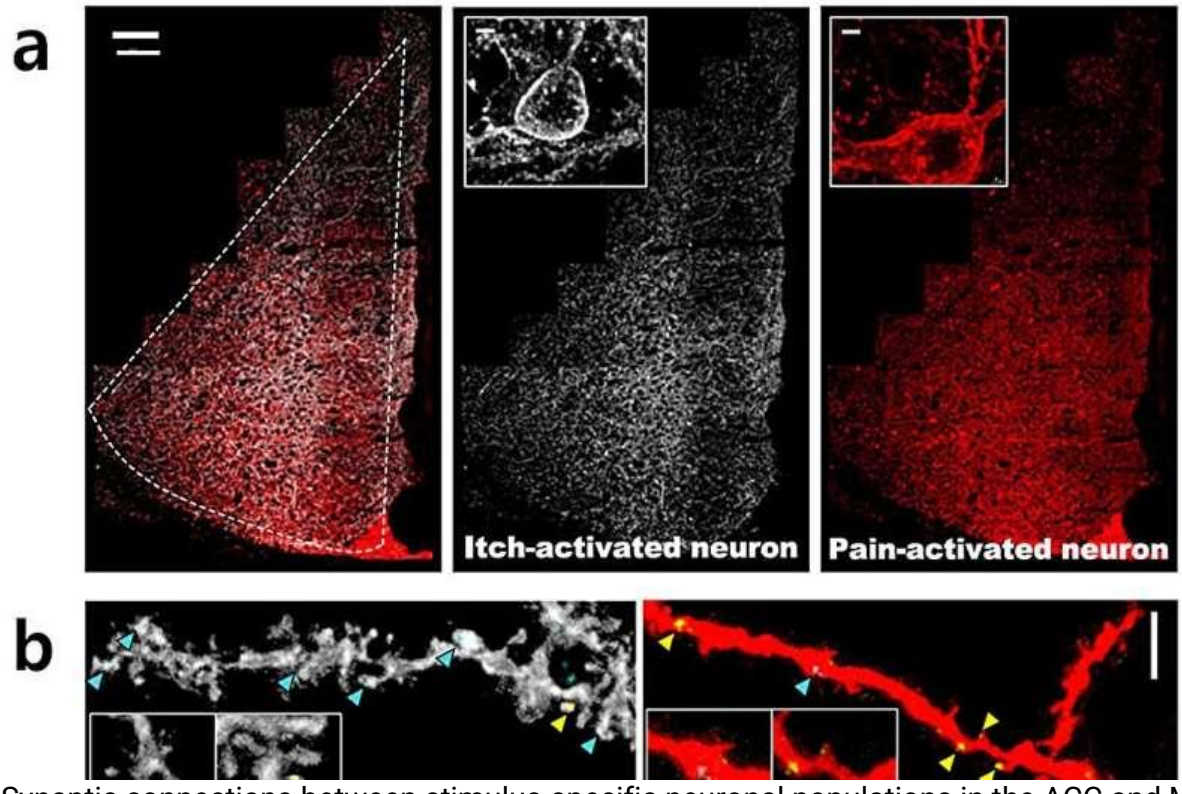
Pain and itch are both unpleasant sensations, but they trigger different responses—pain often prompts withdrawal, while itching leads to scratching. Until now, scientists have struggled to understand how the brain processes these sensations separately, as they share overlapping neural pathways from the spinal cord to the brain.

Both stimuli are transmitted from the spinal cord to the thalamus and brainstem, eventually reaching the ACC. The ACC is a key brain region involved in various functions, ranging from basic sensory processing to higher-order cognition. However, a comprehensive understanding of how a limited number of neurons within the ACC execute such diverse functions has been lacking. This study provides fundamental insights into how ACC neurons selectively process pain and itch information.

By analyzing neuronal response patterns in the ACC to pain and itch stimuli, the research team identified two distinct neuronal populations:

1. Non-selective neurons, which respond to both pain and itch stimuli indiscriminately.
2. Stimulus-specific neurons, which were selectively activated by either pain or itch stimuli.

Furthermore, using the dual-eGRASP technique—an advanced synaptic analysis method developed by Kaang's research team (Science, 2018)—the researchers discovered that stimulus-specific neurons in the ACC receive distinct synaptic inputs from the mediodorsal thalamus (MD). This finding indicates that pain and itch are processed by independent neuronal populations within the ACC, which receive differentiated synaptic inputs, providing fundamental insights into the neural mechanisms of pain and itch processing.



Synaptic connections between stimulus-specific neuronal populations in the ACC and MD. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-57041-z. https://www.nature.com/articles/s41467-025-57041-z

To further confirm the role of these neurons, the team used chemogenetic techniques to selectively deactivate either pain-specific or itch-specific neurons. The results showed

suppressing pain neurons reduced pain perception without affecting itch, and vice versa. This discovery suggests that these neurons play a direct role in shaping how we experience pain and itch.

This study presents a groundbreaking discovery that the role of ACC neurons in processing pain or itch is predetermined. Importantly, the study demonstrates that pain- and itch-specific neurons in the ACC are synaptically paired with corresponding stimulus-specific neurons in the MD, establishing independent neural circuits for pain and itch processing. These findings challenge the conventional assumption that pain and itch signals follow overlapping pathways and instead highlight distinct neural mechanisms for each sensation.

Given that the ACC is known to mediate the affective aspects of pain and itch, this study suggests that separate neuronal populations are responsible for encoding the subjective experience of pain and itch. Building upon these findings, the research team aims to further investigate the brain's complex sensory processing mechanisms.

Corresponding author Bong-Kiun stated, "The ACC is an important brain area not only for memory storage but also for processing higher-order emotions such as pain and conflict. Through this study, we have taken a step further in understanding emotional memory at the synaptic level."

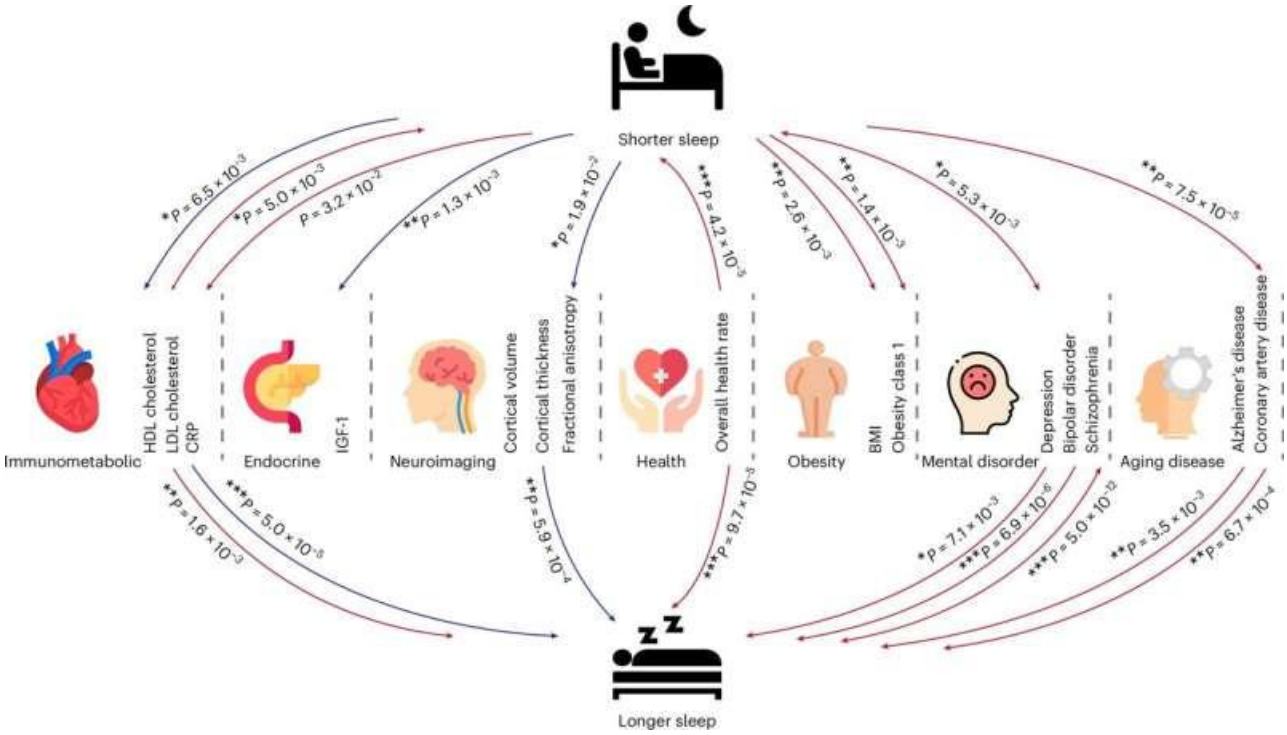
Co-corresponding author and first author Hyoung-Gon commented, "I am particularly interested in how these pain- and itch-selective neural circuits change under pathological conditions. Moving forward, we plan to expand our research to explore the interactions between these circuits."

More information: Hyoung-Gon Ko et al, Processing of pain and itch information by modality-specific neurons within the anterior cingulate cortex in mice, *Nature Communications* (2025). DOI: 10.1038/s41467-025-57041-z. www.nature.com/articles/s41467-025-57041-z
Journal information: Nature Communications

MARCH 4, 2025

Up half the night? Or out like a light? Research finds health consequences for both

by University of Warwick



Causal associations between short and long sleep groups with multiple health conditions. Credit: *Nature Mental Health* (2025). DOI: 10.1038/s44220-025-00395-6

A study led by University of Warwick Professor Jianfeng Feng has found that regularly sleeping too little is associated with depression and brain loss in emotion areas, while sleeping too long is associated with cognitive decline and degenerative diseases.

Sleeping the right amount is crucial for long-term health. Seven hours has recently been proposed as the average amount of sleep to aim for as an adult, yet some people regularly get too little, while others get more than they need.

"How many hours of sleep do you have in every 24 hours?": This question was asked to almost half a million adults aged 38–73 from the UK Biobank database. The researchers in this study then classified them into those who slept fewer than seven hours, aka "short sleepers," and those who slept more than seven hours, aka "long sleepers." Their sleeping

habits were then examined alongside data on their health outcomes, their genetic information and brain imaging data.

Professor Feng, School of Computer Science, The University of Warwick asked, "Is short sleep and long sleep part of the same biological process, or are they distinct pathways with different effects on health? Answering these questions is crucial for developing targeted strategies to improve sleep health among aging populations."

Their analysis, published in *Nature Mental Health*, found that regularly sleeping short durations is linked to psychological problems, such as low mood and fatigue, and poorer muscle and skeletal health (reduced vitamin D and IGF-1).

Brain scans showed that short sleepers have reduced brain matter in brain areas involved in emotion, a biological consequence of cutting sleep short. Sleeping short durations was also found to be a risk factor for a variety of conditions such as depression, heart disease and obesity.

Sleeping long hours, on the other hand, was associated with cognitive decline, higher inflammation and poorer metabolic health (lower "good" cholesterol). Brain scans showed brain matter loss in areas associated with memory and known risk areas for degenerative disease. Long sleep was associated with diseases such as Alzheimer's and schizophrenia. However, sleeping long durations appears to be a symptom, rather than a cause, of these conditions.

Ultimately, genetic analysis showed long sleep and short sleep to be biologically distinct, with their own genetic associations, as opposed to viewing short sleep and long sleep as two extremes of the same process, which is more intuitive.

On the significance of this work, Professor Feng added, "This study represents a paradigm shift in how we understand the relationship between sleep and health. Short sleep is often an underlying cause of health issues, whereas long sleep tends to reflect pre-existing conditions. These findings highlight the importance of personalized interventions to address the unique biological pathways of short and long sleepers.

"Our ultimate goal is to construct a comprehensive sleep health profile across the human lifespan, providing actionable insights for individuals at every stage of life."

This work will be important for establishing meaningful sleep management strategies for aging populations. Future work will expand this research out to more life stages and diverse populations.

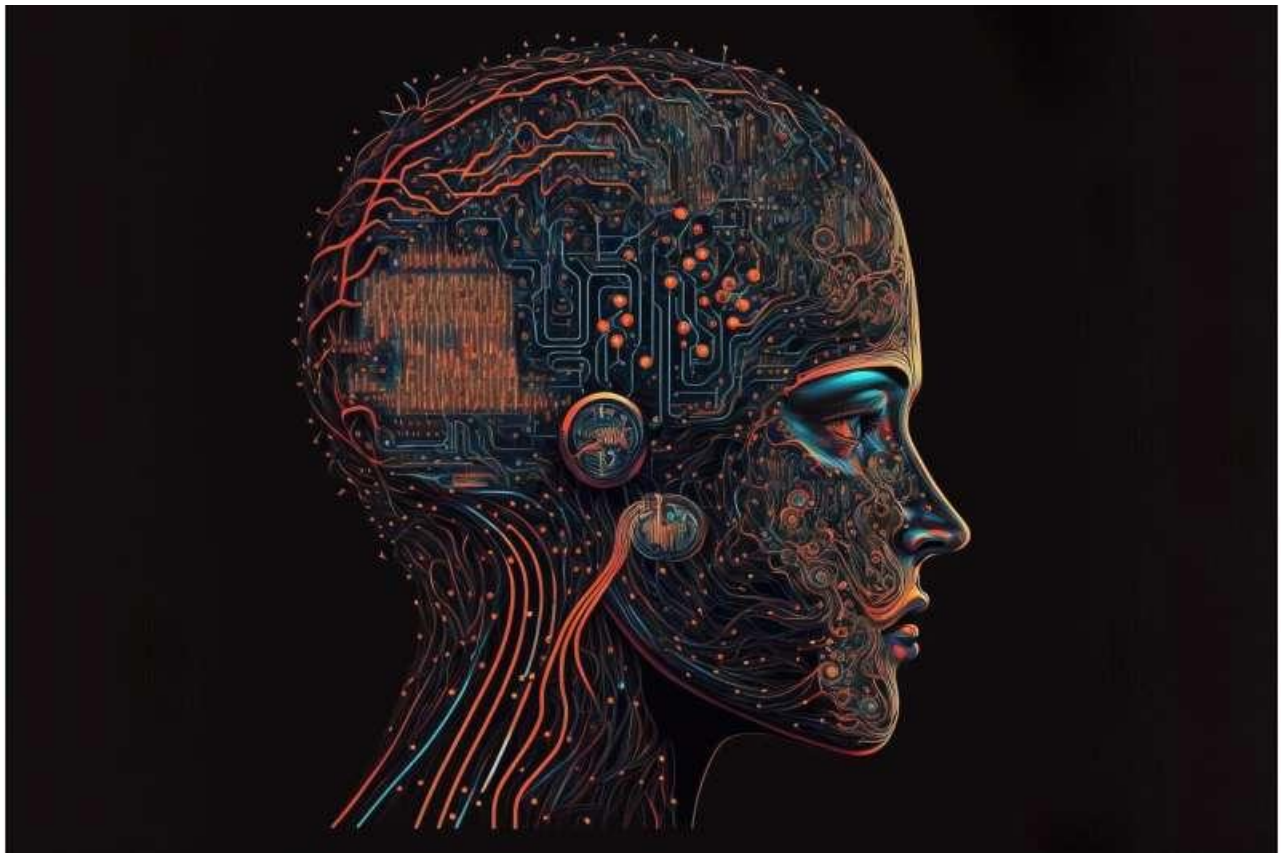
More information: Yuzhu Li et al, Divergent biological pathways linking short and long sleep durations to mental and physical health, *Nature Mental Health* (2025). DOI: 10.1038/s44220-025-00395-6

Journal information: Nature Mental Health

MARCH 4, 2025

AI could supercharge human collective intelligence in everything from disaster relief to medical research

by Hao Cui and Taha Yasseri, The Conversation



Credit: Pixabay/CC0 Public Domain

Imagine a large city recovering from a devastating hurricane. Roads are flooded, the power is down, and local authorities are overwhelmed. Emergency responders are doing their best, but the chaos is massive.

AI-controlled drones survey the damage from above, while intelligent systems process satellite images and data from sensors on the ground and air to identify which neighborhoods are most vulnerable.

Meanwhile, AI-equipped robots are deployed to deliver food, water and medical supplies into areas that human responders can't reach. Emergency teams, guided and coordinated by AI and the insights it produces, are able to prioritize their efforts, sending rescue squads where they're needed most.

This is no longer the realm of science fiction. In a recent paper published in the journal *Patterns*, we argue that it's an emerging and inevitable reality.

Collective intelligence is the shared intelligence of a group or groups of people working together. Different groups of people with diverse skills, such as firefighters and drone operators, for instance, work together to generate better ideas and solutions. AI can enhance this human collective intelligence, and transform how we approach large-scale crises. It's a form of what's called hybrid collective intelligence.

Instead of simply relying on human intuition or traditional tools, experts can use AI to process vast amounts of data, identify patterns and make predictions. By enhancing human decision-making, AI systems offer faster and more accurate insights—whether in medical research, disaster response, or environmental protection.

AI can do this, by for example, processing large datasets and uncovering insights that would take much longer for humans to identify. AI can also get involved in physical tasks. In manufacturing, AI-powered robots can automate assembly lines, helping improve efficiency and reduce downtime.

Equally crucial is information exchange, where AI enhances the flow of information, helping human teams coordinate more effectively and make data-driven decisions faster. Finally, AI can act as social catalysts to facilitate more effective collaboration within human teams or even help build hybrid teams of humans and machines working alongside one another.

AI-driven improvements to all these different aspects can make the entire, interconnected system more adaptive and intelligent.

We're already seeing the impact of AI-enhanced collective intelligence. In disaster response, AI systems already analyze satellite imagery and sensor data, generating risk assessments that help human responders to prioritize rescue efforts and allocate resources efficiently.

In health care, AI already helps doctors make faster and more accurate diagnoses by analyzing large patient datasets. Medical teams refine AI recommendations with their expertise, ensuring the best possible treatment plans. Robots equipped with AI can assist surgeons in performing delicate tasks, allowing for greater precision.

In media, AI curates and verifies news from global sources, assisting journalists in fact-checking and uncovering misinformation. This collaboration can strengthen the accuracy and reliability of information in an era of digital media. However, AI can also drive the dissemination of fake news and disinformation. These include deep fake videos of, for example, politicians, which have the potential to affect elections.

In the public sector, AI-powered policy simulations help governments anticipate the impacts of regulations. Crowd-sourced citizen feedback, combined with AI analysis, can give a sense of the public mood.

Environmental protection is another area benefiting from AI-enhanced collective intelligence. AI systems can analyze data patterns on pollution, deforestation, and wildlife movements, guiding human efforts to address environmental challenges more effectively.

As we can see, AI-enhanced collective intelligence is already here, transforming how we approach some of the world's toughest problems. The key is to recognize that AI is a collaborator, not a competitor. When we combine human creativity, intuition, and ethics with AI's data processing power, the possibilities for what we can achieve are substantial.

As we look towards the future, AI's potential becomes even more exciting. From addressing global health challenges like pandemic prevention to developing solutions to the climate crisis, AI will be at the forefront of tackling issues once thought insurmountable. But this potential comes with responsibility.

It's up to us to guide how this collaboration evolves, ensuring that AI is used responsibly and ethically in ways that enhance human capabilities rather than diminish them. We must engage in shaping policies and frameworks that promote transparency, fairness and inclusivity through a new sociology of humans and machines.

Collaboration across industries, governments, and communities will be crucial to unlocking AI's full potential. Together, we can build a future where AI not only augments human intelligence but also helps solve the challenges of tomorrow, creating a more equitable, sustainable, and prosperous world for all.

More information: Hao Cui et al, AI-enhanced collective intelligence, *Patterns* (2024). DOI: 10.1016/j.patter.2024.101074
Journal information: Patterns
Provided by The Conversation

MARCH 4, 2025

Mind-controlled prosthetic arms could benefit from neural encoding research

by Leila Okahata, University of Oregon

Credit: Michelle Marneweck Human Physiology research

Picking up a cup of coffee, flipping a light switch or grabbing a door handle don't require much apparent thought. But behind the curtain, the brain performs feats to coordinate these seemingly simple hand-to-target motions.

Using functional MRI brain imaging, University of Oregon researchers have unraveled some of the neural circuitry behind these kinds of actions.

Their insights, described in a paper published in the journal *eNeuro*, can potentially be used to improve the design of brain-computer interface technologies, including brain-controlled prosthetic arms that aim to restore movement in people who have lost it.

"While there are already robotic arms or exoskeletons that take signals from brain activity to mimic the motions of a human arm, they haven't quite met the gracefulness of how our arms actually move," said study lead author Alejandra Harris Caceres, an undergraduate senior majoring in neuroscience and human physiology.

"We're hoping to figure out how and when the brain integrates different kinds of sensory information to help make this technology better for patients."

For the brain to plan even a simple, goal-directed action, like reaching out and grabbing a cup of coffee on a table, it needs to make lots of calculations, including the direction and distance of one's hand to the object. To get even more accurate, the brain uses multiple "reference frames" to make calculations from multiple perspectives—for example, from the hand to the cup versus from the eyes to the cup.

In this study, the researchers wanted to understand how the brain combines those different bits of sensory information to plan and generate a goal-directed action.

While this has been investigated extensively in nonhuman primates such as monkeys, this is the first evidence in humans of neural representations of direction and distance in multiple reference frames during reach planning, said study senior author Michelle Marneweck, an assistant professor in human physiology at the UO's College of Arts and Sciences.

"Just like how we use reference frames for navigation, like moving through the woods or driving through fog, we also use it to make the most elementary, everyday actions, such as reaching for a bottle of water," Marneweck said.

"Having a system rich in redundancies allows us to flexibly switch between reference frames, using the most reliable one in the moment, and be good at goal-directed actions, no matter what the environment throws at us."

How the brain plans a reach

As part of the study, human subjects laid flat on a screening table inside an MRI machine. Over their lap was a table with an electronic task board of lights and buttons. Because the participants couldn't sit up during the scan, they wore a helmet-like setup with a mirror attached, allowing them to see and interact with the button-pushing tablet.

The fMRI scan measured blood flow in the brain to highlight active areas when subjects were prompted to reach for a button and when they pressed it.

Analyzing the neural activity patterns across key sensory and motor areas, the results showed the human brain prepares for reaching actions by encoding the target direction first, then the distance. The researchers also found that direction and distance are coordinated in multiple, rather than single, reference frames.

That can help improve the design of tools like bionic arms that use brain signals, Harris Caceres said. Neural interface technology that considers the serial processing of direction into distance and incorporates multiple reference frames—and the multitude of regions encoding this information—could add an extra layer of sophistication to the modeling, she suggested.

"It is a really exciting time for brain-computer interface technology, which has advanced rapidly in recent years with the integration of sensory information," Marneweck said.

"One of the overarching goals of our lab is to further optimize these technologies, by figuring out when, where and how the brain integrates sensory information for skilled actions. This experiment was a step in that direction."

Impacts across the lifespan: From peak performance to aging

The researchers are now performing the same set of experiments but on a skilled performance model: human athletes. Marneweck and her team recruited athletes to check if the neural mechanisms of peak physical performers differ from nonathletes. Their preliminary results suggest athletes require less brain power to complete reaching tasks.

In the future, the researchers also plan to investigate how aging and neurodegenerative disorders, like Alzheimer's disease and Parkinson's disease, affect sensory and motor control.

"Topographical disorientation, which colloquially is known as 'getting lost,' is one of the earliest markers of Alzheimer's disease," Marneweck said. "We and others in the scientific community are interested in determining a causal link between cognitive features of Alzheimer's and sensory and motor changes that show up as early as 10 to 12 years before the hallmark clinical signs."

By studying across the spectrum of human health, Marneweck's lab is shedding light on the complex sensory and motor mechanisms that go on in the background unnoticed.

"Reaching and interacting with objects may seem elementary due to the seamless ease with which we perform these actions," Marneweck said, "but they are among the most complex and least understood feats of human behavior."

More information: Alejandra Harris Caceres et al, Neural Encoding of Direction and Distance across Reference Frames in Visually Guided Reaching, *eNeuro* (2024). DOI: 10.1523/ENEURO.0405-24.2024
Journal information: eNeuro
Provided by University of Oregon

MARCH 4, 2025

Why sleep gets harder with age and how to sleep better

by I. Edwards

Tossing and turning more as you age? You're not alone—and experts think they know why.

Dr. Shelby Harris, a sleep psychologist in White Plains, N.Y., explained that stress, sleep structure and hormonal changes can impact sleep as people age.

"As we start to move into our 60s, 70s, you have more issues with the depth of your sleep, so your sleep is just lighter in general," Harris told CBS News. "There's sleep disorders, like insomnia, that happen, and then you have to go to the bathroom more at night."

Research shows up to 70% of people 65 and older have chronic sleep problems, and hormonal shifts play a big role in that, especially for women. The study is published in the journal *Sleep Medicine Clinics*.

"We have more hot flashes, night sweats. You actually have more sleep apnea in women as well, and just more insomnia too," Harris said.

There may also be some evolutionary reasoning behind why older adults get less deep sleep, Harris added.

"The deepest stage of sleep is where your muscles are repairing, you're growing—and as you're getting older, you don't need that ideally as much as you do when you're younger," Harris said, adding that younger kids get a lot of deep sleep.

"(Older adults) just wake up a lot more because of pain and movement and having to urinate," she added.

What's more, Harris told CBS News it's a myth that older adults don't need much sleep.

"If a doctor tells you that is normal to get a lot less as you get older, definitely seek some other advice," Harris said.

Along with keeping a cool, dark and quiet sleep environment, she offered these tips:

- Meditate during the day. "If you have a busy brain, meditating five minutes during the day can help to actually ease your brain more at night," Harris said.
- Limit daytime sleep. To try and get better sleep at night, you can also try spending less time in bed during the day, Harris added. That means reducing naps.
- Stick to a regular bedtime.

If sleep issues last more than a few weeks, it's important to talk with a doctor, Harris urged.

"We do have a lot of treatments like cognitive behavior therapy for insomnia. You might need a sleep study, medication," she said. "We have lots of options."

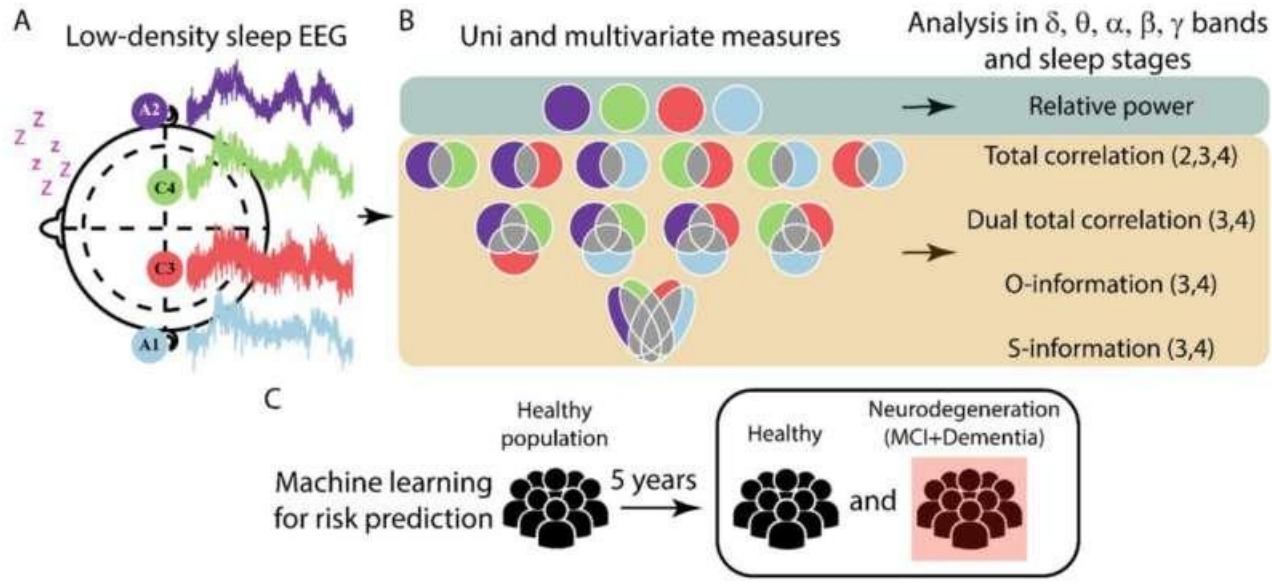
More information: Brienne Miner et al, Sleep in the Aging Population, *Sleep Medicine Clinics* (2016). DOI: 10.1016/j.jsmc.2016.10.008

The Mayo Clinic has more tips to get better sleep.

