JOE R. & TERESA LOZANO LONG SCHOOL OF MEDICINE

FUTURE

SPECIAL RESEARCH EDITION

Mind Shift

Discovering how mind and brain work in concert to help treat neurological disease and mental illness

UT Health San Antonio

A holistic approach to brain health

The brain is the body's central command. It controls every facet of our lives — from our cognitive abilities and physical movements to our sense of self and how we perceive the world around us.

Just as "house" and "home" are distinct yet interdependent concepts, the brain and the mind are similarly intertwined. While the brain, with its billions of neurons and complex circuitry, is the physical structure of consciousness, the mind embodies thoughts, emotions and experiences that seem to transcend its material confines. When this intricate relationship is disrupted from disease or disorder, healing can be complicated. Understanding this connection could unlock breakthroughs in mental health, brain function and human potential.

Despite the enormous strides made in medical prevention and treatment in recent decades — from advanced imaging technologies to precision surgery and interventions — the brain remains one of the most enigmatic organs for physicians and scientists alike.

Researchers at The University of Texas Health Science Center at San Antonio are working to unravel the intricate complexities of the brain and transform discoveries into groundbreaking treatment and care for the full spectrum of conditions affecting the brain and mind, from neurodegenerative diseases to mental health challenges and addiction recovery.

With the opening in 2025 of our new Center for Brain Health, which will serve as a hub for this pioneering work, we are not only advancing the science of brain health, but also investing in the health and future of our community. Brain health challenges are particularly prevalent in our region of South Texas, and this new center will enable us to better serve our community's needs, offering cutting-edge research, innovative treatments and compassionate care.

The center will integrate research efforts and clinical care across a variety of disciplines, with initiatives that pair experts in neurology, mental health and substance use disorder to provide a comprehensive approach to brain health. Working together, we are taking a bold step toward a future where the mysteries of the brain give way to new possibilities for well-being and transformative treatments that can make lives better for those in our community and far beyond.

Francisco Cigarroa, MD
Acting Dean, Long School of Medicine

FUTURE

MEASURES OF SUCCESS

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT SAN ANTONIO IS RATED **#6** AMONG THE **25** TOP RISING INSTITUTIONS IN NORTH AMERICA, ACCORDING TO *NATURE INDEX*

AMA JOY IN MEDICINE™ Recognized Organization BRONZE 2024–2025

2024 RESEARCH FUNDING

NATIONAL INSTITUTES OF HEALTH
$142.8M

U.S. DEPARTMENT OF DEFENSE
$15.3M

ALL FEDERAL FUNDING
$243M

TOTAL ORGANIZED RESEARCH FUNDING
$196.1M

TOTAL SPONSORED PROGRAMS FUNDING
$298.8M

TOP 40 DEPARTMENTAL BLUE RIDGE RANKINGS

#11 PHARMACOLOGY

#20 PHYSIOLOGY (CELLULAR & INTEGRATIVE PHYSIOLOGY)

#20 NEUROLOGY

#22 ANATOMY/CELL BIOLOGY (CELL SYSTEMS & ANATOMY)

#25 UROLOGY

#27 GENETICS (MOLECULAR MEDICINE)

#28 BIOCHEMISTRY & STRUCTURAL BIOLOGY

#29 OBSTETRICS & GYNECOLOGY

THE CENTER FOR BRAIN HEALTH

A multidisciplinary approach to care and research will soon be under one roof

The new Center for Brain Health will feature an imaging suite equipped with a 7-Tesla magnet scanner and dedicated clinical spaces for treatment and rehabilitation.

Opening in 2025, the Center for Brain Health at The University of Texas Health Science Center at San Antonio will be home to the institution's many brain health initiatives to serve the growing need for neurological care in the region.

The new facility will house the health science center's Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, which, in partnership with The University of Texas Rio Grande Valley, is currently the only National Institute on Aging-designated Alzheimer's Disease Research Center in Texas serving patients with conditions that include dementia.

The center will also become home to the university's Department of Neurology, which researches and cares for patients living with neurological diseases including Parkinson's disease and other movement disorders, stroke, Lou Gehrig's disease, muscular dystrophy, peripheral neuropathy, headache, multiple sclerosis, epilepsy and more.

By uniting neurology specialists of all disciplines under one roof, the Center for Brain Health will serve as a comprehensive hub for brain research, fostering collaboration and making discoveries about the brain health issues prevalent in the community. Currently 55 clinical trials and 265 non-interventional cohort studies are underway by investigators.

