

## Health Matters

# Epilepsy: Researchers reveal potential new treatment

In what could one day become a new treatment for epilepsy, researchers at UC San Francisco, UC Santa Cruz and UC Berkeley have used pulses of light to prevent seizure-like activity in neurons. The researchers used brain tissue that had been removed from epilepsy patients as part of their treatment.

Eventually, they hope the technique will replace surgery to remove the brain tissue where seizures originate, providing a less invasive option for patients whose symptoms cannot be controlled with medication.

The team used a method known as optogenetics, which employs a harmless virus to deliver light-sensitive genes from microorganisms to a particular set of neurons in the brain that can be switched on and off with pulses of light.

It is the first demonstration that optogenetics can be used to control seizure activity in living human brain tissue, and it opens the door to new treatments for other neurological diseases and conditions.

"This represents a giant step toward a powerful new way of treating epilepsy and likely other conditions," said Tomasz Nowakowski, PhD, an assistant professor of neurological surgery and a co-senior author of the study published recently.

To keep the tissue alive long enough to complete the study, which took several weeks, the researchers created an environment that mimics conditions inside the skull.

John Andrews, MD, a resident in neurosurgery, placed the tissue on a nutrient medium that resembles the cerebrospinal fluid that bathes the brain.

David Schaffer, PhD, a biomolecular engineer at UC Berkeley found the best virus to deliver the genes, so they would work in the specific neurons the team was targeting.

Andrews then placed the tissue on a bed of electrodes small enough to detect the electrical discharges of neurons communicating with each other.

When the brain is acting normally, neurons send signals at different times and frequencies in a predictable, low-level chatter. But during a seizure, the chatter synchronizes into loud bursts of electrical activity that overwhelm the brain's casual conversation.

The team hoped to use the light pulses to prevent the bursts by switching off neurons that contained light-sensitive proteins.

First, the team needed to find a way to run their experiments without disturbing the tissue. The tiny electrodes were only 17 microns apart -- less than half the width of a human hair -- and the smallest movement of the brain slices could skew their results.

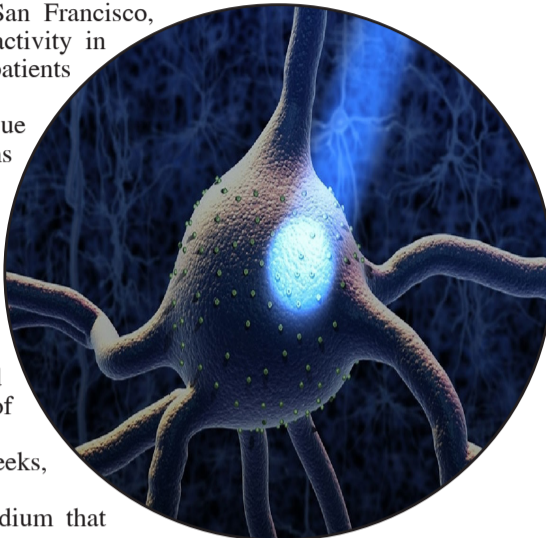
Mircea Teodorescu, PhD, an associate professor of electrical and computer engineering at UCSC and co-senior author of the study, designed a remote-control system to record the neurons' electrical activity and deliver light pulses to the tissue.

Teodorescu's lab wrote software that enabled the scientists to control the apparatus, so the group could direct experiments from Santa Cruz on the tissue in Nowakowski's San Francisco lab.

That way, no one needed to be in the room where the tissue was being kept.

"This was a very unique collaboration to solve an incredibly complex research problem," Teodorescu said. "The fact that we actually accomplished this feat shows how much farther we can reach when we bring the strengths of our institutions together."

Optogenetics enables researchers to zoom in on discrete sets of neurons. The group could see which types of neurons and how many of them were needed to start a seizure. And they determined the lowest intensity of light needed to change the electrical activity of the neurons in live brain slices.



# Diabetes med helps reduce alcohol consumption

New research, led by experts at the University of Nottingham, has found that certain types of medication used to treat diabetes may be effective in reducing alcohol use.

The study, which is published recently, looked at whether a type of diabetes medication, called GLP-1 receptor agonists (GLP-1 RAs), could also be used to help people cut down on drinking.

The study was led by Dr Mohsen Subhani, Clinical Assistant Professor of Gastroenterology at the NIHR Nottingham Biomedical Research Centre, in the School of Medicine, at the University of Nottingham.

It was funded by the National Institute for Health and Care Research (NIHR) and the NIHR Nottingham Biomedical Research Centre. In the new study, researchers evaluated existing literature on GLP-1 RAs use and the change in alcohol consumption.

They gathered studies up to August 2024 that examined whether GLP-1



RAs affect alcohol use, alcohol-related health problems, hospital visits, and brain reactions to alcohol cues.

The team evaluated six articles, including two randomised control trials made up of 88,190 participants, of these 38,740 (43.9%) of participants received GLP-1RA.