MARCH 4, 2025

Brain waves measured during sleep predict cognitive impairment years before symptoms appear, study finds

by Mass General Brigham



Predicting cognitive impairment risk with features from univariate and multivariate EEG analyses. A) Layout of the full night low-density EEG set-up. B) Univariate (relative power) and multivariate EEG analyses (total correlation (TC), dual total correlation (DTC), O and S Information) are computed for each sleep stage and frequency band (see Methods for details). Each circle represents the statistical information present in one electrode (same colors as in A) and the gray zone in the Venn diagrams represents the information shared between them, as measured by metrics from multivariate EEG analyses. The number inside the parentheses denote the order of interactions used to compute these metrics. For pairwise interactions (order = 2) the TC = DTC = Mutual information, so only the TC is computed for order 2. C) Features from univariate and multivariate EEG analyses, and their combination are used as features for a machine learning algorithm to develop early biomarkers of the risk of cognitive impairment. Credit: *Journal of Alzheimer's Disease* (2025). DOI: 10.1177/13872877251319742

Mass General Brigham researchers have developed an AI tool that analyzes brain wave activity recorded during sleep using electroencephalography (EEG), a non-invasive technique that measures electrical activity in the brain through sensors placed on the scalp.

The AI tool was developed using sleep study data from a group of women over 65, who were tracked for five years.

The researchers identified subtle differences in brain wave patterns that predicted which participants would later be diagnosed with cognitive impairment. Published in the *Journal of Alzheimer's Disease*, the study suggests that wearable EEG devices could help identify individuals at risk for dementia, paving the way for earlier interventions.

"Using novel sophisticated analyses, advanced information theory tools, and AI, we can detect subtle changes in brain wave patterns during sleep that signal future cognitive impairment, offering a window of opportunity for intervention years before symptoms appear," said lead author Shahab Haghayegh, Ph.D., a member of the Department of Anesthesia, Critical Care, and Pain Medicine at Massachusetts General Hospital, a founding member of the Mass General Brigham health care system, and Harvard Medical School.

Haghayegh and colleagues analyzed data that was collected for a separate trial on fracture risk in women. For that study, women aged 65 and older underwent a series of cognitive tests around the same time they participated in a sleep study, which included an overnight EEG. Researchers focused on 281 of the participants who had normal cognitive functioning at the time of the initial sleep study and repeated the same cognitive tests five years later. By that second series of assessments, 96 of these women had developed cognitive impairment.

They then applied state-of-art information theory techniques to extract brainwave patterns from the EEG data collected during the sleep study. Using AI, the researchers found that among people who went on to show signs of cognitive impairment, there were changes in subtle brain wave features before symptoms occurred, especially in gamma band frequencies in deep sleep. The AI tool successfully identified 85% of individuals who later developed cognitive impairment, with an overall accuracy of 77%.

The researchers say these findings could help identify patients years before cognitive impairment takes place and suggests a future where wearable EEG devices could become a powerful tool in predicting cognitive decline. Early detection could provide valuable time for individuals to access treatments and make lifestyle modifications that may help maintain cognitive health.

The authors note that further research is necessary to validate these findings across broader populations, including in males and more diverse populations, to verify the link between altered gamma wave activity during deep sleep and future cognitive impairment.

A limitation of the study is that it relied on data from a single night of sleep. However, senior author Kun Hu, Ph.D., physiologist in the Division of Sleep and Circadian Disorders at

Brigham and Women's Hospital and Harvard Medical School, notes that EEG data from multiple nights of sleep could be even more predictive of future cognitive impairment.

"The new, FDA-approved treatments for Alzheimer's disease are effective at the earlier stages of dementia, but not the more advanced stages," said Hu. "Interventions that are performed even earlier—before someone shows signs of cognitive decline—are likely to be even more effective."

The research also opens up another exciting possibility, suggesting that manipulating brain electrical activity during sleep could reduce the risk of cognitive decline. Haghayegh and Hu are currently designing a clinical study that will assess if electrical stimulation can alter EEG patterns in sleep and thereby slow down cognitive decline.

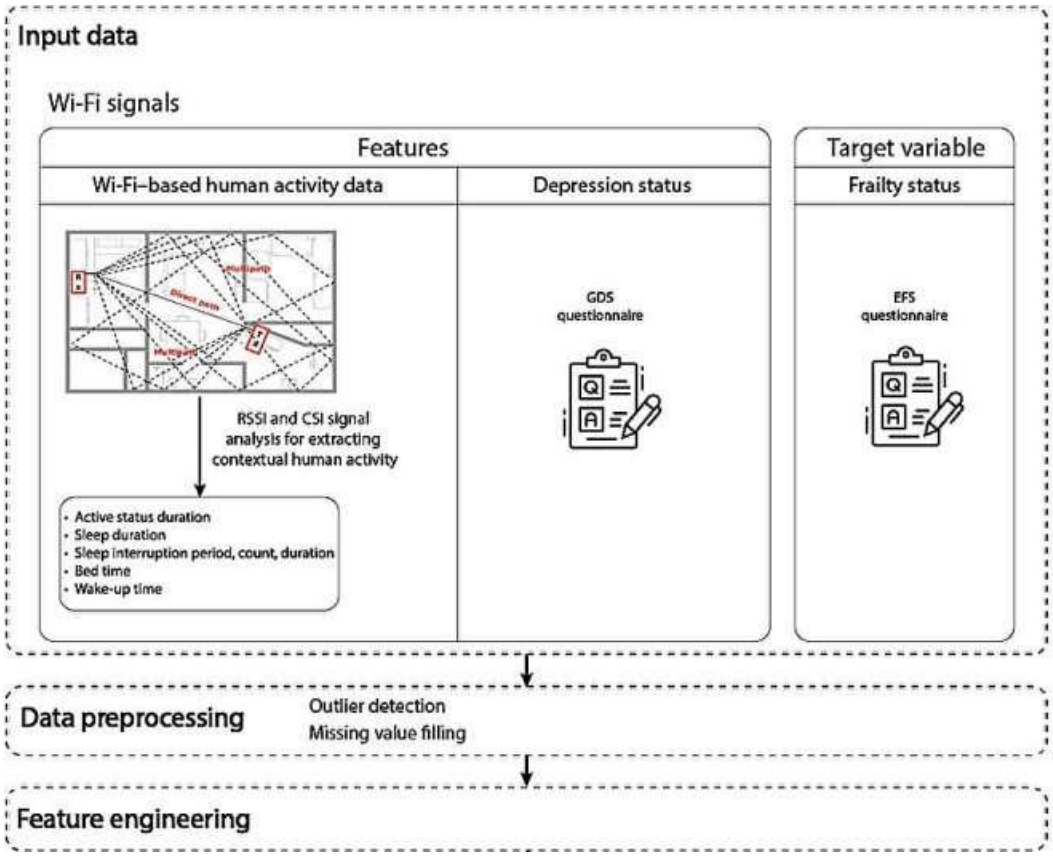
"What makes this research particularly significant is how we can identify those at risk using a simple overnight EEG recording," says Haghayegh. "This could completely change how we approach dementia prevention."

More information: Shahab Haghayegh et al. Predicting future risk of developing cognitive impairment using ambulatory sleep EEG: Integrating Univariate Analysis and Multivariate Information Theory Approach, *Journal of Alzheimer's Disease* (2025). DOI: 10.1177/13872877251319742
Journal information: Journal of Alzheimer's Disease
Provided by Mass General Brigham

MARCH 4, 2025

Wi-Fi-based technology developed to detect depression in older adults

by JMIR Publications



Structure of the automatic Wi-Fi–based depression classification framework. CSI: channel state information; DT: decision tree; EFS: Edmonton Frailty Scale; GDS: Geriatric Depression Scale; LIME: local interpretable model-agnostic explanations; PCA: principal component analysis; RSSI: received signal strength indicator; SFS: sequential forward selection; SHAP: Shapely addictive explanations. Credit: *JMIR Aging* (2025). DOI: 10.2196/67715

A new study published in *JMIR Aging* developed and tested a new AI model called HOPE which uses Wi-Fi-based motion sensor data to detect depression in older adults without relying on intrusive wearable devices. The research highlights a novel machine learning model that accurately detected depression among participants.

Led by principal investigator, Professor Samira A Rhaimi from McGill University and Mila-Quebec AI Institute, the study aimed to determine whether everyday movement and sleep

patterns collected through Wi-Fi-based sensors could provide early indicators of depression in adults 65 years and older. With an accuracy rate above 87%, this innovative approach presents a promising solution for early intervention and nonintrusive mental health monitoring, offering an alternative to traditional methods that require direct patient engagement.

Depression is a growing public health concern among older adults, with studies estimating that 10–15% of community-dwelling older adults and 30–40% of those in long-term care facilities experience this condition. However, nearly half of depression cases remain undiagnosed, leading to detrimental effects on physical health, increased hospitalization rates, and reduced quality of life.

Traditional detection methods, including clinical interviews and wearable-based monitoring, are often resource-intensive, intrusive, or inconvenient, particularly for older adults who may struggle with technology adoption. The HOPE model addresses these challenges by leveraging existing Wi-Fi infrastructure, enabling continuous passive monitoring without requiring any active participation from users.

A key aspect of the HOPE model is the integration of explainable AI (XAI) techniques, ensuring transparency and clinical interpretability. Rahimi's lab used explainable machine learning models to identify the most influential factors in depression detection.

The results underscored the important role of sleep-related features, including average sleep duration, frequency of sleep interruptions, and frailty levels as primary indicators of depression. By making these AI-driven predictions interpretable and clinically meaningful, the HOPE model enhances trust and facilitates early detection of depression among older adults in the community.

The study highlights the importance of sleep-related factors in detecting depression. The analysis revealed that the most influential factors were sleep duration, the number and duration of sleep interruptions, and the level of frailty, which aligns with previous research on the link between sleep and mental health and reinforces the need for further exploration in this area.

"Too often, the mental health of older adults is overlooked, leaving many to suffer in silence without the care and attention they deserve. Our HOPE model could act as a caring friend who looks out for signs of depression in older adults using everyday Wi-Fi data to spot potential issues early on and without being intrusive. It's about using technology to lend a helping hand, especially for those who might find it hard to reach out themselves," said Samira A. Rahimi, one of the McGill University researchers.

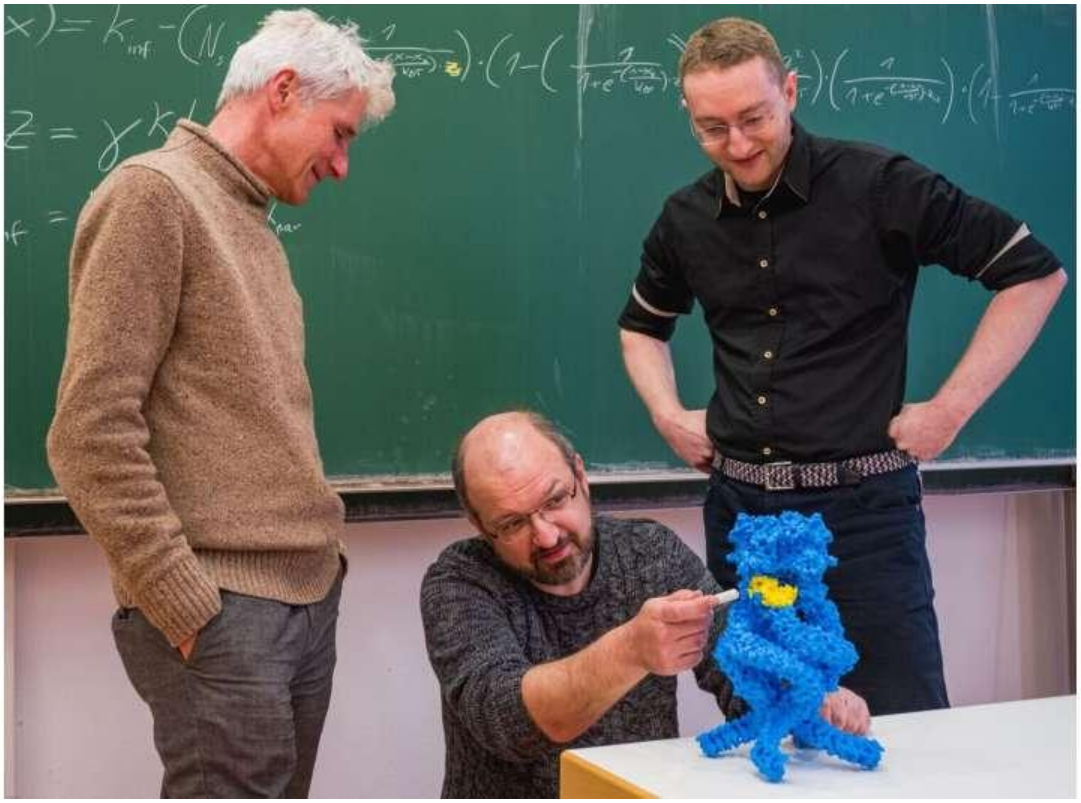
The study demonstrates the feasibility of using smart home technology for mental health assessments. While these findings are promising, larger studies are needed to provide further evidence for this approach. This technology could support early intervention efforts and improve the quality of life for older adults at risk of depression.

More information: Shayan Nejadshamsi et al, Development and Feasibility Study of HOPE Model for Prediction of Depression Among Older Adults Using Wi-Fi-based Motion Sensor Data: Machine Learning Study, *JMIR Aging* (2025). DOI: 10.2196/67715
Provided by JMIR Publications

MARCH 5, 2025

Discovery of molecular 'spring' reveals how hearing is triggered

by University of Göttingen



The 3D model helps researchers to better understand the structure and function of the mechanical spring on the ion channel. From left to right: Professor Martin Göpfert, Dr. Thomas Effertz, Dr. Philip Hehlert. Credit: Philip Hehlert

Hearing begins with the stretching of elastic molecular "springs" that open ion channels in the sensory hair cells of the ear. For decades, researchers have known that these gating springs must exist, but they could not find them. A team from the Cluster of Excellence Multiscale Bioimaging (MBExC) in Göttingen has now discovered just such a spring for the

first time. Their findings shed new light on our understanding of the sense of hearing and the function of ion channels.

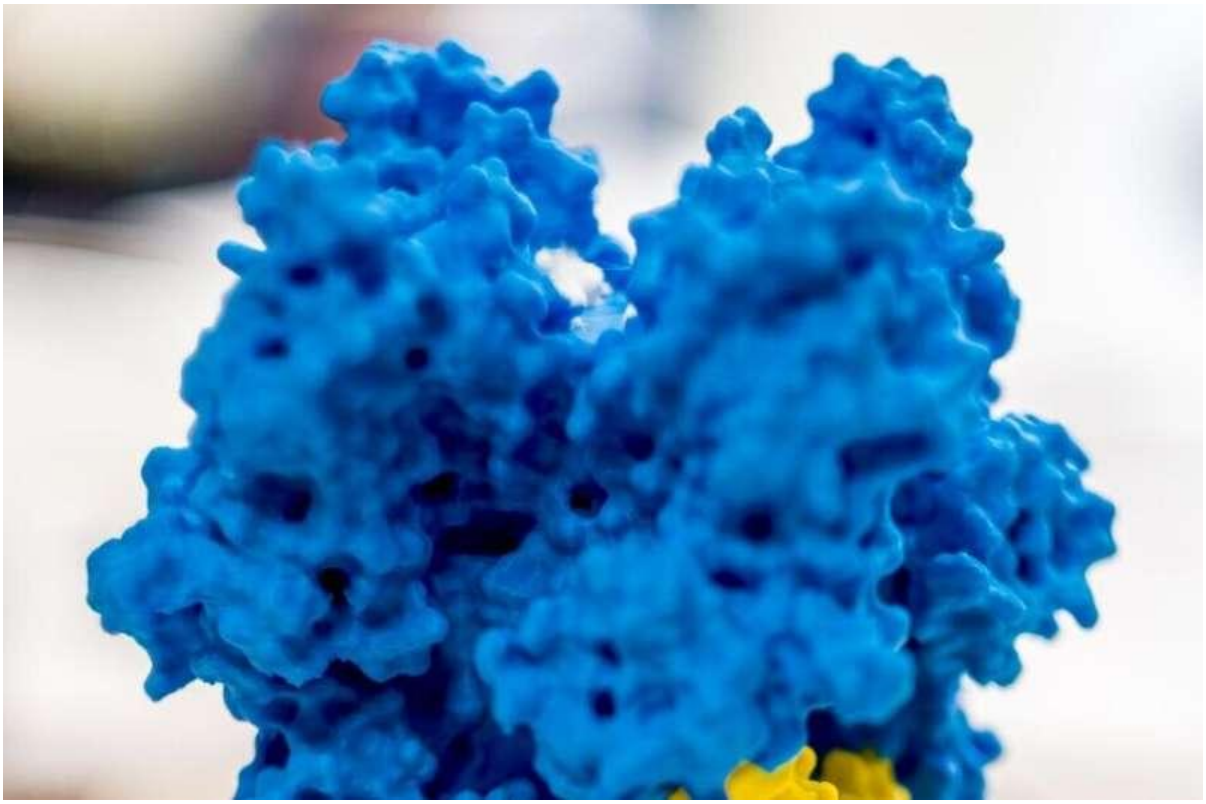
The results appear in *Nature Neuroscience*.

When sound hits the ear, it triggers tiny movements inside. "Hearing cells" register these movements with the help of specialized molecules, known as ion channels. The hearing cells have a pore with a gate that is normally closed. The movements detected inside the ear must be transmitted to the ion channel gates to open them.

PC1, the 'core protein.' Credit: *Nature Neuroscience* (2025). DOI: 10.1038/s41593-024-01849-3
This is done by a gating spring, which—like the spring of a ballpoint pen—is springy and elastic. When these gating springs are stretched, they pull open the channel gates and ions can flow through the pores of the channels.

Researchers have been searching for these springs for over 40 years. They previously found a promising structure in the ear of fruit flies: an ion channel that—in addition to a gate and a pore—also has a region that is wound spirally like a ballpoint pen spring. Researchers therefore suspected that this spiral could be the gating spring.

The research team, led by Professor Martin Göpfert, Head of Göttingen University's Department of Cellular Neurobiology, has now tested this.



Printed 3D model of the ion channel "NompC" with the spring colored yellow. Credit: Philip Hehlert

"Our assumption was that doubling the spiral would halve the stiffness of the gating spring. That was not the case," says Dr. Thomas Effertz, University Medical Center Göttingen (UMG), and one of two lead authors.

The researchers found that the coiled spiral is stiff, but is flexibly attached to the channel gate via a bendy hinge. When the researchers doubled the hinge, putting two hinges in tandem, the stiffness of the opening spring was halved, which shows that the hinge is the gating spring.

"In fact, we were able to observe at the molecular level that it is not the spiral, but the flexible joint that bends under mechanical tension," says Professor Bert de Groot from Göttingen's Max Planck Institute for Multidisciplinary Sciences.

"We suspect," says Dr. Philip Hehlert, also at Göttingen University's Department of Cellular Neurobiology and joint lead author, "that opening springs are hidden in every ion channel, including those in the human ear. Regardless of whether mechanical, electrical or chemical signals open an ion channel, the channel gate must be elastically suspended in order to open at all, and this suspension must serve as a gating spring."

These results not only provide important new insights into how the hearing process is initiated at the molecular level, but also contribute to a better understanding of the basic function of ion channels, which are an essential component of all cells and the basis of all senses.

More information: Philip Hehlert et al, NOMPC ion channel hinge forms a gating spring that initiates mechanosensation, *Nature Neuroscience* (2025). DOI: 10.1038/s41593-024-01849-3
Provided by University of Göttingen

MARCH 5, 2025

The pupil as a window to the sleeping brain: A look under the eyelids shows more is happening than previously assumed

by Peter Rüegg, ETH Zurich

The eye of the sleeping subject was kept open with a special fixation device to record the pupil movements for several hours. Credit: Neural Control of Movement Lab / ETH Zurich

For the first time, researchers have been able to observe how the pupils react during sleep over a period of several hours. A look under the eyelids showed them that more happens in the brain during sleep than was previously assumed. The study is published in the journal *Nature Communications*.

Our eyes are typically closed when we sleep. However, there is a flurry of activity taking place beneath our closed eyelids: a team of researchers, led by principal investigators Caroline Lustenberger, Sarah Meissner and Nicole Wenderoth from the Neural Control of Movement Lab at ETH Zurich, have observed that the size of the pupil fluctuates constantly during sleep. Sometimes it increases in size, sometimes it decreases; sometimes these changes occur within seconds, other times over the course of several minutes.

"These dynamics reflect the state of arousal, or the level of brain activation in regions that are responsible for sleep-wake regulation," says Lustenberger. "These observations contradict the previous assumption that, essentially, the level of arousal during sleep is low."

Instead, these fluctuations in pupil size show that even during sleep, the brain is constantly switching between a higher and lower level of activation.

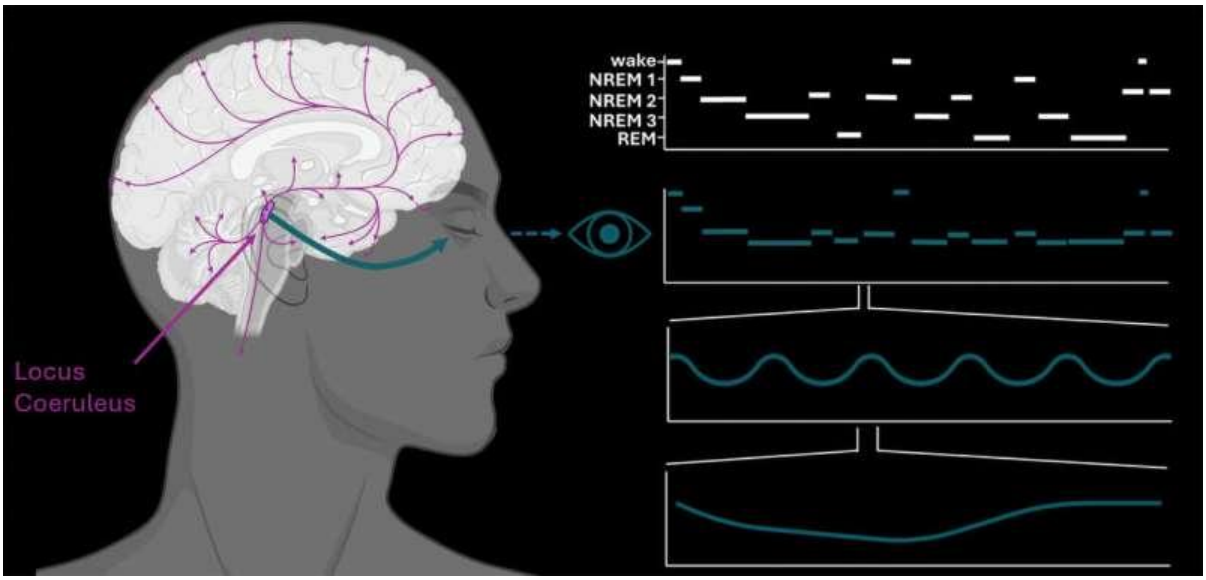
These new findings also confirm for humans what other research groups have recently discovered in studies on rodents, who also exhibit slow fluctuations in the activation level (known in the field as arousal).

New method for an old mystery

The regions of the brain which control the activation level are situated deep within the brainstem, making it previously difficult to directly measure these processes in humans during sleep. Existing methods are technically demanding and have not yet been established in this context.

The ETH researchers' study therefore relies on pupil measurements. Pupils are known to indicate the activation level when a person is awake. They can therefore be used as markers for activity in regions situated deeper within the brain.

The ETH researchers developed a new method for examining the changes in people's pupils while asleep: using a special adhesive technique and a transparent plaster, they were able to keep the eyes of the test subjects open for several hours.



The locus coeruleus regulates various areas of the brain (pink arrows). The graphics on the right show the length and type of sleep phases (white) and the fluctuations in pupil size (blue-green) that occur during them. Credit: M. Carro-Dominguez, ETH Zurich / Biorender

"Our main concern was that the test subjects would be unable to sleep with their eyes open. But in a dark room, most people forget that their eyes are still open and they are able to sleep," explains the study's lead author, Manuel Carro Domínguez, who developed the technique.

Analysis of the data showed that pupil dynamics is related not just to the different stages of sleep, but also to specific patterns of brain activity, such as sleep spindles and pronounced deep sleep waves—brain waves that are important for memory consolidation and sleep stability.

The researchers also discovered that the brain reacts to sounds with varying degrees of intensity, depending on the level of activation, which is reflected in the size of the pupil.

A central regulator of the activation level is a small region in the brainstem, known as the locus coeruleus. In animals, scientists have been able to show that this is important for the regulation of sleep stages and waking. The ETH researchers were unable to prove in this study whether the locus coeruleus is indeed directly responsible for pupil changes.

"We are simply observing pupil changes that are related to the level of brain activation and heart activity," Lustenberger explains.

In a follow-up study, the researchers will attempt to influence the activity of the locus coeruleus using medication, so that they can investigate how this affects pupil dynamics. They hope to discover whether this region of the brain is in fact responsible for controlling the pupils during sleep, and how changes in the level of activation affect sleep and its functions.

Using pupillary dynamics to diagnose illnesses

Understanding pupil dynamics during sleep could also provide important insights for the diagnosis and treatment of sleep disorders and other illnesses. The researchers therefore want to investigate whether pupil changes during sleep can provide indications of dysfunctions of the arousal system. These include disorders such as insomnia, post-traumatic stress disorder and possibly Alzheimer's.

"These are just hypotheses that we want to investigate in the future," says Lustenberger.

Another goal is to make the technology usable outside of sleep laboratories, such as in hospitals, where it could help to monitor waking in coma patients or to diagnose sleep disorders more accurately. The pupil as a window onto the brain could thus pave the way for new opportunities in sleep medicine and neuroscience.

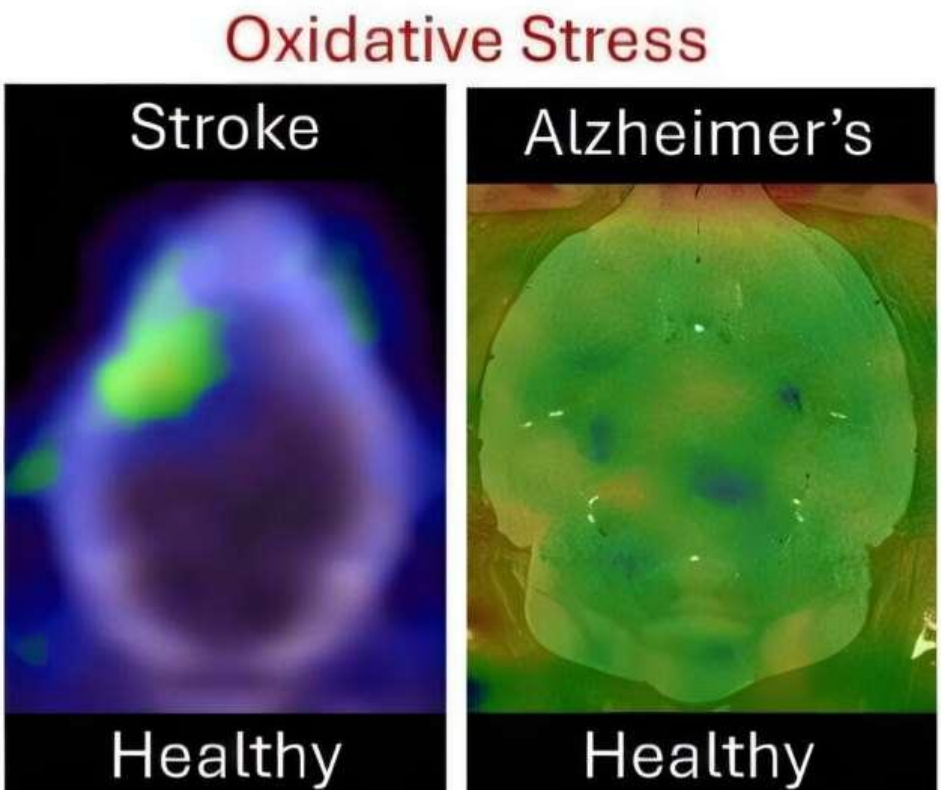
More information: Manuel Carro-Domínguez et al, Pupil size reveals arousal level fluctuations in human sleep, *Nature Communications* (2025). DOI: 10.1038/s41467-025-57289-5
Journal information: Nature Communications

Provided by ETH Zurich

MARCH 5, 2025

Repurposed amyotrophic lateral sclerosis drug becomes imaging probe to help diagnose neurodegeneration

by St. Jude Children's Research Hospital



The researchers u. Credit: sed radiolabeled fluoroedaravone to track the build-up of reactive oxygen and nitrogen species (RONS) in mouse models, the researchers could detect oxidative stress caused by a stroke in just 24 hours (left) and the early widespread signs of Alzheimer's disease (right). *Nature Biomedical Engineering* (2025). DOI: 10.1038/s41551-025-01362-3

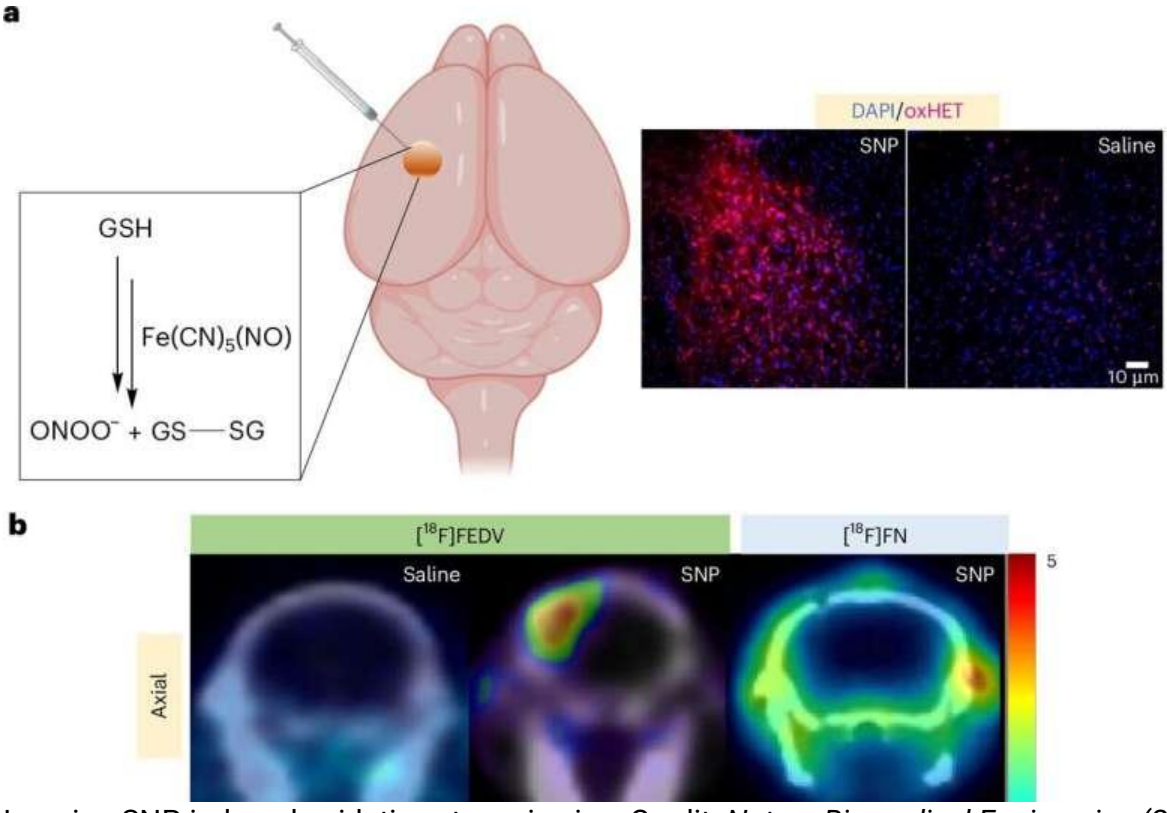
Positron emission tomography (PET) is a nuclear imaging technique used to diagnose conditions such as cancer. An innovative advance from scientists at St. Jude Children's Research Hospital is enhancing the technique's ability to check for signs of neurological disease. The researchers repurposed the drug edaravone, an antioxidant used to treat

amyotrophic lateral sclerosis (ALS), as a probe to be used with central nervous system PET imaging.