"This is where patients receive their diagnosis, get genetic testing, engage with support groups. It's where they receive disease treatment and rehabilitation or therapies such as physical and occupational therapy — all delivered with the highest level of care," said Sudha Seshadri, MD, director of the Biggs Institute.

At the center, patients and their caregivers will benefit from a collaborative approach involving specialists in speech therapy, physical therapy, occupational therapy, psychological counseling and psychiatric advice and coordination with a patient's primary care and non-neurology specialists.

"The Center for Brain Health provides a 'one stop shop' for patients with complex neurologic conditions, where they can get all the services they require in a multidisciplinary clinic in a single morning or afternoon," said Carlayne Jackson, MD, FAAN, chair of the Department of Neurology.

This comprehensive approach ensures that while the new center will streamline access to specialized care, it will also emphasize a broader commitment to supporting the total well-being of patients.

"We focus on holistic care, not only diagnosing and prescribing medications, but also partnering with patients and caregivers to support their function and enhance their quality of life," Seshadri said. In alignment with this integrated approach, Seshadri emphasized the importance of having a team of multilingual providers to serve the diverse patient population of San Antonio and South Texas and to support the needs of families and caregivers.

"We are committed to reaching out to and representing our underserved and minority communities, ensuring they receive culturally competent care from providers who understand their language and cultural backgrounds," she said.

The Center for Brain Health will also expand training programs related to brain health, ensuring the future of neurological care in the community.

CENTERS AND INSTITUTES

Scan here to see the full list of centers and institutes at the Joe R. and Teresa Lozano Long School of Medicine.

STROKE

WHEN ‘TIME IS BRAIN’

Coordinated collaboration and novel therapies help minimize stroke damage

BY JESSICA BINKLEY LAIN

In the world of stroke care, every minute counts. Lee Birnbaum, MD, professor in the departments of neurology and neurosurgery in the Joe R. and Teresa Lozano Long School of Medicine, sheds light on the latest developments in emergency treatments, post-stroke therapies and community education aimed at enhancing patient outcomes.

Current emergency protocols for stroke treatment encompass a range of interventions designed to quickly restore blood flow to the brain. For instance, employing IV thrombolytics and performing intra-arterial catheterizations help dissolve clots and clear blockages, while mechanical thrombectomy allows for precise clot removal directly from brain blood vessels.

Like a competitive swimmer or runner, shaving time is always the goal in stroke care.

“We often use the term ‘door to needle’ to refer to the time it takes a patient to receive treatment, from when they enter the door to when medication is given,” Birnbaum said. Another common mantra, “time is brain,” emphasizes how critical speed and efficiency are when it comes to treatment effectiveness and reducing disability among stroke survivors.

Birnbaum noted that advancements in thrombolytics, like the drug Tenecteplase, and thrombectomy tools continually refine and improve upon treatment protocols. But another critical part of triage relies on what happens before a patient gets to the door.

Collaborating with the South Texas Regional Advisory Council, which includes local emergency response teams like EMS and the fire department, the university is part of an initiative that ensures stroke patients receive fast transport to the appropriate hospital or stroke center where specialized care can be promptly administered.

“If you’re having a stroke or think you’re having a stroke, it’s always best to call 911 and not try to go in a private vehicle,” Birnbaum said. “Time is brain, so you want to make sure you’re getting to the right hospital the first time.”

The recovery role of star-shaped cells

Beyond triage and acute treatment, research into neuroprotective agents to mitigate damage after stroke is rapidly advancing. Ranging from pharmaceuticals to probiotics and vitamins, these treatments aim to reduce stroke size and improve post-stroke outcomes.

In the complex landscape of neuroscience, neurons typically take center stage for their role in nearly everything in the brain. Neurons excel in signaling, but when faced with injury, like from a stroke, they get over-excited, signaling too much. This can lead to toxicities and imbalances that swell the brain and, ultimately, cause cell death.

According to James D. Lechleiter, PhD, it’s the astrocytes that quietly uphold the brain’s delicate environment. Astrocytes maintain and help restore the environment, putting the brake on over-active nerve cells, helping them “get their signaling back to where it’s supposed to be,” explained Lechleiter, a professor in the Department of Cell Systems and Anatomy and director of the health science center’s Optical Imaging Core. He has dedicated his career to these star-shaped “caretaker cells” of the brain and their potential as a target for innovative drug therapies.