Dr Subhani said: "Our findings show that this type of diabetes medication shows promise in reducing alcohol consumption, potentially by targeting the brain's reward centre, especially in people with a BMI over 30."

The key findings: 1. In one main study, the medication exenatide did not significantly reduce

drinking overall after six months, but people with obesity showed some positive results. 2. Another study found that people taking the drug dulaglutide were 29% more likely to reduce drinking than those on a placebo. 3. Observational studies (non-randomised) showed fewer alcohol-related health problems and lower alcohol use in people taking GLP-1 RAs compared to other treatments.

"Whilst further research is needed, our findings suggest this could be a potential treatment option in the future for excessive alcohol use and subsequently could lead to a reduction in alcohol-related deaths," adds Dr Subhani.

# Why teenagers often make unwise decisions

Adults exhibit a general tendency to make better decisions than adolescents, and this improvement drives an increase in specific and more sophisticated choice behaviors, according to a study published recently by Vanessa Scholz and Lorenz Deserno from the University of Würzburg, Germany, and colleagues.

Learning and decision-making change considerably from adolescence into adulthood. Adolescents undergo developmental changes in specific choice behaviors, such as goal-directed behaviors and motivational influences over choice.

They also consistently show high levels of decision noise, i.e., choosing suboptimal options.

However, it remains unknown whether these observations - the development of specific and more sophisticated choice processes and higher decision noise - are independent or related.



It is possible that the development of specific choice processes might be impacted by age-dependent changes in decision noise.

To test this idea, Scholz, Deserno, and colleagues analysed data from 93 participants between 12 and 42 years of age.

The participants completed three reinforcement learning tasks: a task assessing motivational influences over choices, a learning task capturing adaptive decision-making in response to environmental changes, and a task measuring goal-directed behavior.

The results revealed that noise levels were strongly correlated across reinforcement learning tasks.

Critically, noise levels mediated age-dependent increases in more sophisticated choice behaviors and performance gains.

The findings suggest that unspecific noise mediates the development of highly specific functions or strategies.

One reason for these mediation effects could be a limited availability of cognitive resources in adolescents due to the ongoing development of brain areas related to cognitive control.

Having fewer cognitive resources might make adolescents more prone to rely on computationally cheaper decision strategies, rendering them more susceptible to emotional, motivational and social influences.

Overall, the study provides novel insights into the computational processes underlying developmental changes in decision-making.

According to the authors, future work may unravel the neural basis as well as the developmental and clinical real-life relevance of decision noise for neurodevelopmental disorders.

The authors add, "Teenagers make less optimal, so-called 'noisy' decisions. While these noisy decisions decrease when growing older, this decrease is also linked to the development of improved complex decision-making skills, such as planning and flexibility."

# Zinc deficiency promotes lung infection: Study

Dietary zinc deficiency promotes lung infection by *Acinetobacter baumannii* bacteria - a leading cause of ventilator-associated pneumonia, according to a new study published recently.

A Vanderbilt University Medical Center-led team of researchers discovered an unexpected link between the pro-inflammatory cytokine interleukin-13 (IL-13) and *A. baumannii* lung infection, and they demonstrated that blocking IL-13 prevented infection-associated death in an animal model. The findings suggest that anti-IL-13 antibodies, which are FDA-approved for use in humans, may protect against bacterial pneumonia in patients with zinc deficiency.

"To our knowledge, this is the first study showing that neutralization of IL-13 could prevent mortality from a bacterial infection," said Eric Skaar, PhD, MPH, the Ernest W. Goodpasture Professor of Pathology and director of the Vanderbilt Institute for Infection, Immunology and Inflammation. "This discovery points to the possibility of using anti-IL-13 therapy in patients



with zinc deficiency and *A. baumannii* pneumonia as part of a personalized therapy approach."

Nearly 20% of the world's population is at risk for zinc deficiency, which can impair immune function and is a major risk factor for pneumonia. The World Health Organization considers zinc deficiency a leading contributor to disease and death. Patients at risk for zinc deficiency, particularly critically ill and elderly patients, are also at risk for *A. baumannii* infection. Patients in health care settings have the highest risk for infection, especially those who are on ventilators, have devices such as catheters, are in intensive care units, or have prolonged hospital stays. *A. baumannii* is

becoming increasingly resistant to antimicrobial treatments, making it a critical public health threat, Skaar said.

To explore whether and how dietary zinc deficiency contributes to *A. baumannii* pathogenesis, the researchers established a mouse model of dietary zinc deficiency and acute *A. baumannii* pneumonia. Lauren Palmer, PhD, a former postdoctoral fellow at VUMC who is now assistant professor of Microbiology and Immunology at the University of Illinois, Chicago, led the studies.