With this technique, the researchers can detect oxidative stress, which leads to brain damage, offering a clear path to detecting neurological conditions. The findings were published today in *Nature Biomedical Engineering*.

Neurodegenerative diseases, such as ALS and Alzheimer's disease, are largely diagnosed by physical symptoms that occur when treatment is often too late to be effective. Reactive oxygen and nitrogen species (RONS) are a group of chemically reactive molecules that play important roles in cell signaling and growth. However, accumulation of RONS can cause oxidative stress, leading to tissue injury and dysfunction.

Oxidative stress is associated with diseases and conditions affecting the brain and other parts of the central nervous system, resulting in neurodegeneration. Detecting oxidative stress through a noninvasive imaging technique has the potential to shift the diagnosis, and thus treatment, of conditions like ALS and Alzheimer's disease much earlier when such care can be more beneficial.



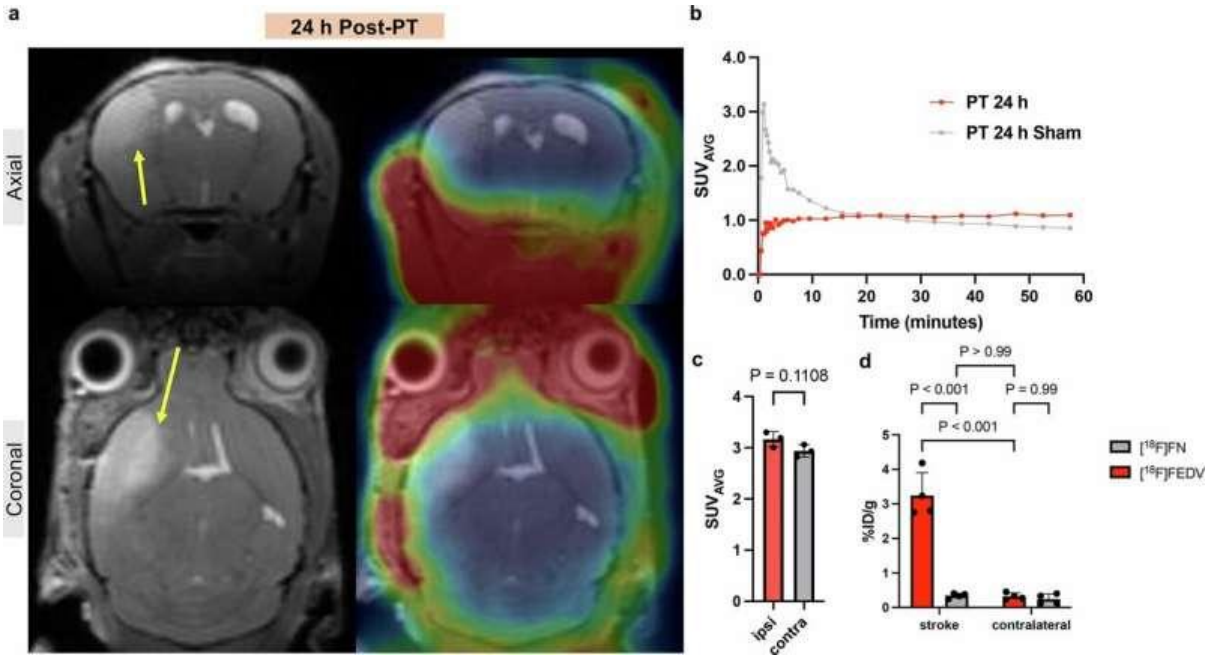
Imaging SNP-induced oxidative stress in vivo. Credit: *Nature Biomedical Engineering* (2025). DOI: 10.1038/s41551-025-01362-3

Radical burst helps track onset of brain damage

In addition to neurodegenerative disease, oxidative stress is a factor in many other neurological diseases, such as stroke. In such cases, the harm does not just come from the initial injury.

"It's the subsequent secondary injury, which usually comes from the immune response, which causes the most neurological damage," explained corresponding author Kiel Neumann, Ph.D., St. Jude Department of Radiology. "Part of that immune response is a burst of reactive oxygen and nitrogen species, sometimes called an oxidative burst."

The reactive chemicals released under oxidative bursts include hydroxyl and peroxyl radicals, short-lived chemicals that, in large amounts, can act as a detonator for a cascade of oxidative damage. As an antioxidant, edaravone naturally interacts with RONS, leading Neumann to hypothesize that the drug could be repurposed to enhance imaging efforts.



[^{18}F]FN is unable to differentiate RONS in a mouse model of stroke. Credit: *Nature Biomedical Engineering* (2025). DOI: 10.1038/s41551-025-01362-3

Neumann's team radiolabeled edaravone, replacing atoms in the molecule with radioactive isotopes to allow him to track the movement and breakdown of the drug. When administered, the radiolabeled drug releases subatomic particles called positrons in amounts unnoticeable by all but a PET scan, wherein it lights up the area where the drug accumulates: alongside the build-up of RONS.

"The goal in imaging is to promote contrast, so we want something that engages with its target rapidly but then also rapidly clears so you can see your target right away," explained Neumann. "What was unique about this drug is that when it reacts with oxidative stress, it undergoes a massive structural and polarity change which keeps it in the cell and promotes contrast."

The drug's excellent ability to bind RONS in tiny doses means it is perfectly suited for PET imaging while it can still be used as an antioxidant treatment at standard doses—a diagnosis and treatment one-two punch. "Our diagnostic tests are on the order of nanograms to micrograms of material, so the body doesn't even know it's there," Neumann said.

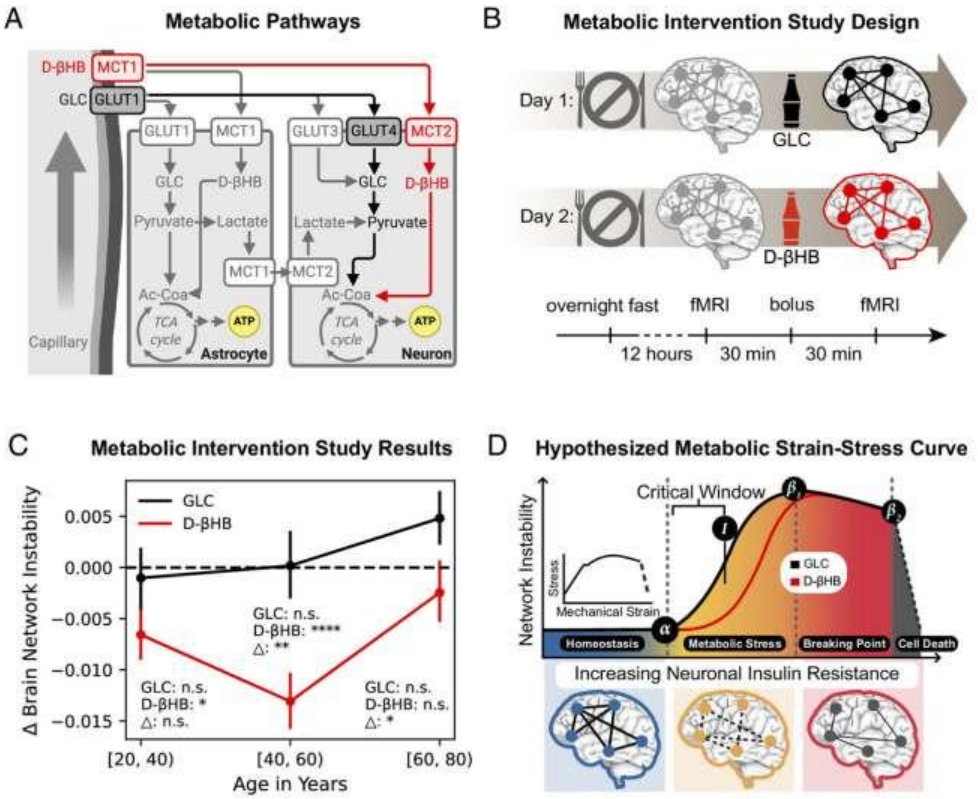
"Ultimately, our goal is to use this to impact clinical care. Therapeutic intervention using this technology for clinical disease management is the future."

More information: Justin H. Wilde et al, A positron emission tomography tracer for the imaging of oxidative stress in the central nervous system, *Nature Biomedical Engineering* (2025). DOI: 10.1038/s41551-025-01362-3
Journal information: Nature Biomedical Engineering
Provided by St. Jude Children's Research Hospital

MARCH 5, 2025

Scientists identify critical 'midlife window' for preventing age-related brain decline

by Stony Brook University



D-β-hydroxybutyrate circumvents insulin resistance to reverse brain network destabilization

during the accelerated phase of brain aging. Credit: *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2416433122
A study published in the *Proceedings of the National Academy of Sciences* has unveiled that brain aging follows a distinct yet nonlinear trajectory with critical transition points. The research, conducted by an international team of scientists led by Lilianne R. Mujica-Parodi, Ph.D., of Stony Brook University, offers new insights into when interventions to prevent cognitive decline might be most effective.

The team analyzed brain networks in more than 19,300 individuals across four large-scale datasets. Their findings reveal that functional communication between brain regions (brain networks) begins to destabilize around age 44, with the degeneration of brain networks accelerating most rapidly at age 67 and plateauing by age 90.

These transition points follow an S-shaped statistical curve with clear transition points, rather than either the late-life clinical onset or gradual linear decline previously assumed, suggesting there are specific windows when intervention could be most impactful.

"Understanding exactly when and how brain aging accelerates gives us strategic timepoints for intervention," says lead author Mujica-Parodi, Director of the Laboratory for Computational Neurodiagnostics (LCNeuro), Baszucki Endowed Chair for Metabolic Neuroscience, and Professor of Biomedical Engineering in the Laufer Center for Physical and Quantitative Biology and the Renaissance School of Medicine at Stony Brook University.

"We've identified a critical midlife window where the brain begins to experience declining access to energy but before irreversible damage occurs, essentially the 'bend' before the 'break.' During midlife, neurons are metabolically stressed due to insufficient fuel; they're struggling, but they're still viable," she explains.

"Therefore, providing an alternative fuel during this critical window can help restore function. However, by later ages, neurons' prolonged starvation may have triggered a cascade of other physiological effects that make intervention less effective."

The researchers not only mapped this aging trajectory but identified its primary driver: neuronal insulin resistance.

By comparing metabolic, vascular, and inflammatory biomarkers, they found that metabolic changes consistently preceded vascular and inflammatory ones. Gene expression analyses further implicated the insulin-dependent glucose transporter GLUT4 and the lipid transport protein APOE (a known Alzheimer's risk factor) in these aging patterns.

However, these same gene expression analyses also identified the neuronal ketone transporter MCT2 as a potential protective factor, suggesting that enhancing the brain's ability to utilize ketones—an alternative brain fuel that neurons can metabolize without insulin—might be beneficial.

This finding of the ketone transporter then motivated an interventional study, in which researchers compared administration of individually weight-dosed and calorically matched glucose and ketones to 101 participants at different stages along the aging trajectory.

The effects were striking in this cohort. Unlike glucose, ketones effectively stabilized deteriorating brain networks, but with effects that differed significantly across critical transition points. Ketones showed moderate benefits in young adults (20–39 years), showed maximum benefits during the midlife "metabolic stress" period (40–59 years), after which networks begin destabilizing, but had diminished impact in older adults (60–79 years) once the network destabilization hit maximum acceleration and the domination of compounding vascular effects.

Mujica-Parodi and co-authors say that these findings could revolutionize approaches to preventing age-related cognitive decline and neurodegenerative diseases like Alzheimer's.

Current treatments typically target symptoms after they appear, often too late for meaningful intervention. This research suggests that metabolic intervention—whether through dietary approaches like ketogenic diets or supplements—might be most effective when started in one's 40s, well before cognitive symptoms appear.

"This represents a paradigm shift in how we think about brain aging prevention," notes Botond Antal, Ph.D., Postdoctoral Associate in Biomedical Engineering at Stony Brook and first author. "Rather than waiting for cognitive symptoms, which may not appear until substantial damage has occurred, we can potentially identify people at risk through neurometabolic markers and intervene during this critical window."

From a public health standpoint, these findings could inform new screening guidelines and preventive approaches, emphasizes Mujica-Parodi. Early (midlife) identification of increasing insulin resistance in the brain (not just the blood), coupled with targeted metabolic interventions, might substantially delay cognitive aging for millions of people.

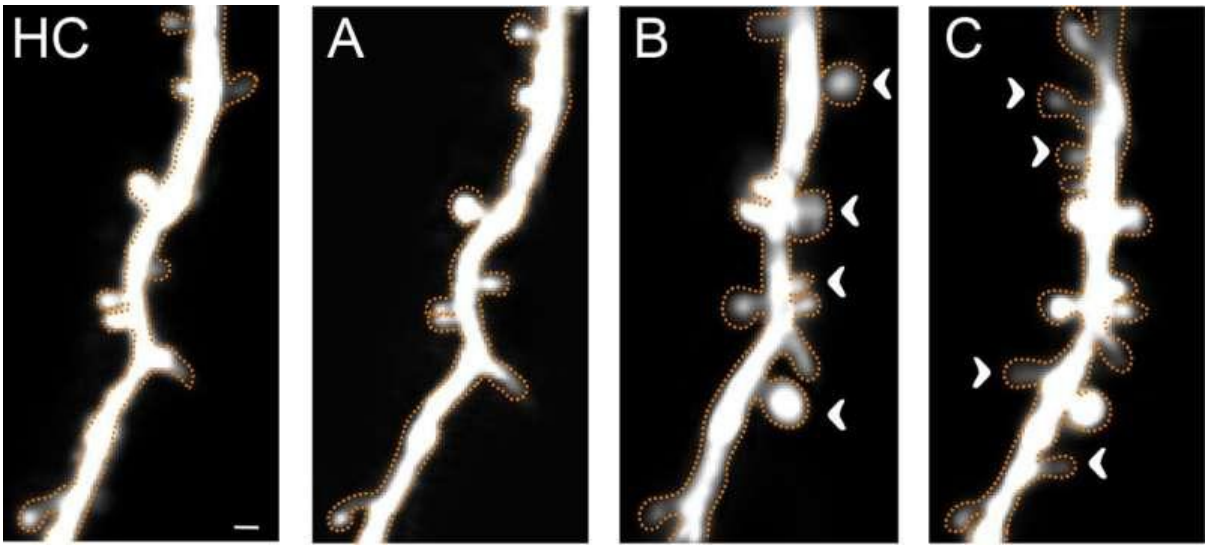
With the global population aging rapidly and dementia cases projected to triple by 2050, these insights into the timing and mechanisms of brain aging offer new hope for preventive strategies that could maintain cognitive health well into later life.

More information: Botond B. Antal et al, Brain aging shows nonlinear transitions, suggesting a midlife "critical window" for metabolic intervention, *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2416433122
Journal information: Proceedings of the National Academy of Sciences
Provided by Stony Brook University

MARCH 7, 2025

Study shows that dendritic plasticity contributes to the integration of memories

by Ingrid Fadelli, Medical Xpress



Representative example of spine dynamics during longitudinal imaging showing clustering of new spines following linked memory formation. Credit: *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01876-8

Past neuroscience studies suggest that memories of events that occurred at short time intervals from one another are often connected, via a process referred to as memory linking. While memory linking is now a well-documented phenomenon, its neural underpinnings have not been fully elucidated.

Researchers at the University of California Los Angeles (UCLA) recently carried out a study aimed at better understanding the neural processes that contribute to memory linking in the mouse brain. Their findings, published in *Nature Neuroscience*, suggest that dendritic plasticity, the adaptation of dendrites (i.e., branch-like extensions of neurons) over time, plays a key role in the linking of memories.

"A few years back, in a landmark study published in *Nature* in 2016, we demonstrated that memories formed a few hours apart are linked because they are stored in a common set of neurons in the hippocampus," Alcino Silva, senior author of the paper, told Medical Xpress. "We wanted to know: Where within these neurons are these memories stored and linked? What was causing these neurons to be recruited?"

While answering these research questions in an experimental setting was unfeasible a few years ago, since then Silva and his colleagues have developed new tools and technologies

to probe subcellular mechanisms. In collaboration with Yiota Poirazi's laboratory at the Foundation for Research and Technology in Crete, they then set out to investigate how dendritic and synaptic dynamics could contribute to memory linking, employing modeling techniques.

"In an earlier theoretical study also published in 2016, we predicted that in addition to being stored in common neuronal populations, linked memories should also reside within common dendrites within these neurons," said Poirazi.

"Inspired by these findings and with the help of our multidisciplinary team, we set out to reveal whether and how dendritic mechanisms may allow the linking of memories across time in rodent brains," added Silva.

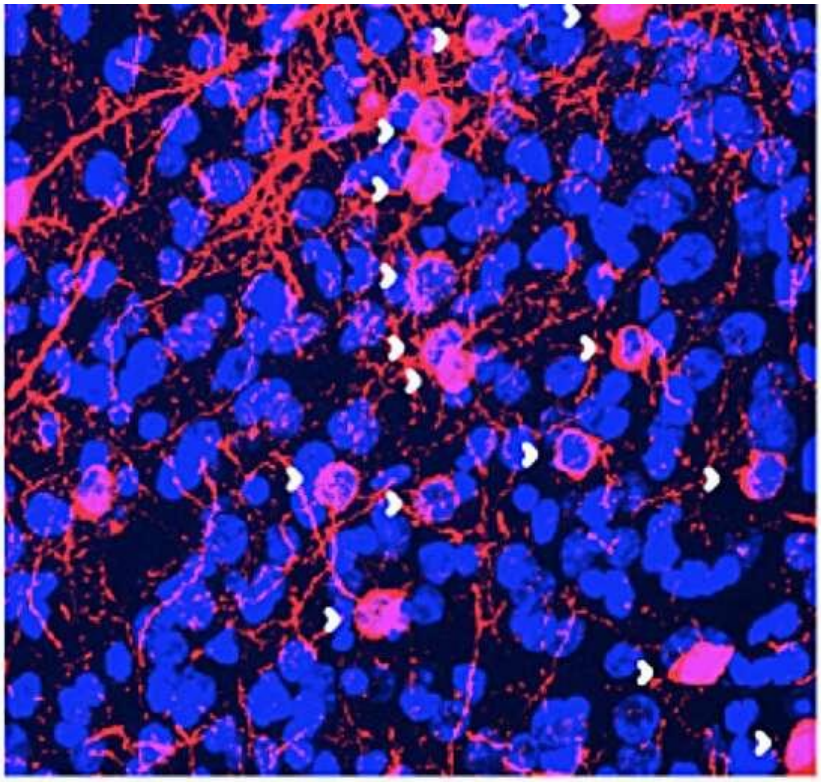
As part of their recent study, the researchers employed three different but complementary imaging techniques. Using these techniques, they visualized three distinct subcellular compartments in living mice, namely the soma, dendrites and spines from neurons.

"We showed that when mice form two memories close in time, we can see that many of the same somas, dendritic branches, and spines are involved in forming these two memories," explained Megha Sehgal, the first author and a co-corresponding author of the paper.

"In a second class of experiments, we used sophisticated genetic tagging techniques to manipulate these neuronal somas and dendrites. When we forced independent memories to be stored in the same neuronal somas or even the dendrites and found just this simple intervention in one brain region, the retrosplenial cortex, was enough to link these memories!"

Silva, Sehgal and their colleagues found that, following their experimental intervention, mice became scared of a box that was previously unimportant to them, simply because the memory of this box was stored in the same dendrites that stored memories of a box in which they experienced an electric shock. In collaboration with Poirazi and her lab, they then used computational modeling techniques to explain their observations.

"By simulating a bio-realistic network of neurons with dendrites and localized plasticity, the model showed that localized dendritic plasticity mechanisms are necessary for replicating key properties of linked memories, such as their recruitment of the same dendrites, clustering of synapses, and stability over time," said Sehgal.



Representative RSC images of cFos-tTa mice injected with TRE-hChR2-mCherry-DTE and TRE-hChR2-mCherry showing selective expression of Channelrhodopsin in dendritic segments in the presence of DTE. Credit: *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01876-8

The findings gathered by this research team suggest that the linking of memories in the mouse brain is supported by highly localized changes (i.e., within a few micrometers) on neuronal dendrites. Silva, Sehgal and their colleagues hypothesize that similar localized dendritic changes could also play a role in other types of memory processes.

"Although such localized changes have been reported in previous studies in cell cultures and brain slices, we did not know their function," said Sehgal. "To the best of our knowledge, this is the first demonstration of their usefulness in animal behavior."

This recent study could soon pave the way for further research exploring the contribution of dendritic plasticity to specific well-documented memory processes. In addition, it could help to better understand disorders associated with an impaired ability to link memories.

"Our findings are important for understanding how memories are linked across time to form memory episodes as well as for addressing memory deficits whereby memory linking is impaired, such as those linked to Alzheimer's disease," explained Poirazi.

"By providing a mechanistic understanding of memory linking, our work serves as a first step towards the development of new treatments that may target such mechanisms in order to remedy respective memory deficits."

In their future research, Sehgal and her lab at The Ohio State University will continue exploring the underpinnings of dendritic plasticity that contributes to the linking and encoding of memories. In addition, they plan to further investigate the memory-related plasticity patterns that they observed as part of their recent study.

"We discovered that compartmentalized plasticity plays a critical role in dictating how memories are stored in the future, but we do not know the underlying mechanisms," said Sehgal. "My lab is now digging deeper into the circuit and molecular processes that allow this plasticity."

Poirazi and her collaborators at the Foundation for Research and Technology are now working to extend their computational models to simulate other brain areas and their contribution to different cognitive tasks. They hope that these models will help them to better understand the role of dendritic mechanisms in learning and memory functions, while also unveiling some of their most important features.

"In parallel, given the key role of dendrites in biological learning and memory, we initiated a new research line whereby we adopt dendritic mechanisms in artificial neural network systems (e.g., Chavlis and Poirazi, *Nature Communications* 2025), with the aim of making machine learning and artificial intelligence systems more robust, intelligent and efficient, like the brain."

More information: Megha Sehgal et al, Compartmentalized dendritic plasticity in the mouse retrosplenial cortex links contextual memories formed close in time, *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01876-8
Journal information: Nature Communications , Nature , Nature Neuroscience

MARCH 7, 2025

How the brain turns sound into conversation: Study uncovers the neural pathways of communication

by Hebrew University of Jerusalem

Credit: Unsplash/CC0 Public Domain
A new study has uncovered how the brain seamlessly transforms sounds, speech patterns, and words into the flow of everyday conversations. Using advanced technology to analyze over 100 hours of brain activity during real-life discussions, researchers revealed the intricate pathways that allow us to effortlessly speak and understand.

These insights not only deepen our understanding of human connection but also pave the way for transformative advancements in speech technology and communication tools.

The study, led by Dr. Ariel Goldstein, from the Department of Cognitive and Brain Sciences and the Business School at the Hebrew University of Jerusalem, Google Research, in collaboration with the Hasson Lab at the Neuroscience Institute at Princeton University, Dr. Flinker and Dr. Devinsky, from the NYU Langone Comprehensive Epilepsy Center, has developed a unified computational framework to explore the neural basis of human conversations.

This research bridges acoustic, speech, and word-level linguistic structures, offering unprecedented insights into how the brain processes everyday speech in real-world settings.

The study, published in *Nature Human Behaviour,* recorded brain activity over 100 hours of natural, open-ended conversations using a technique called electrocorticography (ECoG).

To analyze this data, the team used a speech-to-text model called Whisper, which helps break down language into three levels: simple sounds, speech patterns, and the meaning of words. These layers were then compared to brain activity using advanced computer models.

The results showed that the framework could predict brain activity with great accuracy. Even when applied to conversations that were not part of the original data, the model correctly matched different parts of the brain to specific language functions. For example, regions involved in hearing and speaking aligned with sound and speech patterns, while areas involved in higher-level understanding aligned with the meanings of words.

The study also found that the brain processes language in a sequence. Before we speak, our brain moves from thinking about words to forming sounds, while after we listen, it works backwards to make sense of what was said. The framework used in this study was more effective than older methods at capturing these complex processes.

"Our findings help us understand how the brain processes conversations in real-life settings," said Dr. Goldstein. "By connecting different layers of language, we're uncovering the mechanics behind something we all do naturally—talking and understanding each other."

This research has potential practical applications, from improving speech recognition technology to developing better tools for people with communication challenges. It also offers new insights into how the brain makes conversation feel so effortless, whether it's chatting with a friend or engaging in a debate.

The study marks an important step toward building more advanced tools to study how the brain handles language in real-world situations.