What makes astrocytes such an exciting

SPREADING STROKE AWARENESS

Community education geared at spreading stroke awareness is a significant factor in reducing damage to the brain of affected individuals, according to Lee Birnbaum, MD.

"Health care information that fits the community's needs is essential. For our community in San Antonio, it's important that we offer awareness and education in both English and Spanish. Promoting the 'RAPIDO' mnemonic has been particularly important for our patients in South Texas," Birnbaum said.

While the BE FAST acronym (Balance, Eyes, Facial drooping, Arm weakness, Speech difficulties, Time to call emergency services) remains a crucial mnemonic, the RAPIDO acronym has been embraced as an important mneumonic for Spanish-speaking patients.

James D. Lechleiter, PhD, professor, Department of Cell Systems and Anatomy and director of the university's Optical Imaging Core

target for stroke recovery is that they can function well with little to no oxygen.

"Astrocytes can generate a lot of adenosine triphosphate, or ATP, during a crisis period. ATP is the molecule that gives energy to cells to carry out all their processes," Lechleiter said. "The drug that we developed spurs the astrocyte to use their mitochondria to make more ATP more efficiently. All these ATP-dependent processes that are good for neuroprotection, like restoring the ion balance, maintaining membrane potentials, maintaining good electrical signaling — that all depends on ATP. So, if you can take the brakes off astrocytes' ability to make more ATP, it enhances those neuroprotective processes, which mitigates the damage after a stroke. And that's what this drug can do."

Preserving brain function

The compound, which currently has no official name but is referred to as AST-004, has been successful

Lee Birnbaum, MD, professor in the departments of Neurology and Neurosurgery

in preclinical non-human primate studies and a phase 1 clinical trial, where safety in healthy humans was established. Now Lechleiter and his teammates at Astrocyte Pharmaceuticals — to which UT Health San Antonio has given exclusive licensing rights to develop the drug — are preparing for phase 2 clinical trials. These trials will focus on evaluating the effectiveness of AST-004 in reducing brain tissue loss in patients with large occlusion strokes, a severe type of stroke where blood clots cause substantial brain damage.

"What we want ultimately is for AST-004 to be administered first thing, without concern about what kind of stroke someone is having," Lechleiter said. He explained that, currently, imaging must be done first to determine if a stroke is caused from a clot or from bleeding, which is about a two-hour delay before treatment can be administered.

"But AST-004 doesn't care. It can do both. Its neuroprotective effects are good for either type of stroke, meaning someone can be treated the moment you suspect there's stroke or other injury," Lechleiter said.

Additionally, AST-004 shows promise beyond stroke treatment. The drug's rapid onset and potential for use in portable forms, like dissolvable tablets, make it a candidate for treating traumatic brain injuries on the battlefield or in sports settings. With ongoing research and development, AST-004 has the potential to revolutionize emergency care protocols.

Moreover, preliminary research hints at its efficacy in addressing chronic conditions like Alzheimer's disease and even addiction, which would make AST-004 a transformative, comprehensive therapy in neurological medicine and overall brain health.

PRIMARY AND SECONDARY PREVENTION

"Cardiovascular health is important for brain health, so following heart-healthy guidelines will also help to ensure a healthy brain and is something you can do for stroke prevention," said Lee Birnbaum, MD.

For primary prevention, he recommends following a lifestyle plan outlined by the American Heart Association called "Life's Simple 7" metrics:

- STOP SMOKING
- EAT BETTER
- GET ACTIVE
- LOSE WEIGHT
- MANAGE BLOOD PRESSURE
- CONTROL CHOLESTEROL
- REDUCE BLOOD SUGAR

After having a stroke, addressing secondary stroke prevention is a critical part of comprehensive stroke care. Birnbaum outlines a proactive approach that begins with identifying and mitigating risk factors such as smoking, diabetes and hypertension. Tailored interventions, including lifestyle modifications and targeted medications like blood thinners or cholesterol-lowering drugs, aim to minimize the likelihood of recurrent strokes, safeguarding long-term patient health.

PARKINSON'S DISEASE

A big step forward for movement disorders

Prestigious designation expands and enhances Parkinson's care in Texas

BY JESSICA BINKLEY LAIN

Parkinson's is a neurodegenerative disease that progresses over time. Some symptoms may include shaking or tremors, slow movement, stiffness and balance issues. It is typically diagnosed after age 65, but people under 50 can also have Parkinson's.