The researchers found that zinc-deficient mice had increased *A. baumannii* bacterial burden in the lungs, spread of bacteria to the spleen, and higher mortality compared

to mice with adequate dietary zinc consumption. They showed that the zinc-deficient mice produce more IL-13 during infection and that administration of IL-13 to mice with sufficient zinc promoted spread of *A. baumannii* to the spleen. Anti-IL-13 antibody treatment protected zinc-deficient mice from *A. baumannii*-induced death.

The findings add to a growing set of studies showing that certain nutrient deficiencies are associated with IL-13 production and a "type 2" immune response.

"IL-13 may be an important risk factor for health care-associated and opportunistic lung infections, further supporting exploration of IL-13 as a target for treatment," Skaar noted.

FDA-approved anti-IL-13 antibodies (lebrizumab and tralokinumab) have been extensively investigated as potential therapies for uncontrolled severe asthma. Although they were not found to be effective for that indication, the clinical trials demonstrated their safety.

# New oral drug to calm abdominal pain

University of Queensland researchers have developed a new class of oral painkillers to suppress chronic abdominal pain that is based on the peptide hormone oxytocin that drives childbirth contractions.

Associate Professor Markus Muttenthaler from UQ's Institute for Molecular Bioscience led a team that has changed the chemical structure of oxytocin to make it gut-stable after earlier work revealed the hormone could treat abdominal pain.

Dr. Muttenthaler said there was an urgent need for new treatments for the chronic pain caused by gastrointestinal disorders such as irritable bowel syndrome (IBS) and irritable bowel diseases (IBD).

"This pain affects up to 15 per cent of adults in their lifetime, and all we have are anti-inflammatories and opioids which can cause side effects and addiction," Dr Muttenthaler said. "Our research focuses on peptides that are highly potent and selective molecules and have few side effects. However, nearly all peptide drugs must be injected as they are rapidly digested in the gut.

"We have now developed a way of making peptides gut-stable so they can be given orally. This is a new and highly promising approach to treating gut disorders."

Oxytocin is a peptide hormone produced in the brain which is known as the 'bonding hormone' or

the 'love molecule' due to its effects on relationship building, empathy and trust. Oxytocin is also the key hormone that induces uterine contractions during labour and facilitates milk release during breastfeeding. "We identified the parts of oxytocin that are rapidly broken down by gut enzymes and used medicinal chemistry to render them gut-stable while ensuring that the new molecule was still able to activate the oxytocin receptor," Dr. Muttenthaler said.

"We now have a new class of molecules that are potentially active but do not degrade in the stomach or intestine, meaning they can be taken orally."

The research indicates that

the new molecules work in the colon and do not need to cross the gut barrier into the bloodstream to suppress abdominal pain. "This is a very safe therapeutic approach as it reduces the risk of side effects in the rest of the body, a problem with many other systemic drugs," Dr. Muttenthaler said.

"This is an exciting new mode of action to prevent pain. We are currently looking for investors to accelerate pre-clinical studies, with the goal of taking it into the clinic.

"Now that we have perfected making peptides stable, we are looking at other gut drugs to improve treatment options for gastrointestinal disorders, an unmet medical need."

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AUCTION NOTICE						
The following borrowers of Shivalik Small Finance Bank Ltd. are hereby informed that Gold Loan/s availed by them from the Bank have not been adjusted by them despite various demands and notices including individual notices issued by the Bank. All borrowers are hereby informed that it has been decided to auction the Gold ornaments kept as security with the Bank and accordingly 29.11.2024 has been fixed as the date of auction at 03:00 pm in the branch premises from where the loan was availed. All, including the borrowers, account holders and public at large can participate in this auction on as per the terms and conditions of auction.						
Branch	Account No.	Act Holder name	Father's/ Spouse Name	Address	Ac opening Date	Payoff
CHENNAI	104142510896	PREETHI S	D/O SRIDHAR	78, THIRUVEETHI AMMAN KOIL STREET, VILLIVAKKAM SO, THIRUVALLUR, CHENNAI, TAMIL NADU, 600049	18-07-2024	179,850.63
CHENNAI	104142510642	DHIVAKAR D	S/O DEVANANDAN P C	31 B., CHANDRA PRABU COLONY PONNIAMMANMEDU, THIRUVALLUR, TAMIL NADU, 600110	18-05-2024	207,066.59
CHENNAI	104142510783	SANGEETHA W/O DINESH KUMAR	S/O VILLALAN	5 133, 116 TH STREET, KODUNGAIYUR, MUTHAMIL NAGAR, CHENNAI, TAMIL NADU, 600118	18-06-2024	76,861.28
CHENNAI	104142511104	SANGEETHA W/O DINESH KUMAR	S/O VILLALAN	5 133, 116 TH STREET, KODUNGAIYUR, MUTHAMIL NAGAR, CHENNAI, TAMIL NADU, 600118	18-09-2024	173,511.10

Auction date is 29.11.2024 @ 03:00 pm.

The Bank reserves the right to delete any account from the auction or cancel the auction without any prior notice.

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