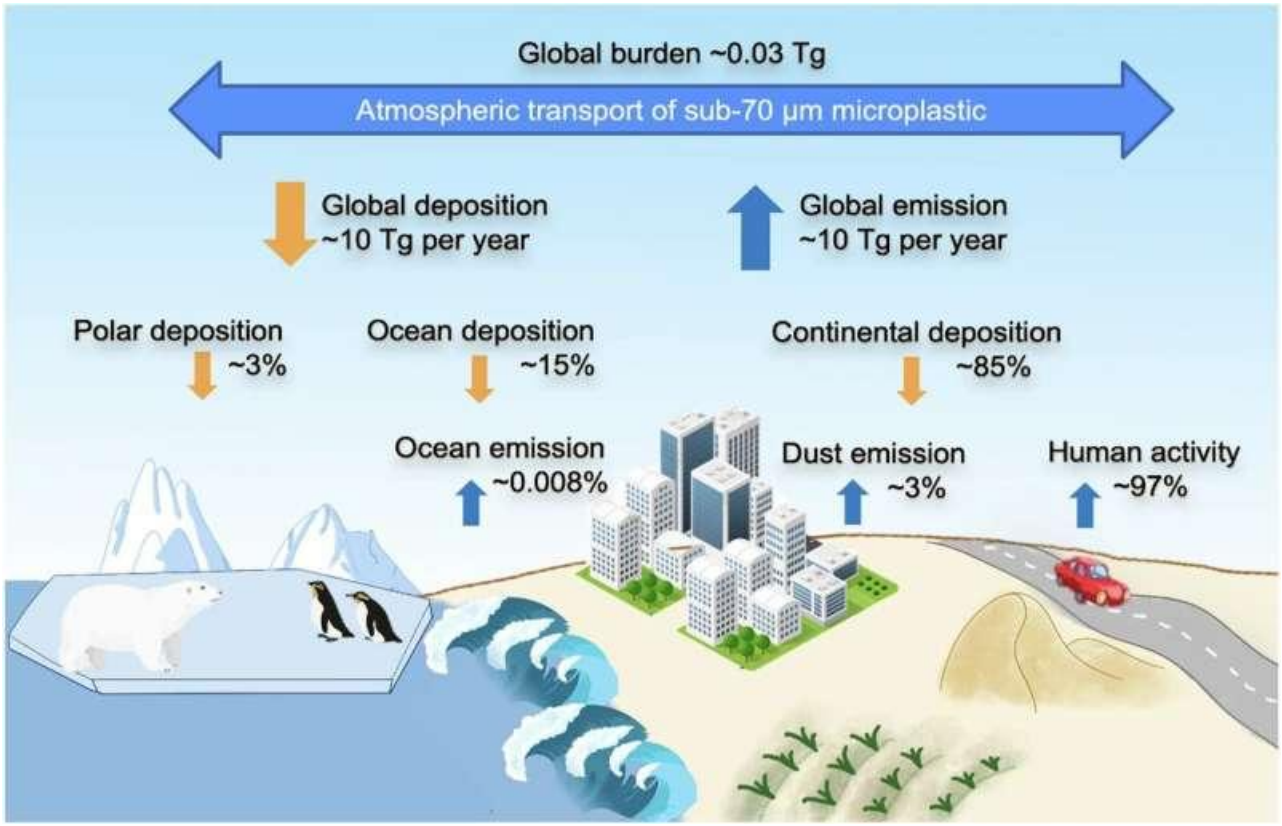
More information: A unified acoustic-to-speech-to-language embedding space captures the neural basis of natural language processing in everyday conversations, *Nature Human Behaviour* (2025). DOI: 10.1038/s41562-025-02105-9
Journal information: Nature Human Behaviour
Provided by Hebrew University of Jerusalem

Explore further

MARCH 7, 2025

Airborne microplastics: Where do they come from, where do they go?

by Denise Müller, Max Planck Society



Sources (blue) and sinks (orange) of atmospheric microplastics. Credit: *npj Climate and Atmospheric Science* (2025). DOI: 10.1038/s41612-025-00914-3

How tiny plastic particles enter the atmosphere is an important question, as airborne microplastics are a potential health threat. Using a global chemical transport model, researchers have provided evidence that, contrary to previous claims, the ocean is not a major source of microplastics to the atmosphere, but a significant sink.

Plastic dust is polluting the global environment: Microplastics—particles less than 5 mm in diameter—have been detected not only in soils, freshwater, and the ocean, but also in the air that we breathe. This could pose a threat to human health, as the smallest particles in particular can enter the respiratory system and the bloodstream.

In addition, atmospheric microplastics are transported to and deposited in the most remote corners of the planet. But how do they enter the atmosphere in the first place?

In general, the sources of microplastics are found on land—for example, fibers from synthetic clothing in domestic sewage, or car tire dust on the streets. Previous studies have suggested that a major pathway for them to enter the atmosphere is through the ocean: Microplastics are washed into rivers and carried out to the sea, where they accumulate.

Air bubbles created by sea spray, wind, and waves can lift them out of the water and into the atmosphere. However, a new study led by researchers from the Max Planck Institute for Meteorology (MPI-M) shows that the ocean's role is mainly that of a sink—not a source, as previously thought.

The ocean: A massive or a negligible source of microplastics?

The assumption that the ocean acts as a source of microplastics to the atmosphere was based on inverse modeling. In this method, the sources of a substance are inferred from measurements of its atmospheric concentration distribution.

Applied to microplastics, it led scientists to believe that there was an oceanic source of microplastics to the atmosphere of several hundred million or even several billion kilograms per year.

The exact mechanism of how this transfer works was then investigated in laboratory experiments which led to a very different conclusion: only a few thousand or hundred thousand kilograms per year seemed plausible.

Using a global atmospheric chemical transport model, an international team of researchers including former visiting researcher at MPI-M Shanye Yang and MPI-M group leader Guy Brasseur investigated whether the assumption of a small oceanic source leads to an atmospheric distribution of microplastics that is consistent with observations. The paper is published in the journal *npj Climate and Atmospheric Science*.

The result was positive. Rather than being a source, the ocean appeared to be a sink, where 15% of all airborne microplastics are deposited.

Informing pollution reduction strategies

The study also shows how size determines the transport of microplastics in the atmosphere: larger particles settle relatively quickly, either still on land or near the coastlines. Small microplastic particles can remain in the atmosphere for up to one year, facilitating their transport around the globe.

For example, the model shows that the small particles, although emitted on the continent, travel as far as the Arctic region and are deposited on snow and ice. This shows the global impact of microplastic pollution. These insights can inform pollution-reduction strategies, which should focus on the continental sources rather than the role of the ocean as a source of microplastics.

More information: Shanye Yang et al, Global atmospheric distribution of microplastics with evidence of low oceanic emissions, *npj Climate and Atmospheric Science* (2025). DOI: 10.1038/s41612-025-00914-3
Journal information: npj Climate and Atmospheric Science
Provided by Max Planck Society

A little-known brain region at the heart of communication

Published March 08, 2025

Nature Communications

When we speak, emphasizing a word or raising our voice on a syllable can radically change the meaning of a sentence.

For example, saying "Did you do it?" with a rising intonation suggests a question, while "You did it." with a falling tone implies a statement. Similarly, stressing a word gives it particular weight and thus intention, as in the case of saying "it was [YOU] who did it": this points an accusatory finger at our interlocutor. A recent study reveals that our brain processes these melodic nuances much earlier than previously thought, thanks to a little-known brain region.

This discovery, published in *Nature Communications*, improves our understanding of language perception. By analyzing the brain activity of epileptic patients, researchers have identified the key role of Heschl's gyrus, in the cerebral cortex, in interpreting

variations in voice pitch, called prosody. These variations, often imperceptible, are nevertheless essential for grasping the intention and emotion behind words.

Heschl's gyrus: much more than a simple sound processor

Heschl's gyrus, a region of the auditory cortex, was until now considered a simple sound detector. Researchers have discovered that it also plays a role in transforming tone variations into meaningful linguistic information. Thus, this region does not merely process raw sounds, but categorizes pitch accents to extract meaning.

This ability to interpret prosody is unique to humans. Experiments conducted on macaques have shown that although these animals perceive the same acoustic variations, they do not process them as linguistic units. This suggests that this skill is the result of our notion of language.

Using intracranial recordings in epileptic patients, researchers observed that Heschl's gyrus encodes voice pitch variations into distinct linguistic units. These units, called pitch accents, are processed separately from the sounds that make up words, revealing an unsuspected specialization of this brain region.

Practical implications for health and technology

These findings could improve the management of language disorders, such as autism or stroke sequelae. By better understanding how the brain processes prosody, therapies could become more targeted and effective. For example, specific exercises could help patients better interpret intonations, thereby improving their daily communication.

Moreover, this discovery could enhance voice recognition systems. Currently, voice assistants struggle to interpret emotional nuances or intentions behind words. By integrating these mechanisms, technologies could become more intuitive and human-like, enabling more natural interaction between humans and machines.

This breakthrough opens up new perspectives for neuroscience research. By studying the role of Heschl's gyrus in more detail, scientists could discover new avenues for treating other neurological disorders related to auditory perception or language. These findings could also shed light on the brain mechanisms involved in language learning.

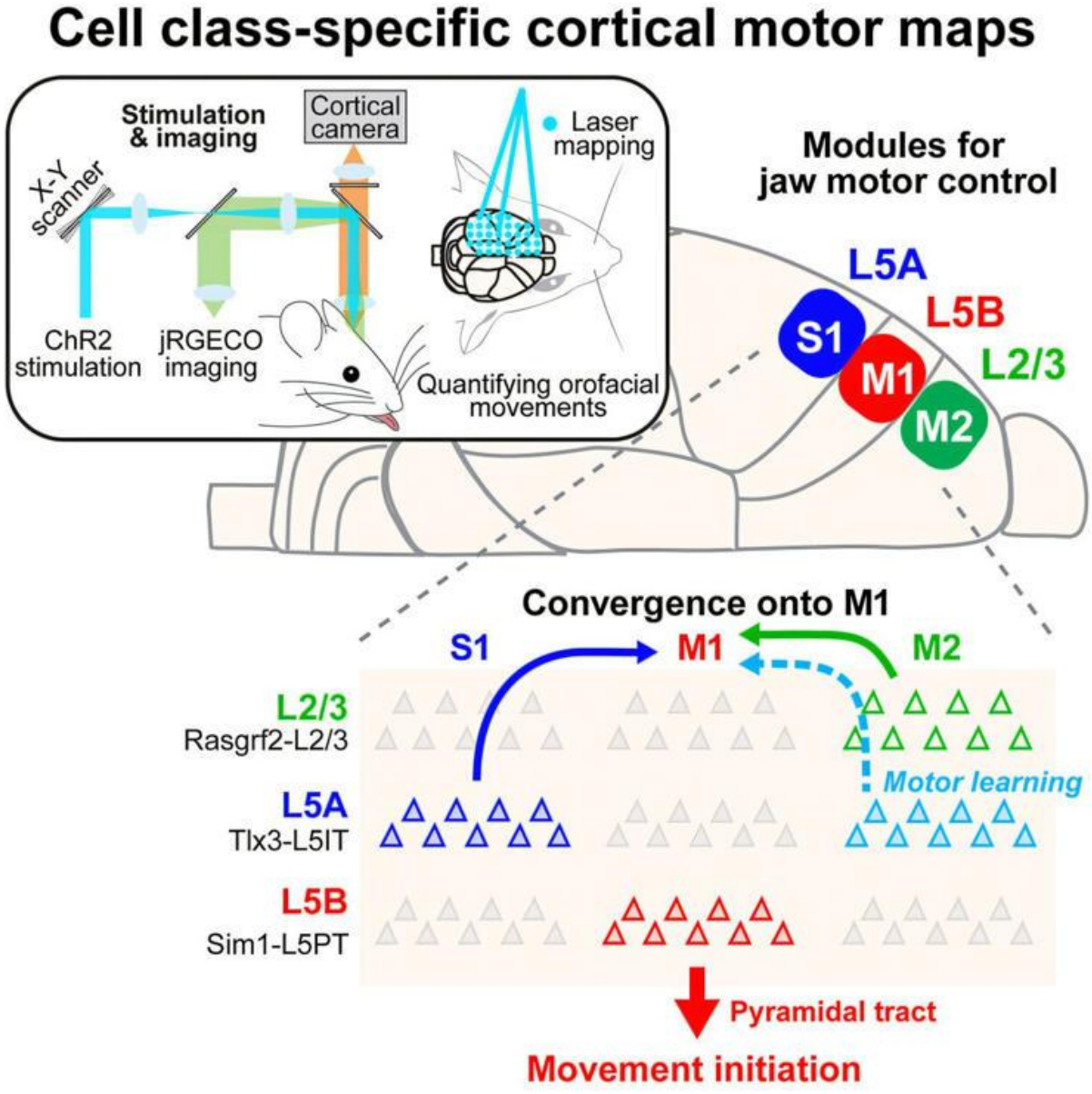
To go further: How does the brain process sounds?

The brain breaks down sounds into several stages. First, primary auditory regions, such as Heschl's gyrus, process basic acoustic characteristics, such as pitch, intensity, and timbre. This information is then transmitted to more specialized areas for further analysis.

Next, regions such as the superior temporal gyrus intervene to interpret these sounds in a linguistic context. They allow for the distinction of phonemes, words, and sentences.

This information is then relayed to associative areas that link it to memory, emotions, and other cognitive functions. This explains why a particular intonation can evoke memories or elicit emotional reactions.

Unraveling the brain's hidden motor modules



Credit: Current Biology (2025). DOI: 10.1016/j.cub.2025.01.056

For nearly a century, scientists have known that different parts of the human brain's cortex control different body movements. This fundamental discovery dates to the 1930s, when neurosurgeons used electrical stimulation to map how different cortical regions correspond to different body parts.

But can these regions be further broken down into even smaller functional components? Researchers have long suspected that cortical units for specific body movements are more complex than simple patches in the cortex. Studies have identified various types of neurons stacked in multiple layers across the neocortex, but without a clear picture of how these neurons interact to produce a specific movement at the level of brain networks.

A new study from EPFL, the University of Cambridge and Kumamoto University, has used advanced optical and genetic techniques to reveal that a movement unit in the neocortex contains distinct neural modules—each localized in different areas that have classically been assigned to planning, executing and sensing movements.

More importantly, these modules change and adapt as skills are learned, providing a new framework for understanding how the brain refines motor control.

The study was led by Keita Tamura, Pol Bech, and Carl Petersen at EPFL's Brain Mind Institute. Keita Tamura is also affiliated with the University of Cambridge and Kumamoto University. The work is published in *Current Biology*.

Horizontal network vs. vertical columns

The researchers studied movement control in mice by combining optogenetics (a technique for controlling neural activity with light), high-speed cortical imaging, and machine learning-based movement tracking. This approach allowed them to selectively activate different types of neurons and observe how the resulting signals traveled through the brain to evoke movements.

To test whether the spatially-broad movement unit of the cortex could be broken down into smaller elements, the researchers first mapped where excitatory

cortical neurons overall control mouth movements. Then, they selectively stimulated different neuron types.

The results were surprising: rather than being evenly distributed, different types of neurons control movement from different, distinct sub-regions within the broad movement unit. These sub-regions form a horizontal network of specialized modules, which challenges the traditional view that the cortex is organized into vertical columns—the idea that different types of neurons are stacked vertically from the brain's surface to its deeper layers and function as processing units.

Instead, the study suggested that a cortical movement unit has a more horizontally distributed and modular organization, where neuron-type-specific modules interact dynamically across different regions of the cortex.

The brain re-networks and adapts

For example, studying mouth movements of the mice, the researchers found that within the broad cortical unit that controls mouth movements there are smaller groups of neurons, each consisting of a specific type of neuron. And even though each type of neuron is spread out evenly, they form functional clusters in distinct cortical regions involved in planning, executing, or sensing movements. In fact, activity in these clusters consistently flowed towards one of those cortical regions for the execution of movements.

This challenges the idea that the brain processes movement in neat, vertical columns. Instead, the study suggests a more flexible and horizontally interconnected system, where different neuron groups work together for a specific function.

Furthermore, the researchers found that as mice learned new motor skills, some of these modules expanded into other cortical areas. This suggests that learning skills involves rewiring connections between these neural modules. In other words, the brain doesn't just get "better" at a movement—it reorganizes itself to optimize control.

The discovery has broad implications. Understanding how motor units are structured and how they change with learning could help researchers develop

better treatments for conditions like stroke or brain injuries. If scientists can reveal how a network of the modules could compensate their function when one of the modules loses its function, they may be able to develop more efficient and precise rehabilitation therapies for example, potentially restoring lost motor function.

More information: Keita Tamura et al, Cell class-specific orofacial motor maps in mouse neocortex, *Current Biology* (2025). DOI: 10.1016/j.cub.2025.01.056. www.cell.com/current-biology/f … 0960-9822(25)00119-8

Provided by Ecole Polytechnique Federale de Lausanne

Pupils reveal our brain activity 👁️

Published by Cédric, March 10, 2025 at 02:00 AM

Article author: Cédric DEPOND

Source: Nature Communications

The pupils, those small black circles at the center of our eyes, could well become a key to understanding sleep. A team of researchers has discovered that their size constantly varies during sleep, reflecting brain activity that is much more intense than previously imagined.

This study, conducted by scientists at ETH Zurich, reveals that the brain remains partially awake even during rest. The pupils, by changing size, betray these

fluctuations in brain activation, thus offering a new tool to explore the mechanisms of sleep.

Pupils, witnesses of brain activity

The researchers have developed a novel technique to observe pupils during sleep. Using a device that keeps the eyes open, they were able to track pupillary variations over several hours. These measurements revealed that pupils react to different stages of sleep, such as slow waves or sleep spindles.

These fluctuations reflect the brain's state of wakefulness, challenging the idea of a completely inactive brain during rest. The researchers also observed that the brain reacts differently to sound stimuli depending on its level of activation, which is reflected in changes in pupil size.

The results suggest that pupils act as precise indicators of brain activity. This discovery opens the way to a better understanding of the mechanisms of sleep and their links with essential functions such as memory or the regulation of wakefulness.

Promising implications for sleep medicine

These findings could transform the diagnosis and treatment of sleep disorders. By analyzing pupillary dynamics, researchers hope to better understand pathologies such as insomnia or post-traumatic stress. These variations could also serve as markers to monitor wakefulness in comatose patients.

In the long term, this technology could be used outside specialized laboratories, for example in hospitals. It would improve the monitoring of patients with sleep disorders or consciousness disorders, offering more precise and less invasive diagnostic tools.

Pupils, as windows to the brain, open new perspectives for research and medicine. These advances could also contribute to the study of neurodegenerative diseases, such as Alzheimer's, by providing clues about dysfunctions in brain activation.

To go further: why do pupils change size?

The size of the pupils is regulated by muscles in the iris, which contract or dilate in response to light and brain activity. These changes are controlled by the autonomic nervous system, which manages the body's involuntary functions. During sleep, pupillary variations reflect the brain's state of activation, thus providing a valuable indicator of neural activity.

Pupils also react to internal stimuli, such as emotions or stress levels. For example, in cases of surprise or fear, they dilate rapidly. These reactions are linked to the activity of deep brain regions, such as the locus coeruleus, which plays a key role in

modulating wakefulness and attention.

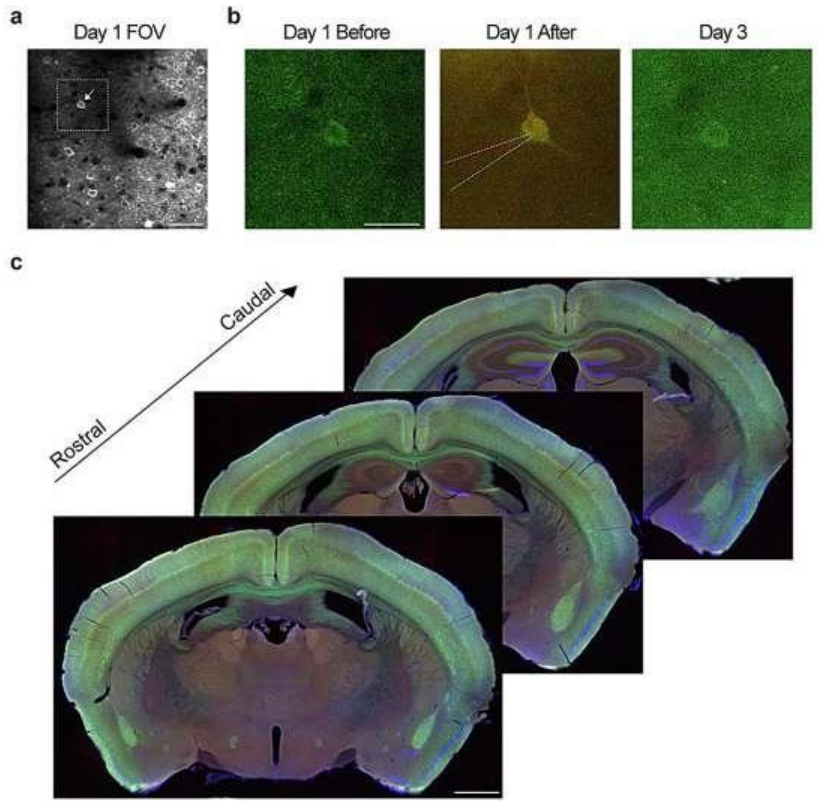
During sleep, pupillary fluctuations are correlated with specific phases, such as sleep spindles or slow waves. These variations allow researchers to study the mechanisms of sleep regulation and better understand how the brain transitions from a state of rest to a state of partial wakefulness.

Finally, changes in pupil size could serve as markers to diagnose sleep disorders or dysfunctions in brain activation. This non-invasive approach opens new perspectives for neuroscience research and sleep medicine.

MARCH 10, 2025

Researchers map how individual neurons encode behavioral states

by Justin Jackson , Medical Xpress



bsence of presynaptic labeling in sham single-cell-based monosynaptic input tracing experiments. Credit: *Nature* (2025). DOI: 10.1038/s41586-025-08631-w

National Institutes of Health researchers have mapped how individual neurons in the primary somatosensory cortex receive brain-wide presynaptic inputs that encode behavioral states, refining our understanding of cortical activity.

Neurons in the primary somatosensory cortex process different types of sensory information and exhibit distinct activity patterns, yet the cause of these differences has remained unclear. Previous research emphasized the role of motor cortical regions in movement-related processing, but also recognized that the thalamus plays a role beyond sensory relay.

Using high-resolution single-cell mapping to trace neuronal connectivity, the team revealed that thalamic input is the primary driver for movement-correlated neurons, while motor cortical input plays a smaller role.

In the study, "Brain-wide presynaptic networks of functionally distinct cortical neurons," published in *Nature*, NIH researchers used two-photon calcium imaging, optogenetics, neuropharmacology, and single-cell-based monosynaptic retrograde tracing to map presynaptic networks of individual neurons in the primary somatosensory cortex of mice. Neuronal activity was recorded over multiple days as the mice engaged in spontaneous movements.

Neurons encoding behavioral states received significantly fewer inputs from motor cortical areas and more from thalamic regions, particularly the ventral posteromedial nucleus. Optogenetic suppression of thalamic input reduced behavioral state-dependent activity, while blocking neuromodulatory inputs such as acetylcholine and noradrenaline had minimal effect.

Cortical state shifts were found to be stable across multiple days, contradicting earlier models that described them as transient. Even after pharmacological blocking of neuromodulatory inputs, the neuronal activity patterns associated with behavioral states remained intact, suggesting that glutamatergic synaptic input plays a dominant role in sustaining these representations.

Mapping presynaptic networks at a single-cell level offers a new perspective on how individual cortical neurons integrate diverse inputs to encode behavior. Findings may inform future research on neurological disorders where disrupted connectivity affects behavior and perception.

A research briefing, "Diversity in neuronal activity could be caused by differences in inputs," by study authors Ana R. Inácio and Soohyun Lee, also published in *Nature*, expands on the significance of these findings.

Functionally distinct neurons, they point out, exhibit characteristic presynaptic networks, with movement neurons receiving a higher proportion of inputs from thalamic nuclei and fewer from motor cortical areas. These anatomical biases shape movement neuron identity within the somatosensory cortex.

They also explore broader implications, noting that behavioral state signals modulate neuronal activity through mechanisms beyond direct sensory feedback. Movement neuron activity persisted even when sensory input from the whisker pad was blocked, suggesting additional influences and supporting the role of thalamic input.

Neuromodulatory signals were considered, but direct release in the somatosensory cortex did not drive movement neuron activity, leaving open the possibility of indirect effects through thalamic projections.

The authors emphasize the need for further research into the nature of these behavioral state signals and their role in neuronal communication. Future studies, they suggest, could compare connectivity patterns across neurological disorders, potentially informing new therapeutic approaches.

More information: Ana R. Inácio et al, Brain-wide presynaptic networks of functionally distinct cortical neurons, *Nature* (2025). DOI: 10.1038/s41586-025-08631-w

Diversity in neuronal activity could be caused by differences in inputs, *Nature* (2025). DOI: 10.1038/d41586-025-00634-x
Journal information: Nature

Scientists issue dire warning: Microplastic accumulation in human brains escalating

A new study published in *Nature Medicine* has revealed the presence of microplastics – tiny fragments of degraded plastic – in human brain tissue. While previous research has identified microplastics in organs such as the liver, kidneys, and placenta, this study suggests that the brain may be especially vulnerable to these tiny synthetic particles. The findings raise pressing questions about the potential effects of plastic buildup on brain health, particularly in relation to neurodegenerative diseases.

The amount of microplastics and nanoplastics in our environment has grown exponentially over the last 50 years. These tiny plastic particles, ranging in size from microscopic to the width of a pencil eraser, are now found everywhere – in the air we breathe, the water we drink, and the soil where our food grows. While it is known that these particles are making their way into the human body, lodging in organs like the liver, kidneys, and even the placenta, the extent of their accumulation and their potential for harm are not fully understood.

Although some studies in cells and animals have shown negative effects, those studies often used amounts of microplastics much higher than what humans are

typically exposed to. A real understanding of the issue requires knowing how much plastic is actually accumulating in different human tissues. Until recently, we lacked reliable methods for measuring these tiny particles, particularly the smallest ones (nanoplastics), in human tissues.

Researchers at the University of New Mexico Health Sciences, led by toxicologist Matthew Campen, developed a new way to detect and measure microplastics in human tissue. They previously used this method to examine placentas and testes. In this new study, they applied the technique to human brain tissue.

The brain tissue samples came from the New Mexico Office of the Medical Investigator, which keeps tissue from autopsies for several years. The researchers compared older tissue samples (from around 2016) with more recent samples (from 2024). All the brain tissue analyzed was from the frontal cortex, the area of the brain located behind the forehead.

To measure the microplastics, the researchers first chemically dissolved the tissue. This created a liquid mixture. They then spun this mixture at very high speeds in a machine called a centrifuge. This process separated out any undissolved materials, including plastics, into a small pellet. Next, they heated this pellet to a very high temperature (600 degrees Celsius), a process that breaks down the plastic.

As the plastics burned, they released gases. The researchers then used a sophisticated instrument called a mass spectrometer to identify the specific types of plastic based on the gases released. This allowed them to determine both the quantity and type of plastic present in the original brain tissue. The team could identify 12 different polymers. In addition to this chemical analysis, the researchers also used powerful microscopes, including a transmission electron microscope, to directly visualize the plastic particles in the tissue.

The researchers found surprisingly high levels of microplastics in the brain tissue. The concentration of plastics in the brain was much greater than that found in the liver or kidney samples. It was also higher than levels previously reported in placentas and testes. The median amount of total plastics for 2024 brain samples was 4917 micrograms per gram, and for 2016 samples, it was 3345 micrograms per gram. For comparison, the 2024 liver and kidney samples were 433 and 404 micrograms per gram, respectively.

Even more concerning was the finding that the amount of plastic in the brain was increasing over time. Brain tissue samples from 2024 had significantly higher levels of microplastics than samples from 2016, representing an approximate 50% increase in just eight years. The predominant type of plastic found in the brain was polyethylene, a common plastic used in packaging, bottles, and cups.

Using electron microscopy, the researchers were able to see very small, sharp-edged plastic particles, some as small as 200 nanometers in size (which is only slightly larger than some viruses). These tiny particles are small enough to potentially cross the protective barrier that normally separates the bloodstream from the brain, although the exact mechanism by which these plastics are entering the brain is still unknown.

To look at trends over a longer time period, the researchers also analyzed brain tissue samples from the eastern United States, dating back as far as 1997. These older samples showed lower levels of microplastics, supporting the idea that plastic accumulation in the brain is increasing over time.

Another striking finding was that brain tissue from individuals who had been diagnosed with dementia contained significantly higher levels of microplastics – up to 10 times more – than brain tissue from people without dementia. While the study does not establish a direct causal link between plastic accumulation and neurodegenerative diseases, it raises important questions. The researchers speculate that microplastics could contribute to neurological conditions by obstructing blood flow, interfering with neural connections, or triggering inflammation in the brain.

“We start thinking that maybe these plastics obstruct blood flow in capillaries,” Campen said. “There’s the potential that these nanomaterials interfere with the connections between axons in the brain. They could also be a seed for aggregation of proteins involved in dementia. We just don’t know.”

He believes that food, especially meat, is the primary source of microplastics entering the body, as commercial meat production tends to accumulate plastic particles within the food chain.

“The way we irrigate fields with plastic-contaminated water, we postulate that the plastics build up there,” Campen said. “We feed those crops to our livestock. We

take the manure and put it back on the field, so there may be a sort of feed-forward biomagnification."

How to Avoid Microplastics and Future Research Directions

A separate commentary on the study, published in *Brain Medicine*, emphasized the significance of these findings and the urgent need for further investigation. The commentary noted that while the presence of microplastics in the human brain is concerning, scientists still do not fully understand their impact on brain function. It is unclear whether microplastics actively contribute to neurodegenerative diseases or whether people with dementia accumulate more plastic simply because their brains are less able to clear it.

"The dramatic increase in brain microplastic concentrations over just eight years, from 2016 to 2024, is particularly alarming," said Nicholas Fabiano from the University of Ottawa's Department of Psychiatry, the lead author of the commentary. "This rise mirrors the exponential increase we're seeing in environmental microplastic levels."

"It is important for the public to be aware of the increasing amounts of microplastics in the environment and uptake into our bodies. We should also understand the methods available to help reduce microplastic intake while research continues seeking methods to their removal from our bodies, which continues to be scarce in evidence."