According to the Parkinson's Foundation, about 90,000 Americans are diagnosed with Parkinson's each year. About 1 million people in the U.S. are currently living with Parkinson's, and that number is expected to increase significantly in the next 20 years due to an aging population.

At a state level, Texas has the third largest number of patients living with Parkinson's disease. The high rates of the disease in the state can be attributed to several factors. Notably, Texas has many people living in rural regions working and living on farmlands that often use harmful pesticides and other chemicals, putting them at a higher risk for developing Parkinson's, which is often caused by exposure to toxic agents, said Okeanis Vaou, MD, associate professor and director of the movement disorders program in the Department of Neurology, Joe R. and Teresa Lozano Long School of Medicine.

"Despite being one of the largest cities, it is evident that San Antonio is considerably underserved in Parkinson's care when compared to other cities of similar or even smaller size," Vaou noted. "This gap in service provision not only hampers the quality of life for those living with Parkinson's, but also places an undue burden on their families and caregivers. It is a situation that warrants immediate attention and action. We're hoping to change that."

> "This designation gives us the leverage to grow and to serve the city as well as the surrounding rural areas."
>
> **Okeanis Vaou,** MD, associate professor and director of the movement disorders program in the Department of Neurology

Leverage to grow

In 2023, The University of Texas Health Science Center at San Antonio's Movement Disorders Program was designated as a Comprehensive Care Center for Parkinson's Disease by the Parkinson's Foundation, one of the largest nonprofit foundations for Parkinson's. The designation — which is the first of its kind in Texas — recognizes centers that provide excellent care to people with Parkinson's disease within a broad geographic region. Each center is required to meet rigorous care, professional training, research, community education and outreach criteria.

"We are the only center in San Antonio for Parkinson's disease and care, and this designation gives us the leverage to grow and to serve the city as well as the surrounding rural areas. And the need is tremendous," said Vaou.

For San Antonio in particular, another high-risk population — veterans — compounds the need for Parkinson's care in the city and surrounding areas.

"San Antonio has a large VA system with a very large population of veterans and active military personnel. We do know that service members exposed to chemicals from burn pits or from Agent Orange in the Vietnam War are at a high risk to develop Parkinson's disease," Vaou said. "So, the need for specialists is high, and part of our vision is to grow and hire more movement disorder specialists to meet that need and better serve our community."

A hub for research and care

By being recognized as the only Comprehensive Care Center for Parkinson's Disease in the state, the university aims to redefine Parkinson's care for San Antonio and surrounding areas, leveraging its designation to expand outreach and research efforts. With a commitment to pioneering early diagnostic approaches and enhancing patient outcomes, the center aspires to serve as a pivotal hub for innovation and support in Parkinson's care, addressing critical needs in the community and beyond.

"Our goal is to establish the center as a beacon of information and hub for Parkinson's research and care, fostering innovation and expanding knowledge in the field," said Vaou.

Early diagnosis and novel diagnostics for Parkinson's are core research objectives for the center. Currently, there is no test or imaging to diagnose Parkinson's disease, and the gold standard of diagnosing Parkinson's relies on the clinical exam. Vaou underscored the center's commitment to changing that.

"Our current focus is on discovering biomarkers or novel diagnostic methods for detecting Parkinson's disease at its earliest stages, as well as new therapies," Vaou said. "Early identification and intervention would make a significant impact by slowing down the progression of the disease, leading to better patient outcomes."

The evolution of epilepsy care

Innovative targets and emerging therapies are reshaping the future of epilepsy treatment

BY JESSICA BINKLEY LAIN

Epilepsy, a neurological condition characterized by recurrent seizures, affects approximately 3 million people in the United States — about 1% of the nation's population — and is considered one of the most prevalent neurological disorders. Charles Akos Szabo, MD, professor in the Department of Neurology, Division of Epilepsy, in the Joe R. and Teresa Lozano Long School of Medicine, sheds light on the changing landscape of epilepsy treatment.

"Epilepsy is a disease defined as having an increased risk for recurring seizures," Szabo said, noting the multifaceted nature of the condition. "Epilepsy has many causes, including head injuries, strokes, neurodevelopmental disorders or genetic predisposition. The treatment depends on several factors, like whether the seizures start in one part of the brain or simultaneously involves both sides, as well as determining the underlying cause."