Animal studies have suggested that microplastics could affect brain health. Experiments on fish have shown that exposure to nanoplastics impairs swimming ability and hunting behavior. In mice, prolonged exposure to microplastics led to memory deficits, inflammation, and reduced levels of key proteins involved in brain function. While these studies indicate potential risks, more research is needed to determine whether similar effects occur in humans.

The commentary also highlighted the increasing presence of microplastics in food and water. People who drink bottled water, for example, ingest significantly more microplastics than those who consume tap water. Heating food in plastic containers has been shown to release billions of plastic particles into food, raising

concerns about dietary exposure. Other sources of microplastic ingestion include seafood, processed foods, and even tea bags, which can release millions of tiny plastic particles when steeped in hot water.

“Bottled water alone can expose people to nearly as many microplastic particles annually as all ingested and inhaled sources combined,” said Brandon Luu, an Internal Medicine Resident at the University of Toronto. “Switching to tap water could reduce this exposure by almost 90%, making it one of the simplest ways to cut down on microplastic intake.”

“Heating food in plastic containers—especially in the microwave— can release substantial amounts of microplastics and nanoplastics,” he explains. “Avoiding plastic food storage and using glass or stainless steel alternatives is a small but meaningful step in limiting exposure.”

Efforts to reduce microplastic exposure may help limit their accumulation in the body, but it is unclear whether this would lead to a reduction in brain plastic levels over time. The commentary suggested that more studies should focus on potential methods of eliminating microplastics from the body. Some research has indicated that plastic-related chemicals like bisphenol A can be excreted through sweat, raising the possibility that exercise or sauna use could aid in microplastic removal. However, no direct evidence currently exists to confirm whether the human body can effectively clear accumulated microplastics.

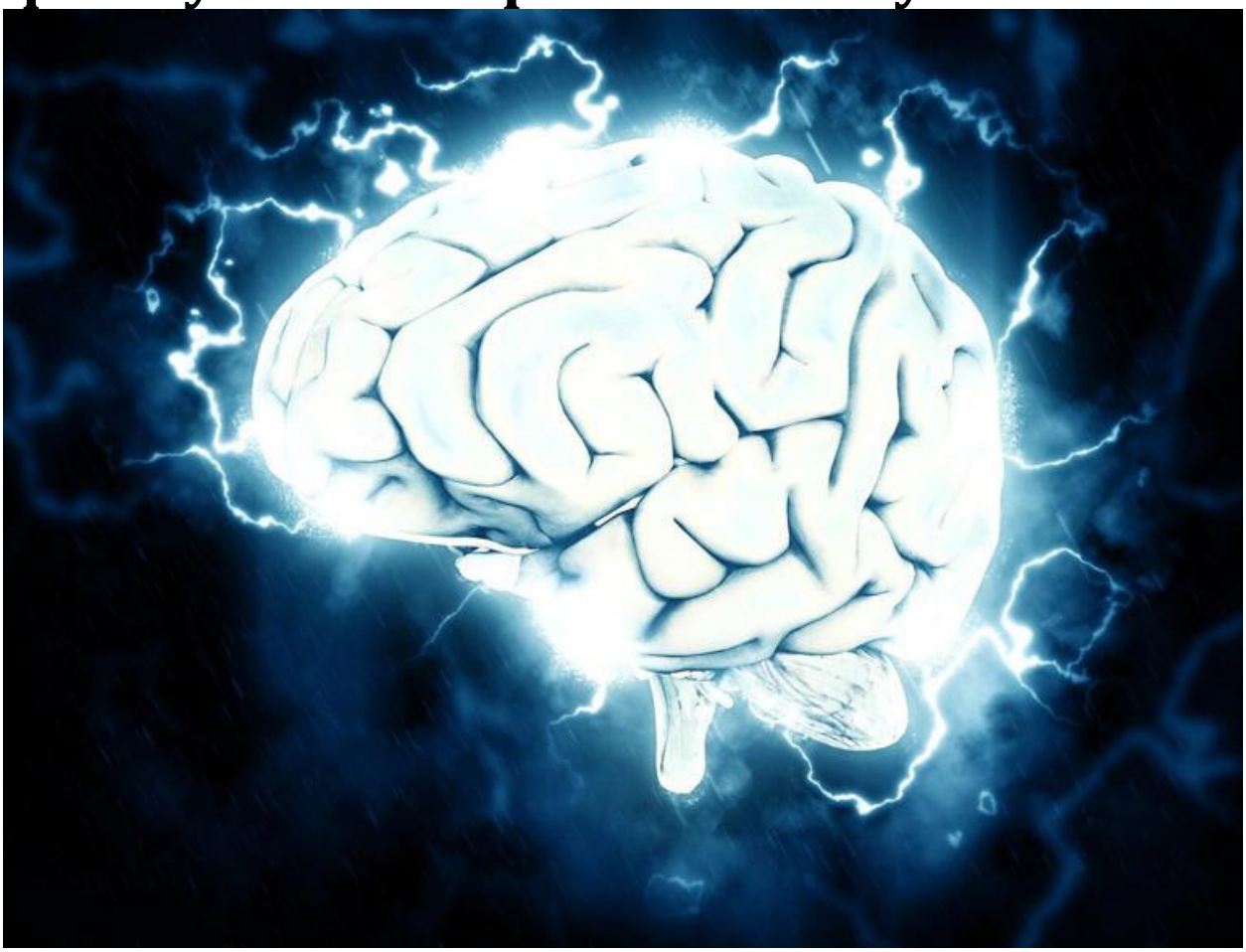
The commentary concludes by emphasizing the need for more research to establish safe exposure limits for microplastics and to understand the long-term health consequences of exposure. Large-scale studies in humans are needed to determine the relationship between microplastic exposure and the development of chronic diseases. Improved methods for measuring microplastics in living humans are also essential for tracking accumulation and assessing the effectiveness of strategies to reduce exposure. It is also important to research ways to remove plastics from the body.

“We need more research to wrap our heads around microplastics—rather than wrapping our brains in them—since this could be one of the biggest environmental storms most people never saw coming,” remarked David Puder, host of the Psychiatry & Psychotherapy Podcast.

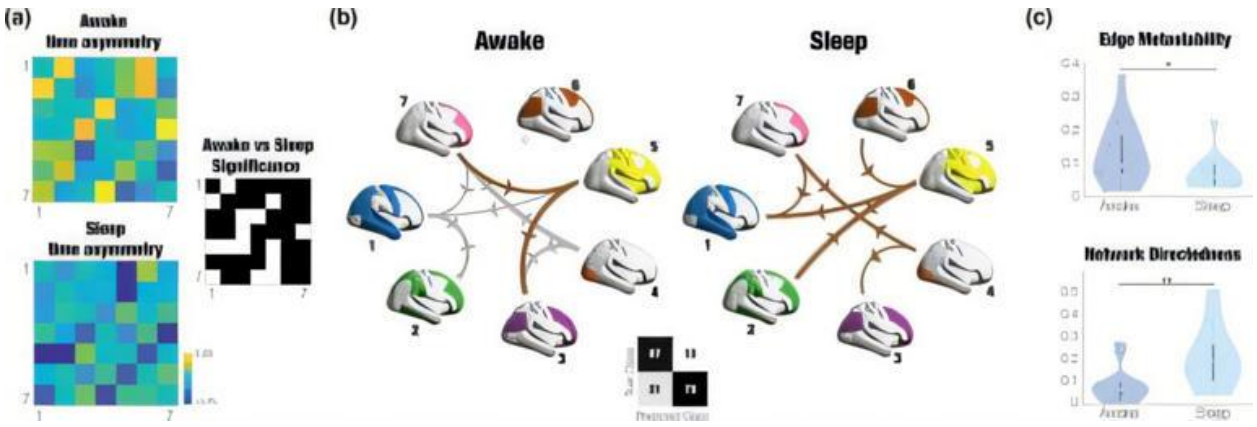
The study, "Bioaccumulation of microplastics in decedent human brains," was authored by Alexander J. Nihart, Marcus A. Garcia, Eliane El Hayek, Rui Liu, Marian Olewine, Josiah D. Kingston, Eliseo F. Castillo, Rama R. Gullapalli, Tamara Howard, Barry Bleske, Justin Scott, Jorge Gonzalez-Estrella, Jessica M. Gross, Michael Spilde, Natalie L. Adolphi, Daniel F. Gallego, Heather S. Jarrell, Gabrielle Dvorscak, Maria E. Zuluaga-Ruiz, Andrew B. West, and Matthew J. Campen.

The commentary, "Human microplastic removal: what does the evidence tell us?," was authored by Nicholas Fabiano, Brandon Luu, and David Puder.

Model uses quantum mechanics to show how the brain makes decisions more quickly than computers in risky situations



In research inspired by the principles of quantum mechanics, researchers from Pompeu Fabra University (UPF) and the University of Oxford reveal new findings to understand why the human brain is able to make decisions quicker than the world's most powerful computer in the face of a critical risk situation. The human brain has this capacity despite the fact that neurons are much slower at transmitting information than microchips, which raises numerous unknown factors in the field of neuroscience.



(a) The two matrices of the shifted functional connectivity between seven manifold networks reflect different interactions in wakefulness (top) and deep sleep (bottom). (b) These time asymmetries are illustrated (for the top 20%) of arrows between the seven manifold networks for awake vs. sleep, where the grey arrows correspond to negative and brown to positive interactions, and their thickness to the value of these interactions. (c) The spatiotemporal characteristics in the CHARM latent space can be captured by the Edge metastability which is significantly different between awake and sleep (upper panel). Credit: Deco, G.; Sanz Perl, Y.; Kringelbach M.L

The research is published in the journal *Physical Review E*.

It should be borne in mind that in many other circumstances, the human brain is not quicker than technological devices. For example, a computer or calculator can resolve mathematical operations far faster than a person. So, why is it that in critical situations—for example, when having to make an urgent decision at the wheel of a car—the human brain can surpass machines?

Most accurate computational model yet to analyze connections between farthest neurons

This recent research clarifies this matter thanks to the design of a new model of brain computational analysis, called CHARM (Complex Harmonics Decomposition). It is the most accurate model to date for examining the

functions of long-distance brain connections, which link neurons that are far apart and play a fundamental role in the brain dynamics that are activated when making critical decisions. It is also the first model to apply quantum mechanics as an instrument for analyzing the brain.

The UPF and Oxford researchers describe this model in their study. The principal author of the article is Gustavo Deco, director of the Computational Neuroscience group at the UPF Center for Brain and Cognition (CBC). The principal investigator is Morten L. Kringelbach (Centre for Eudaimonia and Human Flourishing at Linacre College, University of Oxford and Center for Music in the Brain at the University of Aarhus). Also co-authoring the article is Yonatan Sanz (CBC-UPF and University of Buenos Aires).

Long-distance neural connections are comparable to those connecting computers in distant countries

To design the CHARM model, the researchers started with a paradigm of analysis of brain dynamics that we could compare to the Internet. In certain scenarios, such as risk situations, neurons distributed in different brain regions, both close to and far from each other, are joined by different connections. These connections enable pooling the information processing power of all the neurons in the network.

Thus, although groups of neurons located in different brain regions have a limited capacity to transmit information, when they pool their resources in a network, they attain far greater processing power. This paradigm has gained strength over the past decade, as opposed to the traditional approach whereby neural regions only function in a localized manner.

According to the distributed paradigm, the CHARM model allows examining the specific functions of the connections between neurons of brain regions that are distant from each other. Following the parallel with the Internet, we could compare these connections with the ones that allow us to relate a person located in Barcelona with another in Sydney.

In a critical state, the efficiency of long-distance neural connections is enhanced

The researchers have found that the efficiency of long-distance connections is enhanced when the brain is dominated by critical dynamics, which lead it to a state of transition between order and chaos.

"We could assimilate this state to a transitional phase like the process whereby water becomes ice. At this critical point, the brain has exacerbated properties," Deco explains.

The CHARM model has enabled ascertaining precisely the functions of these long-distance connections in this or other states, for the first time integrating the principles of quantum mechanics into a system of computational brain analysis. Deco (UPF) points out that the functioning of the brain is not quantum, but the equations based on the principles of quantum physics—such as the Schrödinger equation—are an excellent tool for analyzing its dynamics.

In this regard, the UPF full professor says, "The brain's ability to make such complex and sensitive calculations at the same time, despite the lentitude of neuronal transmission, has always been a fascinating enigma. By adopting the Schrödinger equation we can model these interactions with a degree of precision that was previously beyond our reach."

Findings can improve diagnosis of neurological diseases, pave the way towards new AI research

The research findings can also have numerous applications for improving the diagnosis and treatment of various neurological diseases, such as schizophrenia or depression. Long-distance neuronal connection dysfunctions are key to understanding the origin of these diseases.

Moreover, the study opens the door to new lines of research in the field of artificial intelligence (AI). Currently, artificial neural networks are based on a

localized, non-distributed model. In the future, the possible application of the distributed paradigm to AI could multiply its current capabilities, although many technical difficulties must still be overcome to enable this.

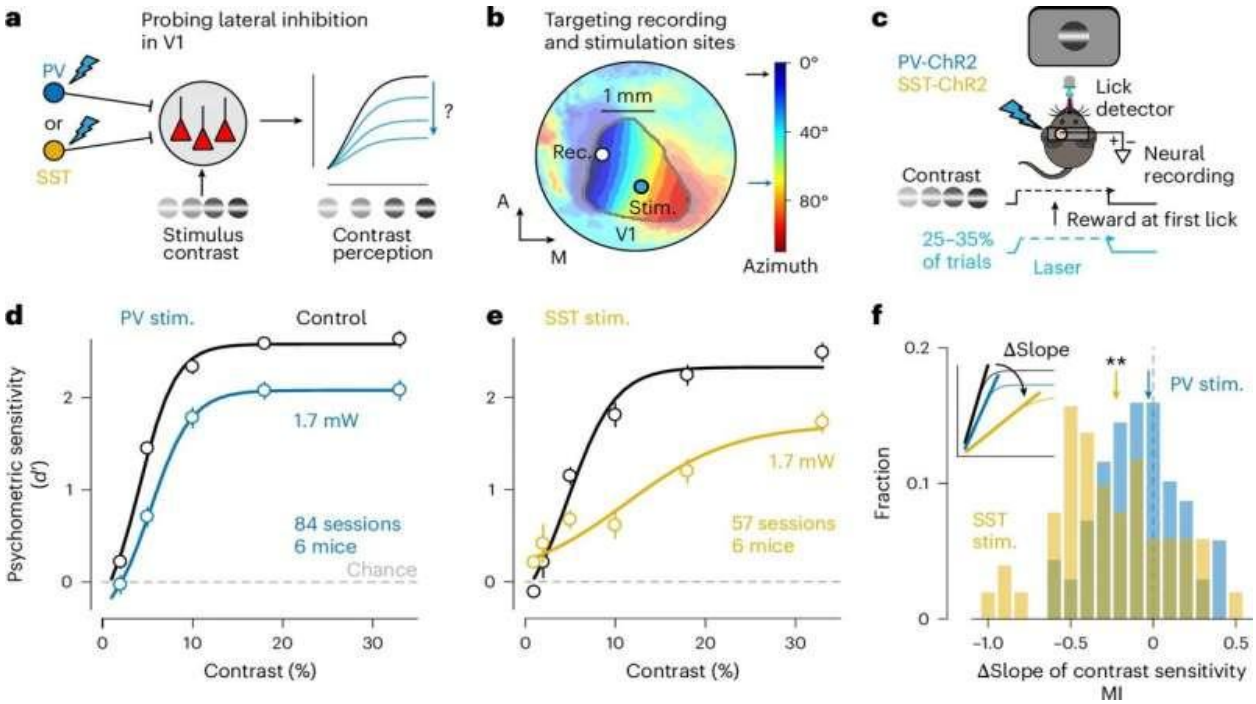
More information: Gustavo Deco et al, Complex harmonics reveal low-dimensional manifolds of critical brain dynamics, *Physical Review E* (2025). DOI: 10.1103/PhysRevE.111.014410

Provided by University at Pompeu Fabra - Barcelona

MARCH 11, 2025

Sharper images: How the brain filters out the noise

by Jerry Grillo, Georgia Institute of Technology



SST lateral inhibition controls the slope of psychometric contrast sensitivity. Credit: *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01888-4

A multidisciplinary team of researchers at Georgia Tech has discovered how lateral inhibition helps our brains process visual information, and it could expand our knowledge of sensory perception, leading to applications in neuro-medicine and artificial intelligence.

Lateral inhibition is when certain neurons suppress the activity of their neighboring neurons. Imagine an artist drawing, darkening the lines around the contours, highlighting the boundaries between objects and space, or objects and other objects. Comparably, in the visual system, lateral inhibition sharpens the contrast between different visual stimuli.

"This research is really getting at how our visual system not only highlights important things, but also actively suppresses irrelevant information in the background," said lead researcher Bilal Haider, associate professor in the Wallace H. Coulter Department of Biomedical Engineering. "That ability to filter out distractions is crucial."

Understanding how these inhibitory mechanisms work could provide insights into why people have trouble filtering out distractions or focusing on what's important in conditions like autism or ADHD.

"Our findings may also influence how we design artificial intelligence and neural networks," said Haider, whose team published its work this month in *Nature Neuroscience*. "Current AI systems treat all the computing units the same, but the brain has figured out how to assign specialized computing roles."

Joseph Del Rosario, a former graduate student in the Haider lab, was the lead author. Another key contributor was Hannah Choi, assistant professor in the School of Mathematics, and her Research Group in Mathematical Neuroscience. Their team built computational models to test the biological findings.

"Collaborating with mathematicians to really understand the computational principles underlying these inhibitory processes is a great example of how neuroscience can inform fields like AI," Haider said.

Fine-tuning perception

The study focused on two types of inhibitory neurons in the visual cortex: parvalbumin (PV) neurons and somatostatin (SST) neurons. The researchers used optogenetics—a technique that uses light to control cell activity—to activate PV and SST neurons in the visual cortex of mice. What they observed was striking.

"What's fascinating is that different types of inhibitory neurons seem to be doing distinct mathematical computations to achieve this suppression of the visual field," Haider said. "It's not a one-size-fits-all process."

When the team activated PV neurons, visual contrast sensitivity was evenly reduced, like lowering the brightness on a computer monitor. Activation of SST neurons resulted in a more nuanced change, altering the slope of the contrast sensitivity curve, which is a graph showing how well your visual system can detect contrast.

"Basically, SST neurons fine-tune our perception of contrast more strongly by reducing extra, unnecessary signals," Haider said. "That's lateral inhibition at work. These inhibitory

neurons play a major role in our perception. The brain has evolved this precise wiring and division of labor among different neuron types to act as the brakes in the visual system, just as important as the accelerator."

The impact of lateral inhibition goes beyond the visual system. Similar processes may also be at work in other senses, like hearing and touch. As scientists develop a better understanding of how the brain filters sensory information, they may discover new ways to enhance or restore our overall sensory experience.

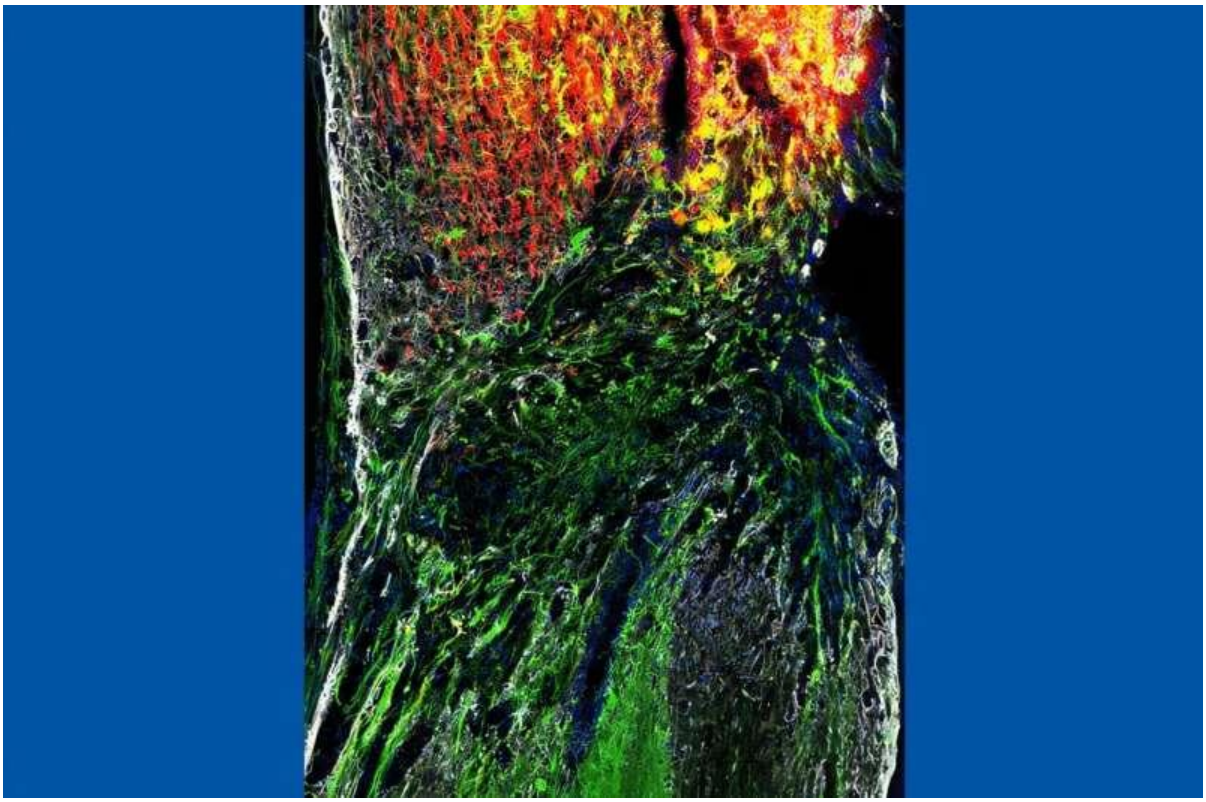
Haider first conceived the idea for this work 10 years ago when he was a postdoc. He believes the research could possibly result in new treatments for visual disorders, and lead to more flexible AI.

More information: Joseph Del Rosario et al, Lateral inhibition in V1 controls neural and perceptual contrast sensitivity, *Nature Neuroscience* (2025). DOI: 10.1038/s41593-025-01888-4
Journal information: Nature Neuroscience
Provided by Georgia Institute of Technology

MARCH 11, 2025

Researchers uncover hidden barrier to spinal cord injury recovery

by Erin Wickey, University of Kentucky



Credit: Cover, *Journal of Neuroscience* Vol. 45, Issue 1

New research from the University of Kentucky has earned a spot on the cover of the *Journal of Neuroscience*, highlighting a major challenge in spinal cord injury recovery.

Andrew Stewart, Ph.D., assistant professor at the Spinal Cord and Brain Injury Research Center (SCoBIRC) in the Department of Neuroscience in the UK College of Medicine, is investigating why treatments that could help repair and regenerate the damaged spinal cord stop working shortly after the injury has occurred. So far, scientists have a limited understanding of why these treatments fail in chronic cases.

"The initial injury is only one part of the problem. It's the inflammation and scarring that peaks a week or two after injury, that disrupts healing," said Stewart. "Inflammation in the spinal cord behaves a lot like inflammation in the skin—except the skin heals, while the spinal cord doesn't. Inflammation can cause more damage over time. Unlike in the skin, these inflammatory cells don't go away. They stick around for life, making recovery even harder."

Stewart began this work in 2020 as a postdoctoral student in John Gensel's UK lab. Alongside Gensel and fellow researchers Chris Bosse-Joseph, Reena Kumari, William M. Bailey, Kennedy A. Park and Victoria K. Slone, he investigated long-term inflammation in spinal cord injuries and tested whether PLX-5622 (PLX), a drug designed to target specific immune cells, could reverse it.

"In animal models, the treatment worked exactly as we hoped—it dramatically reduced the number of inflammatory cells at the injury site," said Stewart. "The real surprise came when

we stopped the treatment. The inflammatory cells quickly returned to the exact same high levels as before. That suggests the body isn't just passively holding onto these cells—something is actively keeping inflammation high."

This unexpected finding led to another important discovery. Stewart and his team set out to determine whether reducing inflammation would help nerve fibers, or axons, regenerate.

"It did but only for one specific type of sensory nerve fiber. The nerve cells we were actually trying to regenerate didn't respond the way we expected," said Stewart. "That led us to a new question: why did these sensory nerves grow back, but not the others? If we can figure that out, we might be able to apply the same principle to other nerve cells and improve treatments for spinal cord injuries."

Stewart says these findings featured in this publication have reshaped how researchers think about chronic inflammation in spinal cord injuries.

"Our discoveries have opened up exciting new research directions. We now have a better understanding of how chronic inflammation influences recovery, and we're exploring new ways to promote healing in the spinal cord."

More information: Andrew N. Stewart et al, Nonresolving Neuroinflammation Regulates Axon Regeneration in Chronic Spinal Cord Injury, *The Journal of Neuroscience* (2024). DOI: 10.1523/JNEUROSCI.1017-24.2024
Journal information: Journal of Neuroscience Provided by University of Kentucky

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MARCH 11, 2025

Liquid nanofoam innovation designed to protect the brain now tested on internal organs

by Derrick L. Turner, Michigan State University

Liquid nanofoam inside a plastic pouch. Credit: Michigan State University

Researchers at Michigan State University have refined an innovation that has the potential to improve safety, reduce severe injury and increase survival rates in situations ranging from car accidents, sports, law enforcement operations and more.

In 2020 and 2022, Weiyi Lu, an associate professor in MSU's College of Engineering, developed a liquid nanofoam material made up of tiny holes surrounded by water that has been shown to protect the brain against traumatic injuries when used as a liner in football helmets. Now, MSU engineers and scientists have improved this technology to shield vital internal organs as well.

Falls, motor vehicle crashes and other kinds of collisions can cause blunt force trauma and damage to bodily organs that can lead to life-threatening emergencies. These injuries are often the result of intense mechanical force or pressure that doesn't penetrate the body like a cut, but causes serious damage to the body's organs, including internal lacerations, ruptures, bleeding and organ failure.

Lu and Yun Liang, an assistant professor in the College of Osteopathic Medicine, have teamed up to see how the liquid nanofoam could protect internal organs in the event of blunt force trauma. Their findings are published in the journal *Scientific Reports*.

"We improved the liquid nanofoam by adjusting its protective response to match biological organs," said Lu. "Then, we sealed the liquid nanofoam material inside a plastic pouch about the size of a quarter and made the new protection layer flexible and moldable enough to be worn comfortably against the body."

To test the capabilities of Lu's liquid nanofoam, the pouch was used as a protective cover and laid over a tissue sample and compressed by a machine with enough force to mimic a blunt force trauma event.

"For the first time, we are trying to understand how trauma is introduced by mechanical force and effectively mitigated it by using liquid nanofoam," said Liang. "We are trying to understand the force needed to damage an internal organ, which will be then converted into the future design criteria for protective materials."

Lu and Liang found that the liquid nanofoam could withstand the mechanical force equal to a blunt force trauma without damaging biological tissue. Liang and her team demonstrated that the liquid nanofoam protected multiple biological tissues, including the liver, kidneys, heart and lungs, from forces and pressures equal to blunt force trauma injuries.

"I could see with my eyes that there's literally no damage," said Liang. "I was totally amazed."

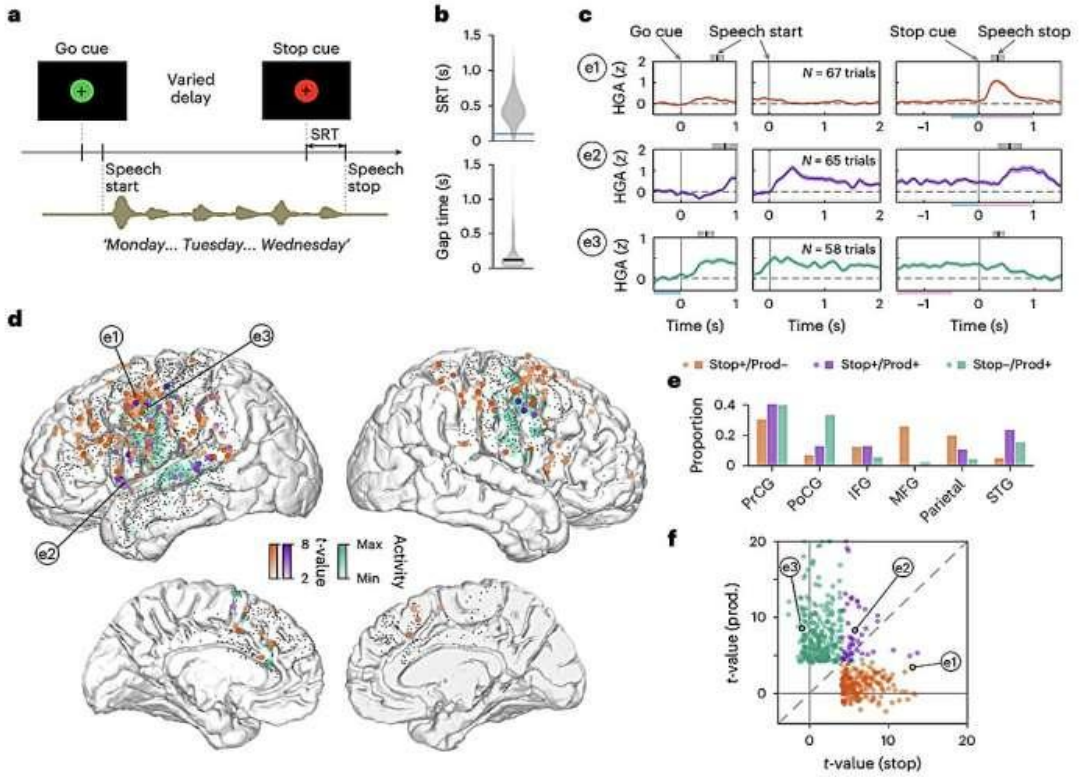
Future applications of the liquid nanofoam could include using it as a protective layer inside an automobile's framework, to line the walls of an earthquake-proof room or to wear it close to the body as a protective vest that could have multiple applications to save lives and prevent tissue and organ damage from blunt force trauma events.

More information: Fuming Yang et al, Effective protection of biological tissues from severe blunt force injury by engineered nanoscale liquid flow, *Scientific Reports* (2024). DOI: 10.1038/s41598-024-80490-3
Journal information: Scientific Reports
Provided by Michigan State University

MARCH 12, 2025

A premotor cortical network in the brain allows people to voluntarily stop speaking, study suggests

by Ingrid Fadelli , Medical Xpress



Premotor neural activation during speech stopping. Credit: *Nature Human Behaviour* (2025). DOI: 10.1038/s41562-025-02118-4

Speech is a unique human ability that is known to be supported by various motor and cognitive processes. When humans start speaking, they can decide to cease at any point; for instance, if they are interrupted by something happening or by another person speaking to them.

The ability to voluntarily stop speaking plays a central role in social interactions, as it allows people to engage in conversations with others while adaptively responding to social cues, environmental stimuli or interruptions. While many past studies explored the neural and cognitive underpinnings of speech itself, the brain processes associated with speech inhibition remain poorly understood.

Researchers at the University of California San Francisco recently set out to better understand how the human brain controls the ceasing of speech using tools to record neurophysiological signals. Their paper, published in *Nature Human Behaviour*, unveils a

previously unknown premotor cortical network that could support voluntary speech inhibition.

"The cognitive and neural mechanisms of speech inhibition are not well understood," wrote Lingyun Zhao, Alexander B. Silva and their colleagues in their paper. "We have recorded direct high-density cortical activity while participants engaged in continuous speech production and were visually cued to stop speaking."

To investigate the neural underpinnings of voluntary speech cessation, Zhao, Silva and their colleagues used a neurophysiological recording technique known as high-density electrocorticography (ECoG). This technique allows researchers to monitor the electrical activity originating from the surface of the brain.

They recruited 13 patients diagnosed with treatment-resistant epilepsy who had electrodes implanted on their brains' surfaces to better understand the brain regions that contribute to their epileptic seizures. These patients were asked to complete a speech-stopping task, which asked them to follow instructions on when to start and stop speaking, while their neural activity was recorded.

"Neural recordings revealed distinct activity in the premotor frontal cortex correlated with stopping speech," wrote the researchers. "This activity was found in largely separate cortical sites from regions encoding vocal tract articulatory movements. Moreover, this activity primarily occurred with abrupt stopping in the middle of an utterance, rather than naturally completing a phrase."

The findings gathered by this team of researchers hint at the existence of a specialized brain mechanism that supports the voluntary control of speech. Zhao, Silva and their colleagues conducted further tests aimed at validating the existence of this mechanism by stimulating specific parts of the premotor frontal cortex.

"Electrocortical stimulation at many premotor sites with inhibitory stop activity caused involuntary speech arrest, which contradicts previous clinical interpretations of this effect as evidence for critical centers of speech production," wrote the team. "Together, these results suggest a previously unknown premotor cortical network that supports the inhibitory control of speech, providing implications for understanding both natural and altered speech production."

Overall, the results of this study suggest that the human ability to voluntarily stop speech is supported by a particular inhibitory control neural network that had not been uncovered before. Future studies could help to further elucidate the functions and contributions of the newly identified premotor cortical network, which could in turn help to better understand some disorders linked to an impaired ability to voluntarily control speech.

More information: Lingyun Zhao et al, Inhibitory control of speech production in the human premotor frontal cortex, *Nature Human Behaviour* (2025). DOI: 10.1038/s41562-025-02118-4
Journal information: Nature Human Behaviour

MARCH 12, 2025

Robotics and spinal stimulation restore movement in paralysis

by Ecole Polytechnique Federale de Lausanne

Close view of the EES triggered legs activation during walking in the robotics exoskeleton Lokomat. Credit: .NeuroRestore / EPFL / CHUV 2025

Spinal cord injuries are life-altering, often leaving individuals with severe mobility impairments. While rehabilitation robotics—devices that guide movement during therapy—have improved training for those with spinal cord injuries, their effectiveness remains limited. Without active muscle engagement, robotic-assisted movement alone does not sufficiently retrain the nervous system.

A team at .NeuroRestore, led by Grégoire Courtine and Jocelyne Bloch, has now developed a system that seamlessly integrates an implanted spinal cord neuroprosthesis with rehabilitation robotics. The researchers' device delivers well-timed electrical pulses to stimulate muscles in harmony with robotic movements, resulting in natural and coordinated muscle activity during therapy.

The work is published in the journal *Science Robotics*.

The neuroprosthetics innovation leveraged the robotic expertise of Professor Auke Ijspeert's lab at EPFL. This advancement not only enhances immediate mobility but also fosters long-term recovery.

"The seamless integration of spinal cord stimulation with rehabilitation or recreational robotics will accelerate the deployment of this therapy into the standard of care and the community of people with spinal cord injury," says Courtine. This adaptability ensures that rehabilitation professionals can incorporate this technology into existing rehabilitation protocols worldwide.

Combining therapies also presents significant challenges, as each requires precise synchronization. Spinal cord stimulation strategies must be modulated in both space and time to match the patient's movement, and integrating them with widely used robotic rehabilitation systems requires a flexible and adaptable framework.

Common robotic devices to safely automate and augment gait rehabilitation across the continuum of care for people suffering from traumatic spinal cord injury interfaced with spinal cord stimulation. Credit: .NeuroRestore / EPFL / CHUV 2025
The technology relies on a fully implanted spinal cord stimulator that delivers biomimetic electrical epidural stimulation. Unlike traditional functional electrical stimulation, this method activates motor neurons more efficiently by mimicking natural nerve signals.

The researchers integrated electrical epidural stimulation with various robotic rehabilitation devices—including treadmills, exoskeletons, and stationary bikes—ensuring that stimulation is precisely timed with each phase of movement. The system uses wireless sensors to detect limb motion and automatically adjust stimulation in real time, allowing for a seamless user experience.

In a proof-of-concept study involving five individuals with spinal cord injuries, the combination of robotics and electrical epidural stimulation resulted in immediate and sustained muscle activation.

Not only did participants regain the ability to engage muscles during robotic-assisted therapy, but some also improved their voluntary movements even after the stimulation was turned off.

EES can engage the neuromuscular system during cycling activities in the lab and also in ecological environment. Credit: .NeuroRestore / EPFL / CHUV 2025
The researchers also worked closely with rehabilitation centers to test how well the stimulation system integrated with widely used robotic devices.

"We visited multiple rehabilitation centers to test our stimulation technology with the robotic systems they routinely use, and it was incredibly rewarding to witness their enthusiasm," say .NeuroRestore researcher Nicolas Hankov and BioRob researcher Miroslav Caban, the study's first authors.

"Seeing firsthand how seamlessly our approach integrates with existing rehabilitation protocols reinforces its potential to transform care for people with spinal cord injury by providing a technological framework that is easy to adopt and deploy across multiple rehabilitation environments."

The study also showed the potential of this approach beyond clinical settings, as participants used the system to walk with a rollator and cycle outdoors, validating its real-world impact.

This innovative technology offers new hope for individuals with spinal cord injuries, presenting a more effective rehabilitation approach than robotics alone. By making rehabilitation more dynamic and engaging, it has the potential to significantly enhance recovery outcomes.

Future clinical trials will be needed to establish long-term benefits, but the initial results suggest that integrating neuroprosthetics with rehabilitation robotics could redefine mobility restoration after paralysis.

More information: Nicolas Hankov et al, Augmenting rehabilitation robotics with spinal cord neuromodulation: a proof of concept, *Science Robotics* (2025). DOI: 10.1126/scirobotics.adn5564. www.science.org/doi/10.1126/scirobotics.adn5564
Journal information: Science Robotics
Provided by Ecole Polytechnique Federale de Lausanne

MARCH 12, 2025

How the brain uses 'building blocks' to navigate social interactions

by University College London

Credit: CC0 Public Domain

Our brains use basic "building blocks" of information to keep track of how people interact, enabling us to navigate complex social interactions, finds a new study led by University College London (UCL) researchers.

For the study, published in *Nature*, the researchers scanned the brains of participants who were playing a simple game involving a teammate and two opponents, to see how their brains were able to keep track of information about the group of players.

The scientists found that rather than keeping track of the performance of each individual player, specific parts of the participants' brains would react to specific patterns of interaction, or 'building blocks' of information that could be combined to understand what was going on.

Lead author Dr. Marco Wittmann (UCL Psychology & Language Sciences and Max Planck UCL Center for Computational Psychiatry and Aging Research) said, "Humans are social creatures that are capable of keeping track of highly complex and fluid social dynamics, requiring a massive amount of brain power to remember not only individual people but also the various relationships between them.

"In order to keep up with a group social interaction in real time, our brains must be using heuristics—mental shortcuts that help people make decisions quickly—to compress and simplify the wealth of information involved, with a system that minimizes complexity while still allowing flexibility and detail.

"In this research, we found that our brains appear to use a set of basic 'building blocks' that represent fundamental aspects of social interactions, enabling us to quickly figure out new and complex social situations."

For the study, the team of scientists from UCL and the University of Oxford used functional magnetic resonance imaging (fMRI) to record the brain activity of 88 participants who were playing a simple game.

While in the scanner, the study participants were given a series of information about how they, a partner, and their opponents were faring in a game, and needed to keep track of the information in order to answer a question comparing performances of different players.

Dr. Wittmann explained, "We were interested to see whether our brains would use an 'agent-centric' frame of reference where specific parts of the brain keep track of each player's performance, or a 'sequential' frame of reference tracking the information in the order it was received. We found that people actually do both, but our brains are able to simplify all of this information into bite-sized chunks."

The scientists were able to pinpoint specific patterns of activity in the brain that represented a few specific 'building blocks," each representing a pattern of interaction between the players.

For example, one building block kept information about how well a participant and their partner were doing relative to the other team. A bigger difference in performance between the two teams corresponded to an increase in brain activity related to this building block. These specific patterns of activity were found in the prefrontal cortex, which is involved in decision-making and social behavior.

The researchers say these fundamental building blocks appear to represent patterns of interaction that are common to many different situations.

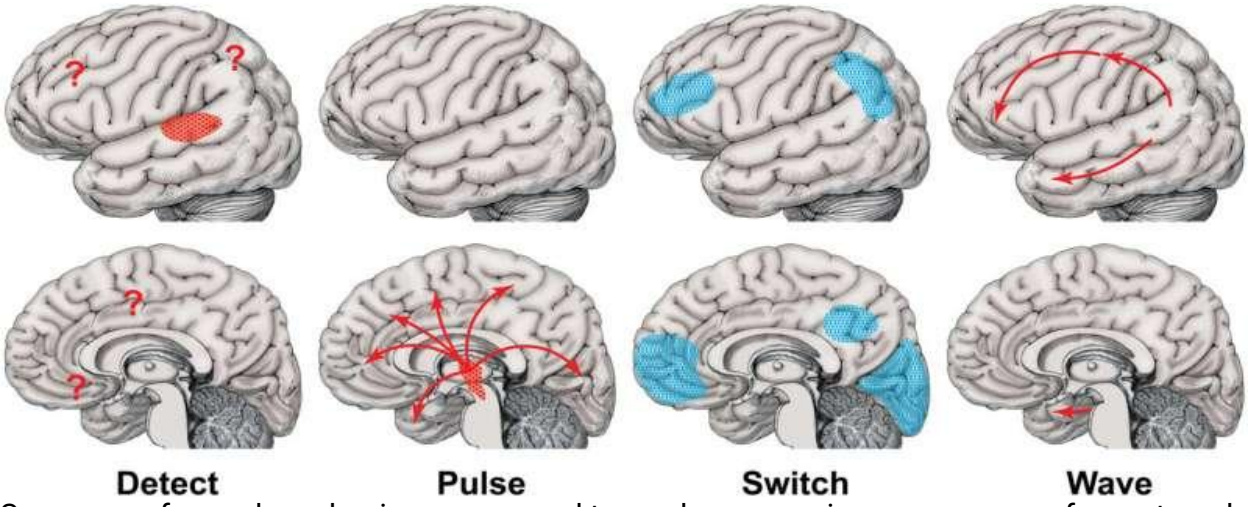
Dr. Wittmann said, "As we develop social skills in life, our brains are likely learning specific interaction patterns that we come across again and again. These patterns may become hard-wired into our brains as building blocks that get assembled and recombined to construct our understanding of any social setting."

More information: Marco Wittmann, Basis functions for complex social decisions in dorsomedial frontal cortex, *Nature* (2025). DOI: 10.1038/s41586-025-08705-9. www.nature.com/articles/s41586-025-08705-9
Journal information: Nature
Provided by University College London

MARCH 12, 2025

Researchers track auditory perception across brain regions

by Yale University



Sequence of neural mechanisms proposed to produce conscious awareness of an external auditory stimulus. Credit: *NeuroImage* (2025). DOI: 10.1016/j.neuroimage.2025.121041

Sounds you consciously perceive affect your brain differently than sounds you don't, a recent Yale study found.

For the study, researchers played participants a series of tones—ranging in intensity from undetectable to fully audible—over a white noise background. Since the participants were also patients undergoing seizure monitoring, and therefore had electrodes implanted on the surface of the brain, this allowed the researchers to record detailed brain activity while the participants listened to the tones.

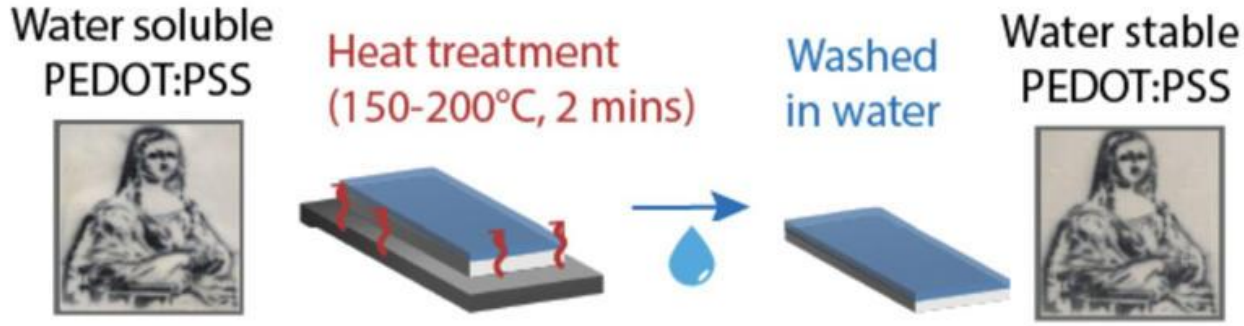
"We found that when sounds were consciously perceived, there was a wave of activity that flowed through widespread areas of the brain," said Hal Blumenfeld, the Mark Loughridge and Michele Williams Professor of Neurology at Yale School of Medicine and senior author of the study, which was published in *NeuroImage*.

"But when the same sounds were not consciously perceived, brain activity was limited to a small region around the auditory cortex."

The activity was similar to what has been observed with visual perception, suggesting there are shared neural mechanisms between the two systems. The findings advance researchers' understanding of what happens in the brain during sensory perception and shed light on the neurological underpinnings of human consciousness.

More information: Kate L. Christison-Lagay et al, The neural activity of auditory conscious perception, *NeuroImage* (2025). DOI: 10.1016/j.neuroimage.2025.121041
Journal information: NeuroImage
Provided by Yale University

Heat-based stabilization of a conductive polymer simplifies bioelectronics fabrication



Overview of the heat treatment process, demonstrated with a screen printed PEDOT:PSS pattern on fabric that remains stable after washing in detergent. Credit: Advanced Materials (2025). DOI: 10.1002/adma.202415827

Recent advances in the field of materials science have opened new possibilities for the fabrication of bioelectronics, devices designed to be worn or implanted in the human body. Bioelectronics can help to track or support the function of organs, tissues and cells, which can contribute to the prevention and treatment of various diseases.

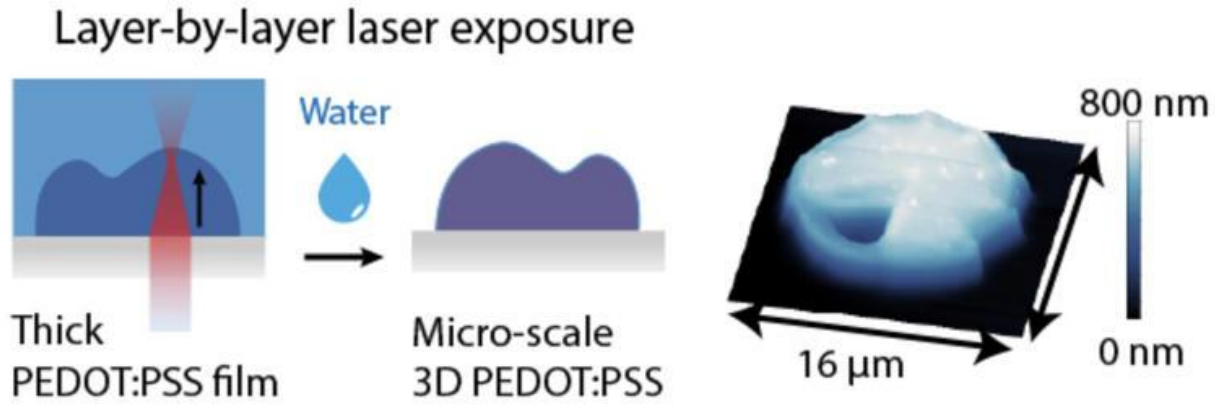
A promising material for the fabrication of bioelectronics is PEDOT:PSS, a polymer known for its high electrical conductivity, flexibility and compatibility with biological tissues. Despite its advantageous properties, PEDOT:PSS is known to gradually dissolve in biological fluids, a limitation that has so far been counteracted using chemical compounds and processes.

Researchers at Stanford University, the University of Cambridge and Rice University recently uncovered an easier and potentially safer strategy to stabilize this bio-compatible polymer using heat. Their proposed thermal treatment, outlined in the journal *Advanced Materials*, was found to make PEDOT:PSS films stable in water without the need for any chemical additives.

"This work started out from a serendipitous discovery during the course of my previous research, where I was using the responsive polymer, PEDOT:PSS to make shape-changing photonic devices," Siddharth Doshi, co-first author of the paper, told Tech Xplore.

"I noticed that films of PEDOT:PSS that I'd accidentally baked at higher than usual temperatures didn't dissolve in water. This was a huge surprise, as PEDOT:PSS is a widely studied conductive polymer, and to get around the fact that it delaminates in water, hundreds of bioelectronics papers use chemical cross-linkers to stabilize their devices."

After making this surprising observation as part of their earlier research, Doshi and his colleagues set out to explore the possibility that heating up PEDOT:PSS films could also stabilize them in fluids. In addition, they wished to determine what exactly happened when the films were heated above certain temperatures, how this heating process affected their properties and whether a heat-based approach could replace existing chemical stabilization processes.



Layer-by-layer exposure to a focused femtosecond laser beam allows for microscale-3D printing of unmodified PEDOT:PSS. Credit: Advanced Materials (2025). DOI: 10.1002/adma.202415827

"The key advantage of our approach is its simplicity—you can simply heat up films of commercial, unmodified PEDOT:PSS on a hot-plate between 150°C and 200°C for 2 mins, and it no longer dissolves in water," explained Doshi. "It works on different substrates, including stretchable plastics and even different fabrics, and avoids many of the complications of chemical crosslinkers, which affect the conductivity and reliability of the films."

The heat treatment devised by the researchers could also enable the direct patterning of PEDOT:PSS simply by applying heat to specific sites on the films

and thus removing the need for complex lithography techniques. As part of their study, Doshi and his colleagues also demonstrated the 3D printing of PEDOT:PSS at the micro-scale, using a focused femtosecond laser beam.

"The PEDOT:PSS absorbs strongly at the near-infrared laser wavelength we used, which causes local heating," said Doshi. "Through layer-by-layer scanning of a focused laser spot, we could locally stabilize 3D patterns within the film which remain even after the unexposed parts of the film are washed away in water. As a nice additional benefit, this gives us an environmentally friendly way to pattern this material, using only water for processing instead of other toxic solvents."

The initial tests run by the researchers yielded very promising results. Ultimately, their heat-based approach was found to make PEDOT:PSS films stable in water, while also improving their performance.

"Heat-treated bioelectronic devices such as transistors, spinal cord stimulators and electrocorticography (ECoG) arrays were easier to fabricate, more reliable, and equally high performing. And they proved to be robust in chronic in vivo experiments, maintaining stability for over 20 days post-implantation," said Margaux Forner, Ph.D. student from the University of Cambridge and co-first author on the paper.

"Notably, the film maintained excellent electrical performance when stretched, highlighting its potential for resilient bioelectronic devices both inside and outside the body."

"Our characterization suggests that heat-treatment drives phase separation of PEDOT and PSS-rich regions, helping stabilize the polymer blend by creating a network of a water-insoluble, PEDOT-rich phase," added Scott Keene, Assistant Professor at Rice University and the senior author of the paper. "In addition to making the polymer water-stable, we found that phase separation improves both the conductivity and capacitance of our films, two critical parameters for bioelectronic devices."

In addition, the simple heat-based treatment introduced by Doshi and his colleagues could be easily integrated with existing manufacturing processes. In the future, it could thus simplify the development of various PEDOT:PSS-based devices, including bioelectronics, as well as wearable electronics and electronic skins.

"We are also really excited about the ability to 3D-print the polymers at the microscale," said Doshi. "This has been a major goal for the community, as writing this functional material in 3D could let you interface with the 3D world of biology. Typically, this is done by combining PEDOT:PSS with different photo-sensitive binders or resins; however, these additions affect the properties of the material or are challenging to scale down to micron-length scales."

The researchers have successfully used their heat-based approach to create complex 3D structures, including blocks, textured surfaces and sculptural test-pieces with curves, bevels and recesses, made of PEDOT:PSS. They achieved this using femtosecond laser patterning, but it could eventually also be attained using other laser-based methods.

The researchers hope that other materials scientists and engineers will start experimenting with their thermal treatment and using it to stabilize PEDOT:PSS films without relying on chemical processes. In the future, their newly introduced approach could facilitate the use of these films for the development of implantable devices and other devices that are meant to be resistant to water or other fluids.

"One direction for future research will be to explore new ways to interface with the 3D world of biology through functional cell-interfaces," said Doshi. "We are also interested in going back to our original motivation of exploring new ways of fabricating PEDOT:PSS, which is in making switchable 3D photonic devices that use the electro-optic tunability of PEDOT:PSS to dynamically change their optical properties.

"There is a lot of interest in the field of micro and nano-optics for devices that change their functionality on demand, and 3D devices could have a lot of advantages over 2D devices that have been most widely explored to date."

In their next studies, Doshi and his colleagues also plan to further investigate the fundamental mechanisms underpinning the stabilization of PEDOT:PSS when it is heated above 150°C for over two minutes. To do this, they will employ advanced imaging and material characterization techniques.

"Techniques like in-situ transmission electron microscopy or in-situ X-ray diffraction could let us visualize what is exactly happening to the PEDOT and PSS chains and the overall microstructure of the material in real-time," added Doshi.

More information: Doshi et al, Thermal Processing Creates Water-Stable PEDOT:PSS Films for Bioelectronics, *Advanced Materials* (2025). DOI: 10.1002/adma.202415827

Scientists Just Discovered That Some Memories Don't Live in Our Brains

Other cells in our body, like nerve cells or kidney cells, pick up on and remember patterns over time.© Yuichiro Chino - Getty Images

- The process of memory is often tied to the brain, but a new study reveals that other cells outside our skulls contain their own kind of "body memory."
- In a new study, scientists also discovered that these memory genes acted similarly to neurons in that they more effectively "learned" through spaced-out repetition rather than just one giant cram session.
- Gaining a deeper understanding of this "body memory" could help scientists and clinicians create new ways to address diseases and other maladies.

Memory—and by extension, learning—is central to life on Earth and its greatest intellectual byproduct: the scientific method. The ability to test hypotheses, draw on past experience, and develop new ways of thinking lies at the cornerstone of our modern society. Our language often describes this process as a purely cerebral pursuit. After all, the smartest among us are often labeled "brainiacs," but a new study suggests that the ability to learn *isn't* exclusive to the brain.

A team of researchers at New York University (NYU) set out to determine if other cells in the body, in this case kidney and nerve cells, could store memory like neurons. This isn't the same as, say, recalling specific moments in your life, but instead memories of specific patterns to help perform their life-sustaining functions. What they found is that other cells do contain a sense of a memory and also follow a specific neurological property known as the massed-spaced effect. The results of the study were published in the journal *Nature Communications*.

"This discovery opens new doors for understanding how memory works and could lead to better ways to enhance learning and treat memory problems," NYU's Nikolay Kukushkin, a co-author of the study, said in a press statement. "At the same time, it suggests that in the future, we will need to treat our body more like the brain—for example, consider what our pancreas remembers about the pattern of our past meals to maintain healthy levels of blood glucose or consider what a cancer cell remembers about the pattern of chemotherapy."

In 1885 German psychologist Hermann Ebbinghaus detailed the idea of "spaced repetition," or massed-spaced effect, in his book *Memory: A Contribution to Experimental Psychology*. This refers to the idea that the best method of learning is through repeated, spaced study sessions rather than massed presentation (or what's commonly known across high school and college campuses as "cramming.") Kukushkin and his team focused on these two types of learning in cells by introducing different patterns of chemical signals, which essentially mimicked brain cells as they're exposed to patterns of neurotransmitters. To study this memory-making effect, the scientists developed the cells with a protein that glowed when the "memory gene" was activated.

The scientists noticed that when the chemical patterns were introduced in space-out intervals, the "memory gene" turned on more strongly and for longer intervals than when exposed to a prolonged exposure.

"This reflects the massed-space effect in action," Kukushkin said in a press statement. "It shows that the ability to learn from spaced repetition isn't unique to brain cells, but, in fact, might be a fundamental property of all cells."

Writing for *Psychology Today*, Kukushkin also notes that this "body memory" could play a profound role in health and disease while also providing powerful evidence of the power of repeated learning, which can strengthen memory instead of slowly losing useful information to Ebbinghaus' "forgetting curve."

So if you've got a big test coming up, it's biologically advantageous to hit books early *and* often rather than slogging through a sleepless night of cramming.

MARCH 13, 2025

Engineers turn skin cells directly into neurons for cell therapy

by Massachusetts Institute of Technology

Credit: Pixabay/CC0 Public Domain

Converting one type of cell to another—for example, a skin cell to a neuron—can be done through a process that requires the skin cell to be induced into a "pluripotent" stem cell, then differentiated into a neuron. Researchers at MIT have now devised a simplified process that bypasses the stem cell stage, converting a skin cell directly into a neuron.

Working with mouse cells, the researchers developed a conversion method that is highly efficient and can produce more than 10 neurons from a single skin cell. If replicated in human cells, this approach could enable the generation of large quantities of motor neurons, which could potentially be used to treat patients with spinal cord injuries or diseases that impair mobility.

"We were able to get to yields where we could ask questions about whether these cells can be viable candidates for the cell replacement therapies, which we hope they could be. That's where these types of reprogramming technologies can take us," says Katie Galloway, the W. M. Keck Career Development Professor in Biomedical Engineering and Chemical Engineering.

As a first step toward developing these cells as a therapy, the researchers showed that they could generate motor neurons and engraft them into the brains of mice, where they integrated with host tissue.

Galloway is the senior author of two papers describing the new method, which appear in *Cell Systems*. MIT graduate student Nathan Wang is the lead author of both papers.

From skin to neurons

Nearly 20 years ago, scientists in Japan showed that by delivering four transcription factors to skin cells, they could coax them to become induced pluripotent stem cells (iPSCs). Similar to embryonic stem cells, iPSCs can be differentiated into many other cell types. This technique works well, but it takes several weeks, and many of the cells don't end up fully transitioning to mature cell types.