Mitigation treatments

Anti-seizure medications can control seizures in most people with epilepsy. However, in some people whose seizures do not respond to medications, surgical resective procedures to remove identifiable lesions underlying epilepsy, such as tumors, scar tissue or cortical dysplasias, are highly effective at alleviating seizures. Minimally invasive techniques like laser ablation offer similar results with reduced risk and faster recovery.

Newer implanted neurostimulation devices like responsive neurostimulation or deep brain stimulation are also safe and effective treatment options to reduce seizure activity when resective or ablative approaches may not be successful or are too risky.

"With these methods we can modulate brain activity to mitigate seizures. In addition, responsive neurostimulation also helps physicians to monitor their patients' seizures," Szabo said. He explained that the technique involves implanting devices that deliver targeted electrical stimulation to certain areas of the brain to brake or prevent seizures.

New drug therapies

Novel pharmacological treatments currently under investigation at the university target potassium channels rather than traditional anti-seizure therapies that target sodium channels.

"The traditional treatments work by blocking or modulating sodium and calcium channels that cause increased excitation, aiming to stabilize neuronal activity and reduce seizure susceptibility. But the newer class of medications that target the potassium channel stabilize neuronal activity by rendering neurons less electrically responsive to abnormal stimulation," Szabo explained. The new compounds are currently in phase 2 and 3 clinical trials at the university.

Szabo and his team are also engaged in pioneering research investigating sudden unexpected death in epilepsy, or SUDEP, a fatal complication of epilepsy that happens when a person with epilepsy dies unexpectedly and without an apparent cause. These studies explore potential biomarkers to better predict which people with epilepsy may be at increased risk for this potentially devastating yet avoidable outcome. Their research includes population-based studies evaluating brain or cardiac electrophysiological markers, as well as neuroimaging biomarkers, and testing of seizure-detection devices that can warn people with epilepsy and their caregivers of potentially hazardous seizures.

Animal model comparisons

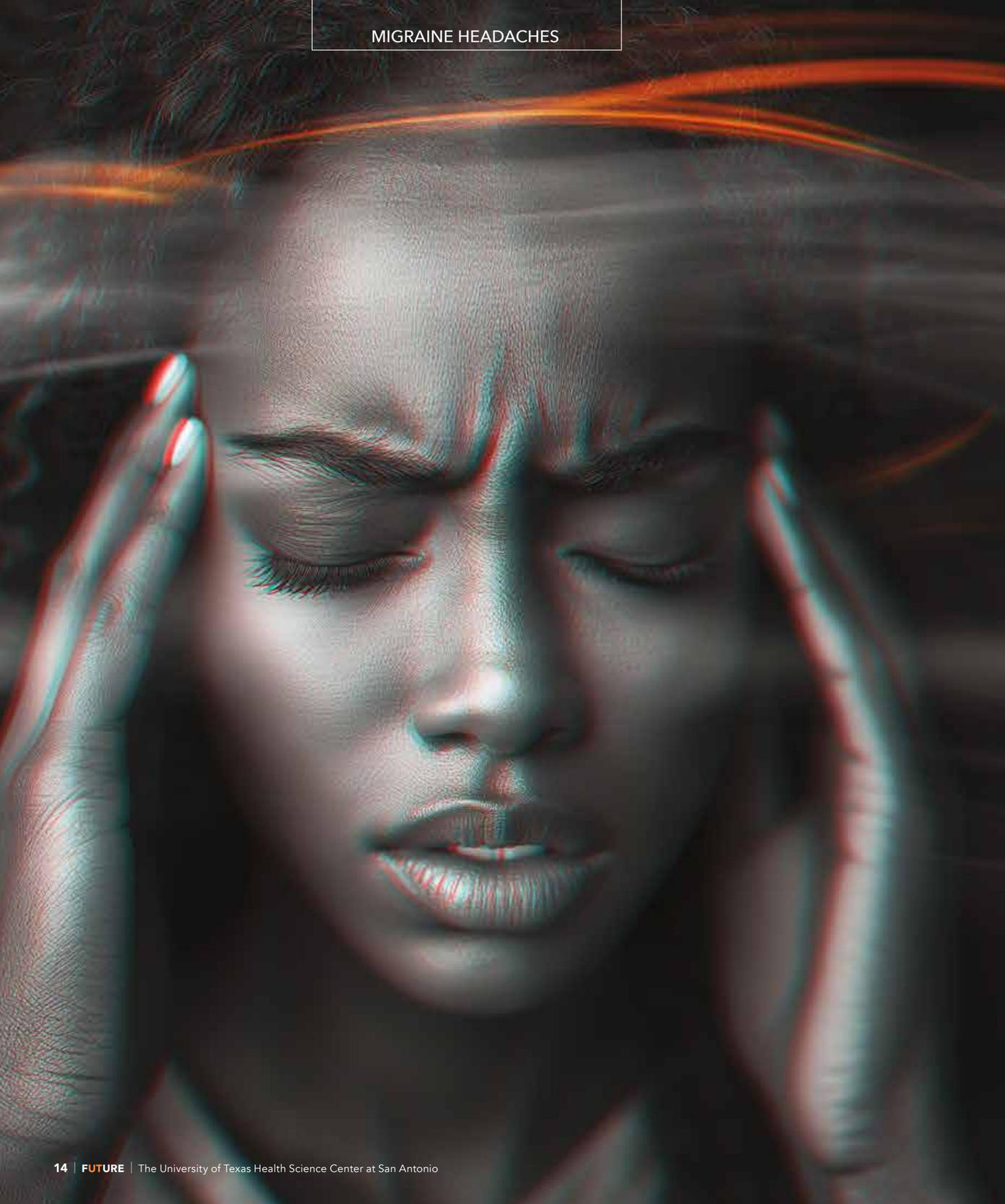
For these studies, Szabo is working closely with the Texas Biomedical Research Institute, which houses a large baboon colony that includes baboons with natural genetic epilepsy. These animal models allow Szabo to evaluate physiological, neuroanatomical, genetic and epigenetic markers that may contribute to sudden unexpected death in baboons with epilepsy similar to that in humans.