"Oftentimes, one of the challenges in reprogramming is that cells can get stuck in intermediate states," Galloway says. "So, we're using direct conversion, where instead of going through an iPSC intermediate, we're going directly from a somatic cell to a motor neuron."

Galloway's research group and others have demonstrated this type of direct conversion before, but with very low yields—fewer than 1%. In Galloway's previous work, she used a combination of six transcription factors plus two other proteins that stimulate cell proliferation. Each of those eight genes was delivered using a separate viral vector, making it difficult to ensure that each was expressed at the correct level in each cell.

In the first of the new *Cell Systems* papers, Galloway and her students reported a way to streamline the process so that skin cells can be converted to motor neurons using just three transcription factors, plus the two genes that drive cells into a highly proliferative state.

Using mouse cells, the researchers started with the original six transcription factors and experimented with dropping them out, one at a time, until they reached a combination of three—NGN2, ISL1, and LHX3—that could successfully complete the conversion to neurons.

Once the number of genes was down to three, the researchers could use a single modified virus to deliver all three of them, allowing them to ensure that each cell expresses each gene at the correct levels.

Using a separate virus, the researchers also delivered genes encoding p53DD and a mutated version of HRAS. These genes drive the skin cells to divide many times before they start converting to neurons, allowing for a much higher yield of neurons, about 1,100%.

"If you were to express the transcription factors at really high levels in nonproliferative cells, the reprogramming rates would be really low, but hyperproliferative cells are more receptive. It's like they've been potentiated for conversion, and then they become much more receptive to the levels of the transcription factors," Galloway says.

The researchers also developed a slightly different combination of transcription factors that allowed them to perform the same direct conversion using human cells, but with a lower efficiency rate—between 10 and 30%, the researchers estimate. This process takes about five weeks, which is slightly faster than converting the cells to iPSCs first and then turning them into neurons.

Subscribe

Implanting cells

Once the researchers identified the optimal combination of genes to deliver, they began working on the best ways to deliver them, which was the focus of the second *Cell Systems* paper.

They tried out three different delivery viruses and found that a retrovirus achieved the most efficient rate of conversion. Reducing the density of cells grown in the dish also helped to improve the overall yield of motor neurons. This optimized process, which takes about two weeks in mouse cells, achieved a yield of more than 1,000%.

Working with colleagues at Boston University, the researchers then tested whether these motor neurons could be successfully engrafted into mice. They delivered the cells to a part of the brain known as the striatum, which is involved in motor control and other functions.

After two weeks, the researchers found that many of the neurons had survived and seemed to be forming connections with other brain cells. When grown in a dish, these cells showed measurable electrical activity and calcium signaling, suggesting the ability to communicate with other neurons. The researchers now hope to explore the possibility of implanting these neurons into the spinal cord.

The MIT team also hopes to increase the efficiency of this process for human cell conversion, which could allow for the generation of large quantities of neurons that could be used to treat spinal cord injuries or diseases that affect motor control, such as ALS.

Clinical trials using neurons derived from iPSCs to treat ALS are now underway, but expanding the number of cells available for such treatments could make it easier to test and develop them for more widespread use in humans, Galloway says.

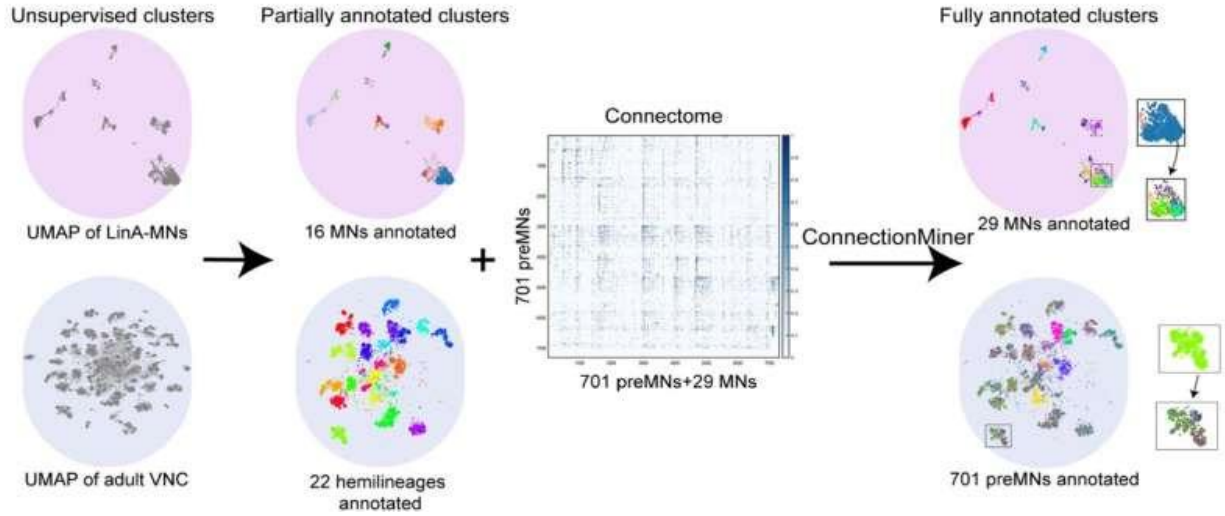
More information: Proliferation history and transcription factor levels drive direct conversion to motor neurons, *Cell Systems* (2025). DOI: 10.1016/j.cels.2025.101205. www.cell.com/cell-systems/full … 2405-4712(25)00038-9

Compact transcription factor cassettes generate functional, engraftable motor neurons by direct conversion, *Cell Systems* (2025). DOI: 10.1016/j.cels.2025.101206. www.cell.com/cell-systems/full … 2405-4712(25)00039-0
Journal information: Cell Systems
Provided by Massachusetts Institute of Technology

MARCH 13, 2025

New research uses AI to unravel the complex neuronal wiring of the motor system

by NYU Tandon School of Engineering



Overview of ConnectionMiner. Credit: *Neuroscience* (2025). DOI: 10.1101/2025.03.04.640006

The nervous system is a marvel of biological engineering, composed of intricate networks that control every aspect of an animal's movement and behavior. A fundamental question in neuroscience is how these vast, complex circuits are assembled during development.

A recent study by a group of researchers including Erdem Varol, Assistant Professor of Computer Science and Engineering and a member of the Visualization, Imaging and Data Analysis Center, has provided new insights into this problem by studying how the neurons responsible for leg movement in fruit flies (Drosophila melanogaster) establish their connections.

The researchers developed ConnectionMiner, a novel computational tool that integrates gene expression data with electron microscopy-derived connectomes. This tool enabled them to infer neuronal identities and predict synaptic connectivity with remarkable accuracy. Their findings, posted to the *bioRxiv* preprint server, offer a blueprint for understanding how neurons wire themselves into functional circuits.

Neurons form connections based on genetic and molecular cues, but identifying the precise mechanisms behind this process has been difficult. In the fruit fly, roughly 69 motor

neurons (MNs) in each leg are responsible for controlling movement. These neurons receive input from more than 1,500 premotor neurons (preMNs) through over 200,000 synapses. The challenge lies in understanding how each MN finds the right preMN partners and how these connections are established at the molecular level.

By applying single-cell RNA sequencing (scRNAseq) at multiple developmental stages, the researchers tracked how different gene families, particularly transcription factors (TFs) and cell adhesion molecules (CAMs), shape the unique identities of MNs. They discovered that these molecular signals not only define neuronal types but also correlate with the strength of their synaptic connections.

Traditional methods of studying neuronal circuits rely on either gene expression data (which tells us what molecules neurons produce) or connectomics (which maps how neurons are wired together). However, integrating these two datasets has been a major challenge. ConnectionMiner bridges this gap by using machine learning to refine ambiguous neuronal annotations, effectively reconstructing the genetic and synaptic landscape of the nervous system.

The researchers tested their tool on the Drosophila leg motor system, identifying combinatorial gene signatures that likely orchestrate the assembly of circuits from preMNs to MNs and ultimately to muscles. By leveraging both transcriptomic (gene expression) and connectomic (wiring) data, ConnectionMiner successfully resolved previously uncharacterized neuronal identities and predicted the molecular interactions driving connectivity.

By mapping these relationships, ConnectionMiner provides a predictive framework for understanding how the nervous system assembles itself.

"The nervous system is one of the most complex networks that we know of, and deciphering its molecular building blocks is key to understanding much about our health, our behavior and our lives in general," says Varol. "Tools like ConnectionMiner are a major stepping stone towards unlocking the brain's molecular blueprint—enabling us to identify the genes that build neural circuits, revolutionize the diagnosis and treatment of neurological disorders, and fundamentally enhance our understanding of how brain wiring drives behavior."

This research has far-reaching implications. Understanding the molecular rules that govern neural connectivity in fruit flies could inform studies of more complex nervous systems, including our own. The principles uncovered here might help explain how neural circuits form during development, how they recover from injury, and even how neurodevelopmental disorders arise when connectivity goes awry.

Furthermore, computational tools like ConnectionMiner represent a paradigm shift in neuroscience. By integrating artificial intelligence with biological data, researchers can now tackle questions that were previously too complex to analyze. The approach outlined in this

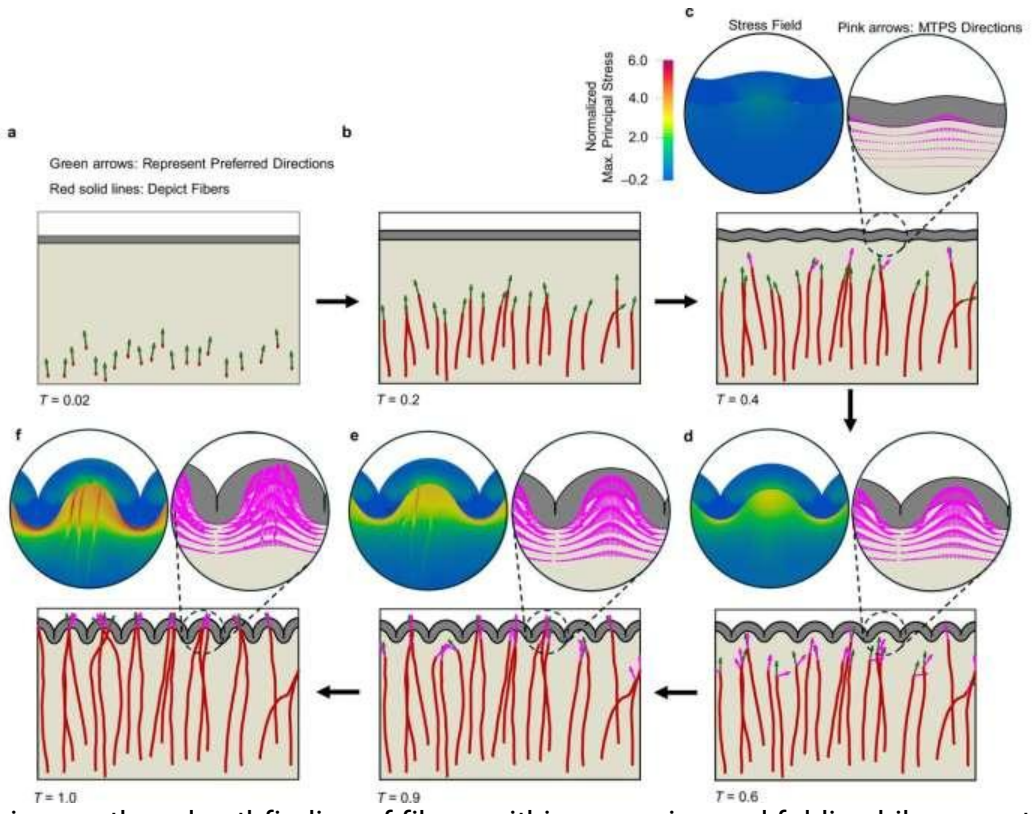
study could be applied to other model organisms, potentially unlocking new insights into brain development, neural repair, and artificial intelligence itself.

More information: Himanshu Pawankumar Gupta et al, Decoding neuronal wiring by joint inference of cell identity and synaptic connectivity, *bioRxiv* (2025). DOI: 10.1101/2025.03.04.640006
Journal information: Neuroscience , bioRxiv
Provided by NYU Tandon School of Engineering

MARCH 18, 2025

New research looks at how axons connect as brains grow

by Chris Kocher, Binghamton University



Dynamic growth and pathfinding of fibers within a growing and folding bilayer system. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-56362-3

How a person's brain grows and makes connections can determine intelligence as well as susceptibility to disorders such as epilepsy and mental illness. However, a lot of questions remain about how the process works, especially the mechanics of brain folding.

In a study recently published in the journal *Nature Communications*, researchers from Binghamton University propose the first dynamic model predicting the complicated mechanics of connectivity development and folding in the cerebral cortex—the outermost layer of the brain where memory and reasoning occur.

Assistant Professor Mir Jalil Razavi—a faculty member at the Thomas J. Watson College of Engineering and Applied Science's Department of Mechanical Engineering—led the research, with contributions from Ph.D. students Akbar Solhtalab and Ali H. Foroughi. Dr. Lana Pierotich from Harvard Medical School and Boston Children's Hospital also contributed to the study, providing insights into the biological relevance of the proposed model.

"Our motivation," Razavi said, "was to look at the physical interplay between the folding of the brain and connectivity development, and why if we have an alteration in one of them, there will be disruption in the other one. How are they connected?"

From left, PhD student Akbar Solhtalab, Assistant Professor Mir Jalil Razavi and PhD student Ali H. Foroughi are part of the Mechanics of Soft/Bio Materials Lab at Binghamton University. Credit: Binghamton University

The researchers studied why axons—the long, slender projections of neurons that transmit electrical impulses—have a much higher density in the gyri (convex parts) than in the sulci (concave parts). Because of what they are calling axon reorientation theory, axons grow differently when exposed to tensile or compressive forces within the brain's white matter.

"The folding brain creates a stress landscape," Razavi said. "Where we have convex and concave patterns because of folding, we have tensile stresses and compressive stresses. When axons move or expand from the core of the brain toward the cortex or outer layer of the brain and they experience a stress created by the folding in the white matter, they just change their direction. They reorient themselves toward the tensile stresses, not compressive stresses.

"They love to be under tension rather than on compression. Although they grow faster in a stiffer medium, they tend to move toward a softer medium. The folding of the brain, which generates tensile and compressive forces, can alter the stiffness of the white matter, influencing the environment in which axons grow."

Razavi has spent the last 10 years looking at the brain from a mechanical standpoint, since his Ph.D. studies at the University of Georgia. Now that he has a model for axon growth behavior, his next step would be to validate it through experimentation. He knows other researchers who are ready to collaborate—all he needs is funding.

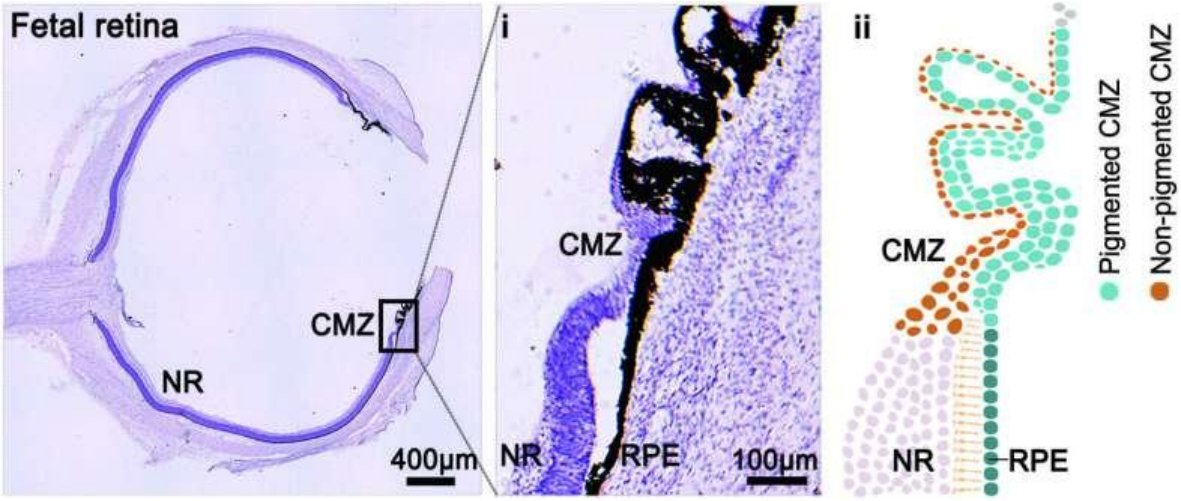
"This research has a lot of potential to reveal brain disorders and mechanisms, so if we have funding, we will extend this to a true scale model," Razavi said. "We could initiate fibers in different locations and let them grow to see what happens when we have the unfolding of the brain. Can we see the same pattern that we have predicted?"

More information: Akbar Solhtalab et al, Stress landscape of folding brain serves as a map for axonal pathfinding, *Nature Communications* (2025). DOI: 10.1038/s41467-025-56362-3
Journal information: Nature Communications
Provided by Binghamton University

MARCH 28, 2025

Human retinal stem-like cells with potential to repair vision loss discovered

by Justin Jackson , Medical Xpress



H&E staining of an 18-week human fetal retina, showing the spatial distribution and differentiation potential of human retinal stem cells in the ciliary marginal zone. Credit: Jianzhong Su, State Key Laboratory of Eye Health, Eye Hospital, Wenzhou Medical University

Wenzhou Medical University and collaborating institutions have identified a population of human neural retinal stem-like cells able to regenerate retinal tissue and support visual recovery.

Vision loss caused by retinal degeneration affects millions worldwide. Conditions such as retinitis pigmentosa and age-related macular degeneration involve the irreversible loss of light-sensitive neural cells in the retina. While current treatments may slow progression, they do not replace damaged tissue.

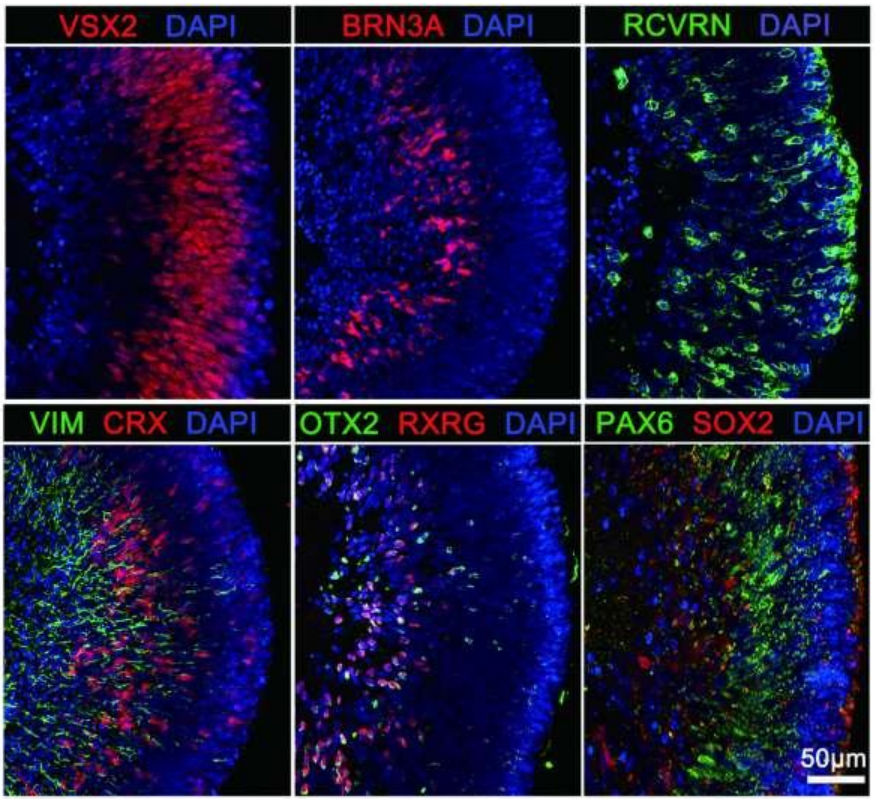
For decades, scientists have explored whether stem cells could be used to regenerate the retina, but the existence of true retinal stem cells in humans has remained uncertain. In fish and amphibians, the outer edge of the retina houses stem cells that regenerate tissue continuously. Whether a comparable system exists in the human eye has been debated for more than two decades.

In the study, "Identification and characterization of human retinal stem cells capable of retinal regeneration," published in *Science Translational Medicine*, researchers used single-cell and spatial transcriptomic methods to investigate the presence and identity of retinal stem-like cells in humans.

Researchers examined human fetal retinal tissue from four donors at 21 weeks of gestation, using spatial transcriptomics and single-nucleus sequencing to identify and localize cell types in the retina.

Researchers analyzed gene expression and chromatin accessibility to detect populations with stem cell–like properties. Additional samples from donors between 16 and 22 weeks of gestation were used to confirm the location of these cells in the peripheral retina.

A distinct population of neural retinal stem-like cells was identified in the peripheral retina of human fetal tissue. Located in the ciliary marginal zone, these cells showed molecular features consistent with self-renewal and the ability to differentiate into all major retinal cell types. Similar cells appeared in the same anatomical region of retinal organoids, with overlapping gene expression profiles.



Immunostaining of retinal organoid sections at repair stage day 40, highlighting different types of retinal cells. Credit: Jianzhong Su, State Key Laboratory of Eye Health, Eye Hospital, Wenzhou Medical University

Following injury in organoids, stem-like cells migrated into the damaged area and produced new retinal cells. Gene activity during the repair process matched patterns observed during natural fetal development.

In a mouse model of inherited retinal degeneration, transplanted cells remained viable for up to 24 weeks. Donor cells integrated into the host retina, developed into mature retinal types, and formed connections with neighboring cells. Treated animals exhibited improved retinal structure and stronger visual responses compared to controls.

Human retinal stem-like cells demonstrated the capacity to regenerate tissue and restore visual function across both fetal tissue and retinal organoid models. In both injury models and transplant experiments, the cells demonstrated the ability to restore retinal structure and contribute to visual function.

Post-transplantation, the cells remained viable for at least 24 weeks, differentiated into photoreceptors, ganglion cells, and bipolar cells, and formed functional synapses with host tissue. Treated mice demonstrated improved retinal morphology and performance in visual function assays across multiple time points. No intraocular tumors were observed following transplantation.

Compared to previously studied retinal progenitor cells, this population showed broader differentiation capacity and longer-term viability. Transplanted cells contributed to retinal structure and restored visual function in mice, without adverse effects.

Results suggest that retinal organoids may serve as a source of human stem-like cells for future research and therapeutic development. Further studies will be needed to assess safety, immune compatibility, and effectiveness in models that more closely resemble human disease.

More information: Hui Liu et al, Identification and characterization of human retinal stem cells capable of retinal regeneration, *Science Translational Medicine* (2025). DOI: 10.1126/scitranslmed.adp6864
Journal information: Science Translational Medicine

Woman's Brain Implant Turns Her Thoughts Into Speech in Real Time

digital brain image

Nearly two decades after suffering a brainstem stroke at the age of 30 that left her unable to speak, a woman in the US regained the ability to turn her thoughts into words in real time thanks to a new brain-computer interface (BCI) process.

By analyzing her brain activity in 80-millisecond increments and translating it into a synthesized version of her voice, the innovative method by US researchers dispelled a frustrating delay that plagued previous versions of the technology.

Our body's ability to communicate sounds as we think them is a function we often take for granted. Only in rare moments when we're forced to pause for a translator, or hear our speech delayed through a speaker, do we appreciate the speed of our own anatomy.

For individuals whose ability to shape sound has been severed from their brain's speech centers, whether through conditions such as amyotrophic lateral sclerosis or lesions in critical parts of the nervous system, brain implants coupled to specialized software have promised a new lease on life.

A number of BCI speech-translation projects have seen monumental breakthroughs recently, each aiming to whittle away at the time taken to generate speech from thoughts.

Most existing methods require a complete chunk of text to be considered before software can decipher its meaning, which can significantly drag out the seconds between speech initiation and vocalization.

Not only is this unnatural, it can also be frustrating and uncomfortable for those using the system.

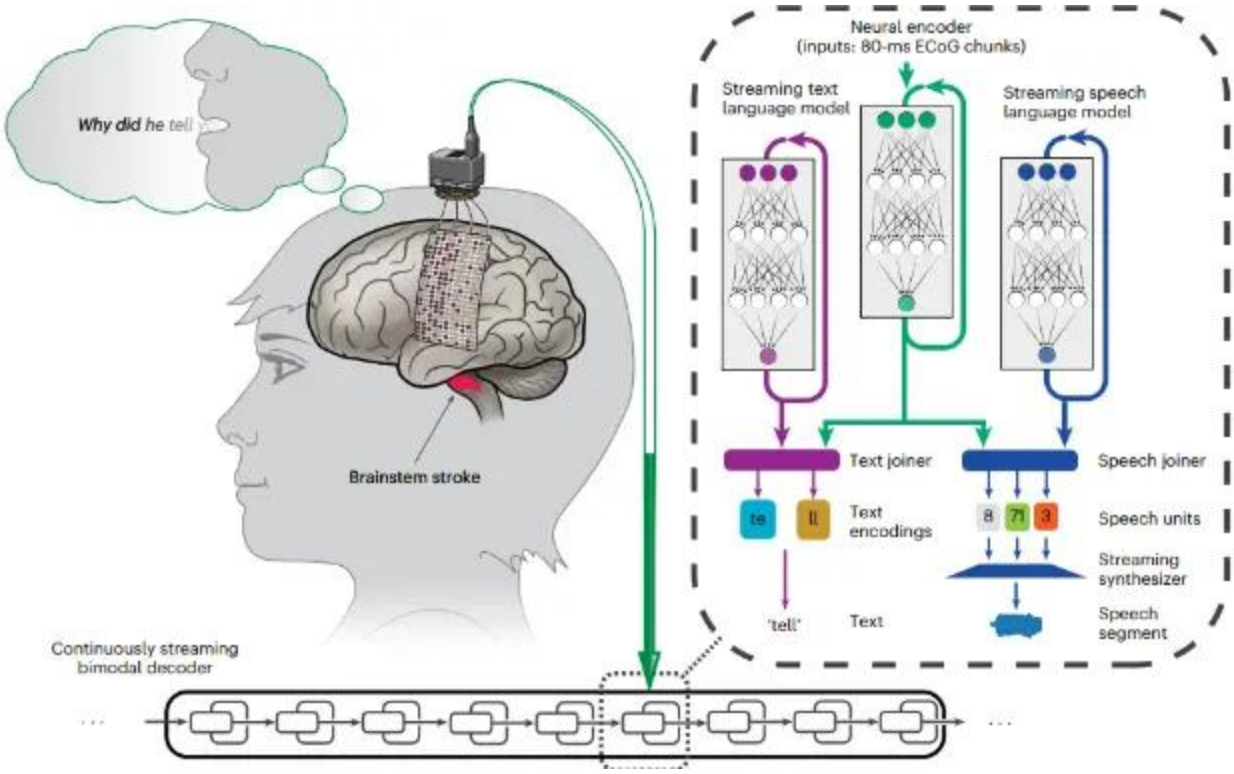
"Improving speech synthesis latency and decoding speed is essential for dynamic conversation and fluent communication," the researchers from the University of California in Berkeley and San Francisco write in their published report.

This is "compounded by the fact that speech synthesis requires additional time to play and for the user and listener to comprehend the synthesized audio," explains the team, led by University of California, Berkeley computing engineer Kaylo Littlejohn.

What's more, most existing methods rely on the 'speaker' training the interface by overtly going through the motions of vocalizing. For individuals who are out of practice, or have always had difficulty speaking, providing their decoding software with enough data might be a challenge.

To overcome both of these hurdles, the researchers trained a flexible, deep learning neural network on the 47-year-old participant's sensorimotor cortex activity while she silently 'spoke' 100 unique sentences from a vocabulary of just over 1,000 words.

Littlejohn and colleagues also used an assisted form of communication based on 50 phrases using a smaller set of words.



Operating in increments of 80 milliseconds, this latest method of translating neural commands into speech can communicate in an almost natural manner. (Littlejohn et al., Nature Neuroscience , 2025)

Unlike previous methods, this process did not involve the participant attempting to vocalize – just to think the sentences out in her mind.

The system's decoding of both methods of communication was significant, with the average number of words per minute translated close to double that of previous methods.

Importantly, using a predictive method that could continuously interpret on the fly allowed the participant's speech to flow in a far more natural manner that was 8 times faster than other methods. It even sounded like her own voice, thanks to a voice synthesis program based on prior recordings of her speech.

Running the process offline without limitations on time, the team showed their strategy could even interpret neural signals representing words it hadn't been deliberately trained on.

The authors note there is still much room for improvement before the method could be considered clinically viable. Though the speech was intelligible, it fell well short of methods that decode text.

Considering how far the technology has come in just a few years, however, there is reason to be optimistic that those without a voice could soon be singing the praises of researchers and their mind-reading devices.

This research was published in *Nature Neuroscience*.

Here's more of what you'll see through Meta's $1,000 smart glasses

Here's more of what you'll see through Meta's $1,000 smart glasses

Meta is reportedly preparing a higher-end version of its Ray-Ban Meta smart glasses with a built-in screen to launch as early as by the end of the year, *Bloomberg* reports.

The new glasses, codenamed Hypernova, can run apps and display photos, all controlled using hand gestures and capacitive touch on the sides of the frame. *Bloomberg* reports that the screen will only be visible on the right lens at the lower-right quadrant, and is best viewed when looking downward. When the device is turned on, a home screen appears and displays icons horizontally, similar to a Meta Quest.

Hypernova will also feature an improved camera compared to the current model, and will continue building upon the idea of having an AI chatbot on your face, according to *Bloomberg*.

Bloomberg says that Hypernova will cost over $1,000 and could sell for as high as $1,300 to $1,400. For comparison, the current Meta Ray-Ban smart glasses start at $299.

Meta is reserving advanced augmented reality technology for its still-in-development Orion glasses. In contrast, the Hypernova will target the "mid-tier" smart glasses shown off in droves at CES, such as the Rokid Glasses that display green text.

However, the Hypernova will command a higher price tag than other options, likely since it will come with the Orion's "neural" wristband controller, codenamed Ceres.

Meta is also working on a next version of Hypernova, with the codename Hypernova 2, that will have two screens, *Bloomberg* reports. The company is apparently planning to launch Hypernova 2 in 2027.

Scientists observe possible ‘foundation of human intelligence’ for first time

In a nutshell

- Human brain neurons maintain consistent responses to people and objects regardless of context—unlike animal brains which show different neural responses to the same thing in different environments.
- This “context-independent” memory coding was observed in 97% of responsive neurons during memory formation and 100% during recall, suggesting a fundamental difference in how humans process information.
- This unique brain processing may explain why humans can think abstractly and transfer knowledge across different contexts—potentially revealing a key foundation of human intelligence.

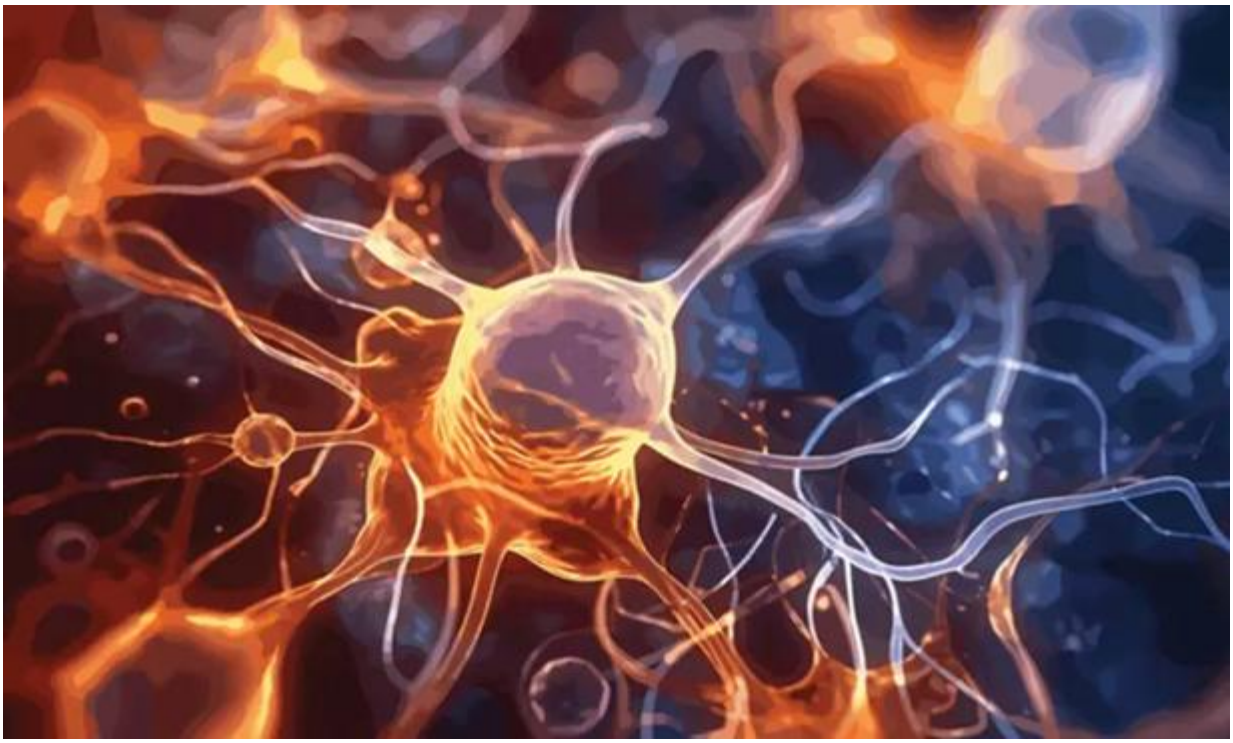
BARCELONA — For the first time, scientists have confirmed that the human brain processes memories in a way that’s remarkably different from other species — a finding that may reveal a key foundation of human intelligence. Their research shows that individual neurons in the human brain represent concepts consistently, regardless of the context in which we encounter them. It’s a stark contrast to what happens in the brains of rodents and monkeys.

This finding may help explain some uniquely human cognitive abilities, including our capacity for abstract thought, metacognition, and forming connections across vastly different situations. It indicates that the way our brains encode memories might be a key evolutionary adaptation that separates the human mind from that of other species.

“This context-invariant coding could be a key, unique feature of human intelligence,” the researchers note in their paper.

More specifically, the study, published in *Cell Reports*, suggests this ability to maintain stable neural representations across different situations may be what enables our unique capacity for abstract thinking.

“The basic principle of neuronal coding in humans is the opposite of what has been observed in other species, which has significant implications,” notes Dr. Rodrigo Quian Quiroga, who led the research at the Hospital del Mar Research Institute, in a statement. This fundamentally different approach to memory storage represents a radical departure from existing neuroscience models.



A 3D rendering of neurons and how they connect and communicate through synaptic connections. (credit: Sanford Burnham Prebys)

Why Neuronal Behavior Matters

The research team studied the activity of individual neurons in the brains of nine epilepsy patients who had electrodes implanted as part of their treatment. This rare opportunity allowed the scientists to observe how single neurons behave when forming and recalling memories—something that cannot be done with standard brain imaging techniques.

The study revealed something unexpected: When a neuron responded to a specific person (like the Argentinian TV host Diego Topa used in one example), it fired in almost exactly the same way regardless of whether that person appeared in story context A or story context B. This contradicts decades of animal research

showing that neurons in other species significantly modify their firing patterns based on context.

When a rat encounters a familiar object in two different locations, its brain activates different sets of neurons—essentially creating separate memories for the same object in different contexts. This has been well-documented across animal studies.

Human brains, however, appear to work differently. Our neurons recognize concepts consistently, regardless of where we encounter them. It's as though our brains prioritize the "what" over the "where" or "when."

How the Study Worked

The researchers used a clever experimental design to investigate this phenomenon. Patients learned and recalled four simple stories, with two different stories featuring the same person in entirely different contexts. By recording the activity of individual neurons as participants learned and recalled these stories, the scientists could directly observe how context influenced neural responses.

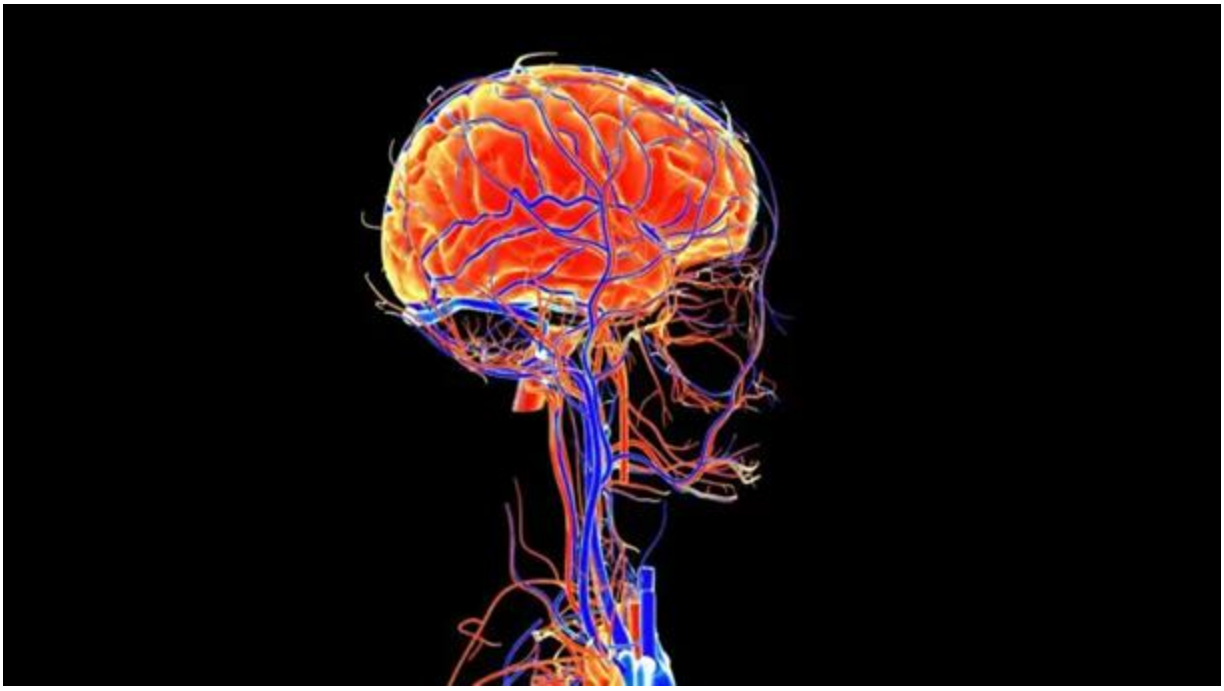
Incredibly, nearly all neurons (97% during encoding and 100% during recall) maintained consistent firing patterns regardless of which story context was being processed. The neurons fired robustly to the presence of a specific person regardless of where they appeared in the narrative.

This consistency held true across different tasks as well. The same neurons activated whether participants were passively viewing images of people, actively learning stories about them, or recalling those stories from memory.

The researchers also looked for evidence of "conjunctive coding"—neurons that might fire only to specific combinations, such as "Jackie Chan at the waterfall" but not "Jackie Chan at another location." Such conjunctive coding is common in animal studies but was almost entirely absent in the human participants. Less than 1% of neurons showed any evidence of responding to specific person-context combinations.

Statistical models built by the team could successfully predict which person a participant was processing but failed to predict which specific story context was

involved—further evidence that the neural representations were context-independent.



The ability to think abstractly separates the human brain from that of other mammals. (Credit: Shot4Sell/Shutterstock)

A New Perspective of Human Intelligence

"Memories are stored in a much more abstract manner in humans compared to other animals. You can think of concepts or anything else in more abstract terms, independent of the context in which you learned them," explains Dr. Quian Quiroga, suggesting that this could be one of the "foundations of human intelligence."

This ability to maintain consistent mental representations across different contexts might be what enables humans to think abstractly and make connections between seemingly unrelated scenarios.

"This ability allows us to make much more abstract and complex associations and inferences than if we were forced to think of each concept within a specific, concrete context," Dr. Quian Quiroga asserts. "In other words, humans can decontextualize their memories to create more abstract thought."

These findings challenge the prevailing view that human memory works similarly to that of other mammals, just with greater complexity. Instead, they point to a key difference in information processing that could help explain uniquely human cognitive abilities.

This mechanism might be what allows us to recognize the same person in completely different contexts, take lessons learned in one domain and apply them to entirely different scenarios, or understand abstract concepts like justice or democracy regardless of the specific examples we encounter.

The human brain, it seems, plays by different rules than we've long believed—rules that might help explain our unique place in the animal kingdom.

Paper Summary

Methodology

The study examined nine epilepsy patients who had electrodes implanted in their brains as part of their clinical treatment. These electrodes allowed direct recording from the hippocampus and amygdala, brain regions crucial for memory formation. Patients first viewed over 100 pictures to identify which stimuli triggered responses in specific neurons. Researchers then created four stories with similar structures, where two stories featured one person in different contexts, and two featured another person in different contexts. Participants learned these stories through repeated presentations and then recalled them when prompted. By recording brain activity during both learning and recall, researchers could directly observe how individual neurons responded to the same person in different narrative contexts.

Results Breakdown

The key findings revealed that human memory neurons behave consistently across contexts. Out of all neurons that responded to a specific person during memory encoding, 97% showed no significant difference in their response when that person appeared in two completely different story contexts. During recall,

this consistency rose to 100%. The team could predict which person a participant was thinking about with 84% accuracy during encoding and 75% during recall but could not reliably determine which specific story context was being processed. This provided strong evidence that human memory neurons maintain consistent responses regardless of context—a fundamental difference from how animal brains process memories.

Limitations

This study has important limitations to consider. The small sample of nine epilepsy patients may not represent how all human brains function. The recordings were limited to specific brain regions determined by clinical needs. The researchers used familiar identities in their design, and it remains unknown whether novel, unfamiliar stimuli would show similar patterns. During the encoding phase, identical pictures were used across different stories, which might have influenced the results, though similar findings were observed during recall when no pictures were shown.

Discussion and Takeaways

The significance of this research extends beyond basic neuroscience. The authors suggest that context-invariant neural coding might explain uniquely human cognitive abilities. While the hippocampus is known to be critical for context-dependent memories across species, the mechanisms appear to differ fundamentally in humans. Rather than neurons changing their firing patterns based on context, humans might represent different contexts through the co-activation of different neuronal assemblies, each encoding specific elements in a context-independent way. This mechanism could facilitate metacognition (thinking about thoughts independent of specific contexts), making inferences across diverse situations, and generalizing concepts across contexts – all hallmarks of human intelligence. The authors suggest this might reflect an evolutionary adaptation connected to language, which allows humans to think about meaning independently from specific sensory experiences. This discovery challenges prevailing models of memory that assume human memory works similarly to that of other mammals but with greater complexity. Instead, it

suggests a qualitatively different information processing approach that may help explain the unique nature of human cognition.

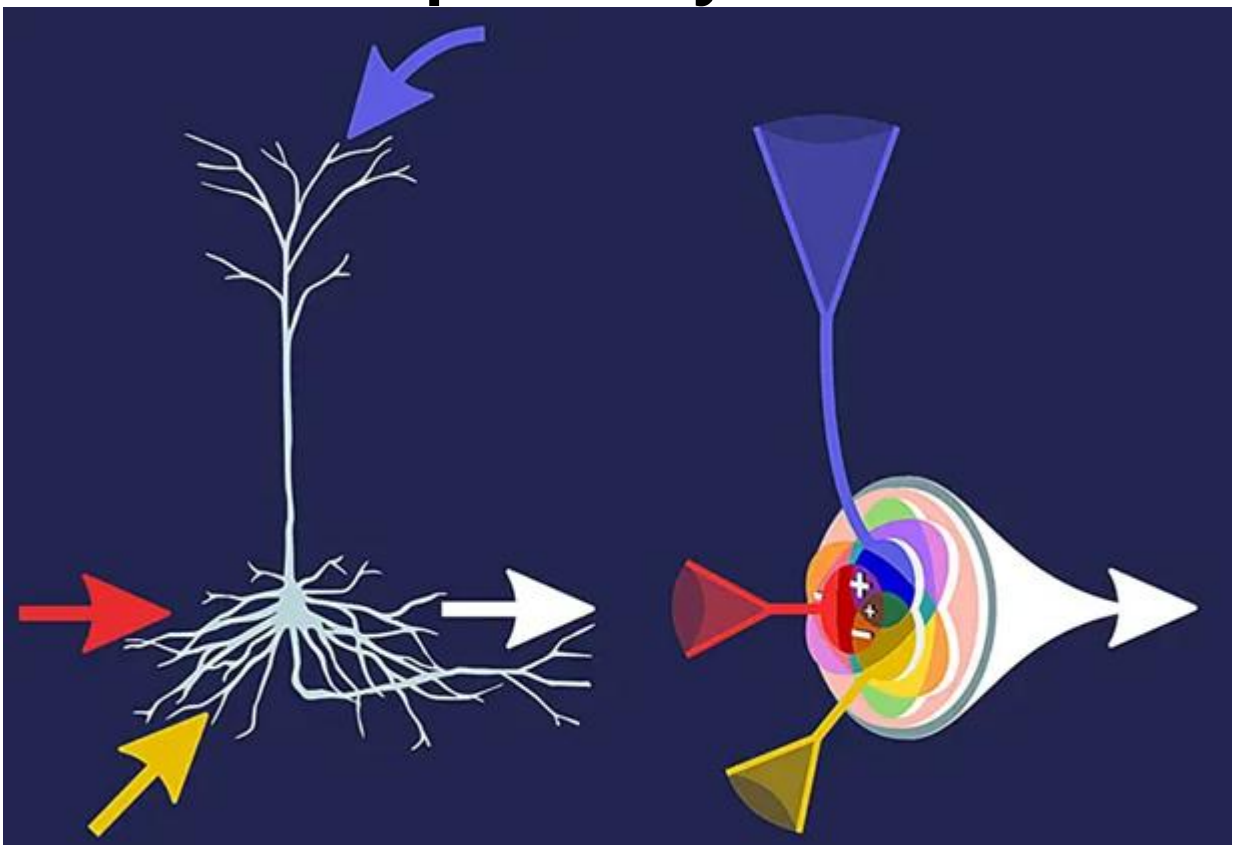
Funding and Disclosures

The research was supported by grants from several organizations including the Medical Research Council, the Biotechnology and Biological Sciences Research Council, the Human Frontiers Science Project, the Royal Society, and CONICET (Argentina's National Scientific and Technical Research Council). The authors declared no competing interests related to the research.

Publication Information

The study, titled "Lack of context modulation in human single neuron responses in the medial temporal lobe," was authored by Hernan G. Rey, Theofanis I. Panagiotaropoulos, Lorenzo Gutierrez, Fernando J. Chaure, Alejandro Nasimbera, Santiago Cordisco, Fabian Nishida, Antonio Valentin, Gonzalo Alarcon, Mark P. Richardson, Silvia Kochen, and Rodrigo Quian Quiroga. It was published in *Cell Reports* (Volume 44, 115218) on January 28, 2025. The research represents a collaborative effort involving scientists from the University of Leicester (UK), Medical College of Wisconsin (USA), INSERM (France), University of Buenos Aires (Argentina), ENyS CEMET (Argentina), King's College London (UK), Royal Manchester Children's Hospital (UK), El Cruce Hospital (Argentina), Hospital Del Mar Medical Research Institute (Spain), and several other institutions.

Self-organizing 'infomorphic neurons' can learn independently



Living neurons receive signals from different sources, process them and pass an output signal on to other neurons (left). In the artificial neuron model, this information processing can be described and improved by a learning objective (right). Similar to their biological models, this independent learning allows novel artificial neurons to solve tasks in a self-organized way. Credit: Andreas Schneider, MPI-DS

Researchers have developed "infomorphic neurons" that learn independently, mimicking their biological counterparts more accurately than previous artificial neurons. A team of researchers from the Göttingen Campus Institute for Dynamics of Biological Networks (CIDBN) at the University of Göttingen and the Max Planck Institute for Dynamics and Self-Organization (MPI-DS) has programmed these infomorphic neurons and constructed artificial neural networks from them.

The special feature is that the individual artificial neurons learn in a self-organized way and draw the necessary information from their immediate environment in the network. Their findings are published in the journal *Proceedings of the National Academy of Sciences*.

Both the human brain and modern artificial neural networks are extremely powerful. At the lowest level, the neurons work together as rather simple computing units.

An artificial neural network typically consists of several layers composed of individual neurons. An input signal passes through these layers and is processed by artificial neurons in order to extract relevant information. However, conventional artificial neurons differ significantly from their biological models in the way they learn.

While most artificial neural networks depend on overarching coordination outside the network in order to learn, biological neurons only receive and process signals from other neurons in their immediate vicinity in the network. Biological neural networks are still far superior to artificial ones in terms of both flexibility and energy efficiency.

The new artificial neurons, known as "infomorphic neurons," are capable of learning independently and self-organizing among their neighboring neurons. This means that the smallest unit in the network has to be controlled no longer from the outside, but decides itself which input is relevant and which is not.

In developing the infomorphic neurons, the team was inspired by the way the brain works, especially by the pyramidal cells in the cerebral cortex. These also process stimuli from different sources in their immediate environment and use them to adapt and learn. The new artificial neurons pursue very general, easy-to-understand learning goals.

"We now directly understand what is happening inside the network and how the individual artificial neurons learn independently," emphasizes Marcel Graetz from CIDBN.

By defining the learning objectives, the researchers enabled the neurons to find their specific learning rules themselves. The team focused on the learning process of each individual neuron.

They applied a novel information-theoretic measure to precisely adjust whether a neuron should seek more redundancy with its neighbors, collaborate synergistically, or try to specialize in its own part of the network's information.

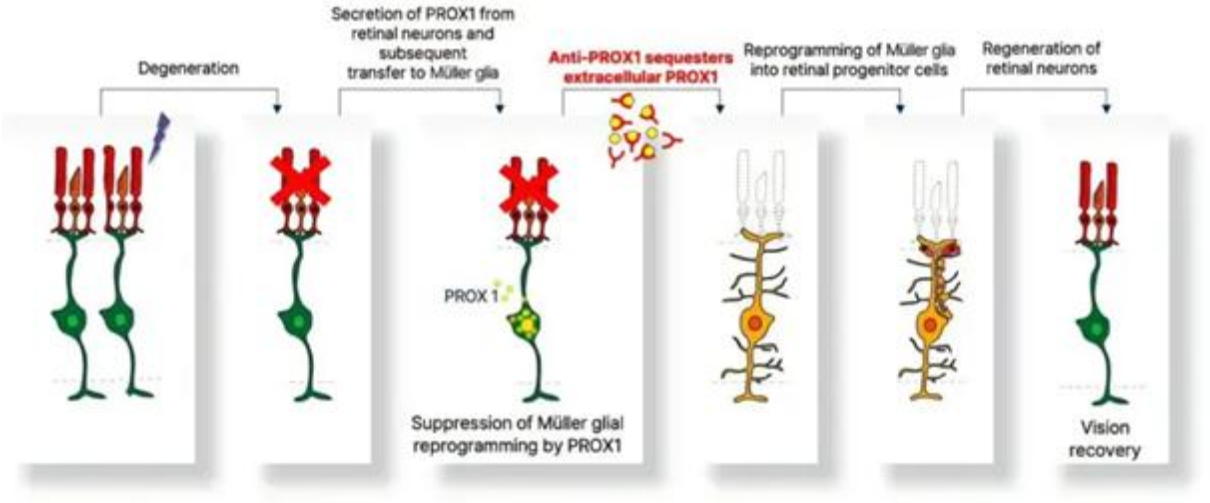
"By specializing in certain aspects of the input and coordinating with their neighbors, our infomorphic neurons learn how to contribute to the overall task of the network," explains Valentin Neuhaus from MPI-DS.

With the infomorphic neurons, the team is not only developing a novel method for machine learning, but is also contributing to a better understanding of learning in the brain.

More information: Abdullah Makkeh et al, A general framework for interpretable neural learning based on local information-theoretic goal functions, *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2408125122

Provided by Max Planck Society

Vision restored: Retinal therapy research marks first successful induction of long-term neural regeneration



Schematic diagram of the mechanism of retinal regeneration through inhibition of PROX1 migration. PROX1 protein secreted from damaged retinal nerve cells migrates to Müller glia and inhibits dedifferentiation into neural progenitor cells and neural regeneration. When PROX1 is captured outside the cells with a neutralizing antibody against PROX1 and its migration to Müller glia is inhibited, dedifferentiation of Müller glia cells and neural cell regeneration processes are resumed, restoring retinal function. Credit: Nature Communications (2025). DOI: 10.1038/s41467-025-58290-8

Vision is one of the most crucial human senses, yet more than 300 million people worldwide are at risk of vision loss due to various retinal diseases. While recent

advancements in retinal disease treatments have successfully slowed disease progression, no effective therapy has been developed to restore already lost vision—until now.

KAIST researchers led by Professor Jinwoo Kim from the Department of Biological Sciences have successfully developed a novel drug to restore vision through retinal nerve regeneration. The research is published in the journal *Nature Communications*. The study was co-authored by Dr. Eun Jung Lee of Celliaz Inc. and Museong Kim, a Ph.D. candidate at KAIST, as joint first authors.

The research team successfully induced neural regeneration and vision recovery in a disease-model mouse by administering a compound that blocks the PROX1 (Prospero Homeobox 1) protein, which suppresses retinal regeneration. The effect lasted for more than six months.

This study marks the world's first successful induction of long-term neural regeneration in mammalian retinas, offering new hope to patients with degenerative retinal diseases who previously had no treatment options.

As the global population continues to age, the number of retinal disease patients is steadily increasing. However, no treatments exist to restore damaged retinas and vision. The primary reason for this is the mammalian retina's inability to regenerate once damaged.

Studies on cold-blooded animals, such as fish—known for their robust retinal regeneration—have shown that retinal injuries trigger Müller glia cells to dedifferentiate into neural progenitor cells, which then generate new neurons. However, in mammals, this function is lost, leading to permanent retinal damage.

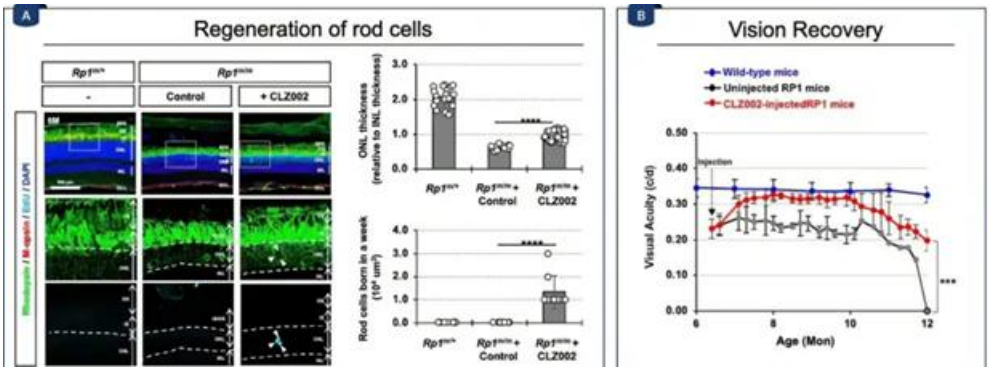
Through this study, the research team identified the PROX1 protein as a key inhibitor of Müller glia dedifferentiation in mammals. PROX1 is a protein found in neurons of the retina, hippocampus, and spinal cord, where it suppresses neural stem cell proliferation and promotes differentiation into neurons.

The researchers discovered that PROX1 accumulates in damaged mouse retinal Müller glia, but is absent in the highly regenerative Müller glia of fish. Furthermore, they demonstrated that the PROX1 found in Müller glia is not synthesized internally but rather taken up from surrounding neurons, which fail to degrade and instead secrete the protein. Based on this finding, the team

developed a method to restore Müller glia's regenerative ability by eliminating extracellular PROX1 before it reaches these cells. This approach involves using an antibody that binds to PROX1, discovered by Celliaz Inc., a biotech startup founded by Professor Jinwoo Kim's research lab. This PROX1-neutralizing antibody exhibited superior binding affinity compared to existing antibodies. When administered to disease-model mouse retinas, this antibody significantly promoted neural regeneration. Additionally, when delivered as a type of gene therapy in mice with congenital retinal degeneration, it enabled sustained neuronal production and vision restoration for over six months.

The retinal regeneration-inducing therapy is currently being developed by Celliaz Inc. for application in various degenerative retinal diseases that currently lack effective treatments. The company aims to begin clinical trials by 2028.

Dr. Eun Jung Lee stated, "We are finalizing improvements to the efficacy of the PROX1-neutralizing antibody (CLZ001) and aim to complete vision restoration efficacy and safety evaluations in multiple animal models before administering it to retinal disease patients. Our goal is to provide a real solution for patients at risk of blindness who currently lack proper treatment options."



Retinal regeneration and visual recovery in a retinitis pigmentosa model mouse through administration of AAV2-Anti-PROX1 gene therapy. We demonstrate that after administration of adeno-associated virus (AAV2-Anti-PROX1) expressing PROX1 neutralizing antibodies to the eyes of RP1 retinitis pigmentosa model mice with vision loss, the photoreceptor cell layer of the retina is restored (A) and vision is restored (B). Credit: Nature Communications (2025).

DOI: 10.1038/s41467-025-58290-8 **More information:** Eun Jung Lee et al, Restoration of retinal regenerative potential of Müller glia by disrupting intercellular Prox1 transfer, *Nature Communications* (2025). DOI: 10.1038/s41467-025-58290-8

Provided by The Korea Advanced Institute of Science and Technology (KAIST)