"Baboons, like humans, have naturally occurring epilepsy, which makes them a valuable non-human primate model for studying genetic and epigenetic factors underlying epilepsy in humans," Szabo said.

"Furthermore, their similarity to humans allows us to translate seizure characteristics and epilepsy-related changes in the brain and cardiac functioning back to the human condition," he said, adding that the baboon provides a model not only to validate prospective human SUDEP biomarkers, but also to test treatments or devices to prevent this outcome in people with epilepsy.

As the field of epilepsy treatment continues to evolve, driven by technological innovations and a deeper understanding of underlying mechanisms, the future holds promise for more effective therapies and improved quality of life for individuals living with epilepsy, said Szabo.

> "With these methods we can modulate brain activity to mitigate seizures. In addition, responsive neurostimulation also helps physicians to monitor their patients' seizures."
>
> **Charles Akos Szabo,** MD, professor in the Department of Neurology, Division of Epilepsy



MIGRAINE HEADACHES

BREAKING THE GRIP OF MIGRAINES

The latest medications for pain relief show great promise for reducing the frequency and severity of attacks

BY JESSICA BINKLEY LAIN

Throbbing. Stabbing. Fiery. Electric. Like being in a vice. There are many ways that migraine sufferers describe their pain, but no matter the word to describe it, having migraines is a debilitating condition that often causes significant disruption to a person's quality of life.

"A lot of people will suffer because they don't know there's something better out there. But there are many options and things that we can do for patients," said Deborah Carver-Hodges, MD, a headache specialist and professor in the Department of Neurology at the Joe R. and Teresa Lozano Long School of Medicine.

Migraines are a type of headache disorder characterized by moderate to severe pain, often presenting on only one side of the head and worsened by physical activity, Carver-Hodges explained. The pain is frequently accompanied by nausea, vomiting and sensitivity to light and sound.

The welcome arrival of triptans

The introduction of triptans in the 1990s saw the rise of a class of medication specifically created for migraine pain relief, revolutionizing acute treatment. Triptans work by blocking the pain impulses in the brain and decreasing the release of inflammatory molecules and neuropeptides, including calcitonin gene-related peptide, one of the key culprits causing migraine attacks.

Calcitonin gene-related peptide, or CGRP, is a neuropeptide found in the nervous system that plays a pivotal role in triggering migraines, Carver-Hodges explained. This peptide has been found to be elevated in migraine sufferers and even further increased during a migraine attack.

CGRP's release in the trigeminal nerve leads to a domino effect of localized neuroinflammation and vasoconstriction in the brain, resulting in profound pain. Triptans have been shown to decrease levels of CGRP, resulting in significant relief from pain during an acute migraine attack.

Yet, it wasn't until 2018 that preventive medication designed specifically for migraine emerged.

Innovations in preventing pain

"In the past, the only medications available to prevent migraine headaches were repurposed from other categories of drugs, like antidepressants, blood pressure medicines and anti-seizure medicines, but we didn't have any prevention medication specifically created for migraine headaches until recently," Carver-Hodges said.

There are two types of this new class of medicine, which either block the CGRP receptor or the peptide itself, she explained. One type are monoclonal antibodies, administered as injections, which help to prevent migraines. The other class, known as gepants, are oral tablets that provide options for both acute treatment and prevention. Both types have shown promising clinical results, with approximately 50% of patients experiencing significant headache reduction. Their efficacy, coupled with minimal side

> There's a lot about these medications that give providers reason to be optimistic. One is that they are specific to migraines, focusing on the pathophysiology of migraines. Another is that, in clinical studies so far, we've seen that the majority of patients respond really well, having low side-effect profiles and significant improvement in their migraine frequency."

Deborah Carver-Hodges, MD, headache specialist and professor in the Department of Neurology

effects compared to previous treatments, marks a substantial improvement in migraine care.

"There's a lot about these medications that give providers reason to be optimistic," Carver-Hodges said. "One is that they are specific to migraines, focusing on the pathophysiology of migraines. Another is that, in clinical studies so far, we've seen that the majority of patients respond really well, having low side-effect profiles and significant improvement in their migraine frequency."

Reclaiming quality of life

This is especially good news for chronic migraine sufferers — typically defined as people who experience 15 or more migraine headaches per month. The recent monoclonal antibodies and gepants medications reduce both frequency and severity of attacks and can greatly enhance daily functioning for those with migraine, minimizing negative impacts to their work and family life.

"If you're having several migraines per month, or losing a week of productivity due to migraine, you should really consider starting a preventative medication. It can help reduce not only migraine frequency, but also makes the attack less severe, which can have a huge impact on your life," Carver-Hodges said. "For now, we might not be able to get rid of your migraines completely, but we can definitely make you more functional and improve quality of life."

Ongoing research promises further insights into migraine pathophysiology and the development of even more effective therapies, noted Carver-Hodges. By understanding the complexities of migraines, migraine sufferers can reclaim their lives from the grasp of this debilitating condition.

TRAJECTORY OF A MIGRAINE

A typical migraine can last several days as it moves along a pathway of four distinct phases. Migraine sufferers may experience symptoms both before and after the pain itself.

PRODROME
The prodromal phase of a migraine attack can begin hours to days before the aura or acute phases. Symptoms in this phase may include mood changes, feeling foggy, appetite changes, fatigue, insomnia or neck pain.

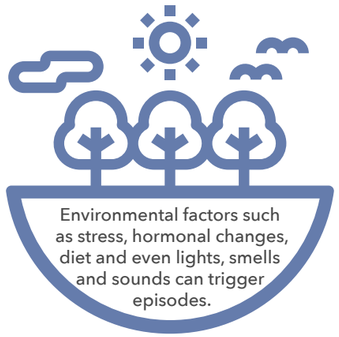
AURA
The aura phase of a migraine attack occurs in only about 25% of those living with migraine. It can serve as a warning of a coming attack, occurring five minutes to an hour before the acute phase begins. The most common aura people experience is visual and may include seeing zig-zags or sparklers or having tunnel vision and blind spots. Other aura symptoms can include numbness, tingling, vertigo, tinnitus and even temporary paralysis on one side of the body.

ACUTE
This phase is the peak of the migraine attack, which can last from four hours up to several days. During this phase, symptoms are debilitating and can include profoundly painful, intense headache; nausea; vomiting; sensitivity to light, sound or smell; vertigo; fatigue and body aches.

POSTDROME
This phase occurs after the acute pain and other symptoms have subsided. Sometimes known as a "migraine hangover," it can last up to 48 hours. The postdrome phase can cause fatigue, trouble concentrating and mood changes.

FACTS ABOUT MIGRAINE

The word "migraine" is derived from the Greek word "hemikrania," meaning half (hemi) skull (kranion), referring to the typically unilateral presentation of the disorder. Later, the term converted into Latin as "hemigranea" and then into a French translation that became "migraine." (National Library of Medicine)

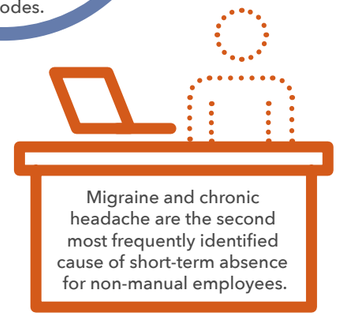


Environmental factors such as stress, hormonal changes, diet and even lights, smells and sounds can trigger episodes.

38M

people in the United States are afflicted with migraine.

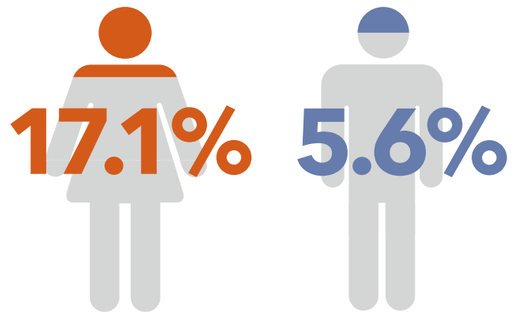
Lifestyle adjustments such as regular exercise, stress-reduction techniques and maintaining a balanced diet can complement medical treatments.



Migraine and chronic headache are the second most frequently identified cause of short-term absence for non-manual employees.

Caution is advised with over-the-counter medications, which, if overused, can lead to medication-overuse headaches.

Both men and women can experience migraine, but women are more likely. In a large U.S. survey, 17.1% of women and 5.6% of men reported having migraine symptoms. (National Library of Medicine and JAMA network)



THE SEARCH TO PREVENT ALZHEIMER'S

ALZHEIMER'S DISEASE

Investigators are testing a new drug for its potential to slow and prevent the disease

BY JESSICA BINKLEY LAIN

Alzheimer's disease continues to challenge medical science with its complex and devastating effects on cognition and memory. In a significant stride forward, the Food and Drug Administration recently approved lecanemab as a promising new compound found to slow the progression of the disease.

Researchers at The University of Texas Health Science Center at San Antonio are now diving deeper into the mechanisms of lecanemab to determine if this innovative drug also has preventive potential.

What happens in the brain

Lecanemab is a humanized monoclonal antibody that removes amyloid buildup, which is a protein that is one of the key features of Alzheimer's disease. The antibodies bind to and clear away the amyloid that builds up in the spaces between the neurons, which hinders the messages buzzing from synapse to synapse throughout the brain.

This amyloid protein starts building up in the brain about 20 years before the first symptoms of Alzheimer's emerge. As amyloid accumulates, an abnormal form of a second protein, called tau, also starts to build up, and the buildup of this abnormal tau can kill the neurons.

"The location of where these neurons die in the brain seems to determine the symptoms a patient will experience," explained Sudha Seshadri, MD, director of the university's Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases.

"If the neurons die in the part of the brain that is responsible for making new memories, then memory issues will be the symptom. If it's a part of the brain that's responsible for communication, then you may see primary progressive aphasia. If it's mostly in the posterior cortex of the brain, then a patient may have difficulty making sense of what they see," Seshadri said.

In a 2019 study called Clarity AD, lecanemab was shown to reduce the amyloid burden to a level that is seen in healthy brains. This is a highly effective treatment in slowing disease progression, but it can't undo the damage of neuronal death in the brain, explained Seshadri.

Sudha Seshadri, MD, director of the Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases

"This type of treatment doesn't typically bring back function that has already been lost, but it does slow down the decline," Seshadri said. "That's why we're looking at the effects of removing amyloid buildup in earlier stages of the disease, before function is lost."

Tracking amyloid levels

Currently, the health science center is part of a national, multisite study called AHEAD 3-45. The ongoing study investigates lecanemab's effects when administered before the onset of symptoms, at the preclinical stage of the disease. The findings of this study will have significant impacts on potential preventive treatment.

"We want to see if completely asymptomatic, cognitively normal people who have excess amyloid in the brain will benefit from receiving lecanemab," Seshadri said.

The study will span five years, with participants undergoing regular positron emission tomography scans and infusions of lecanemab to observe and track the amount of amyloid in the brain.

How often a participant receives the treatment depends on how much amyloid is found in their scan when they begin, Seshadri explained.

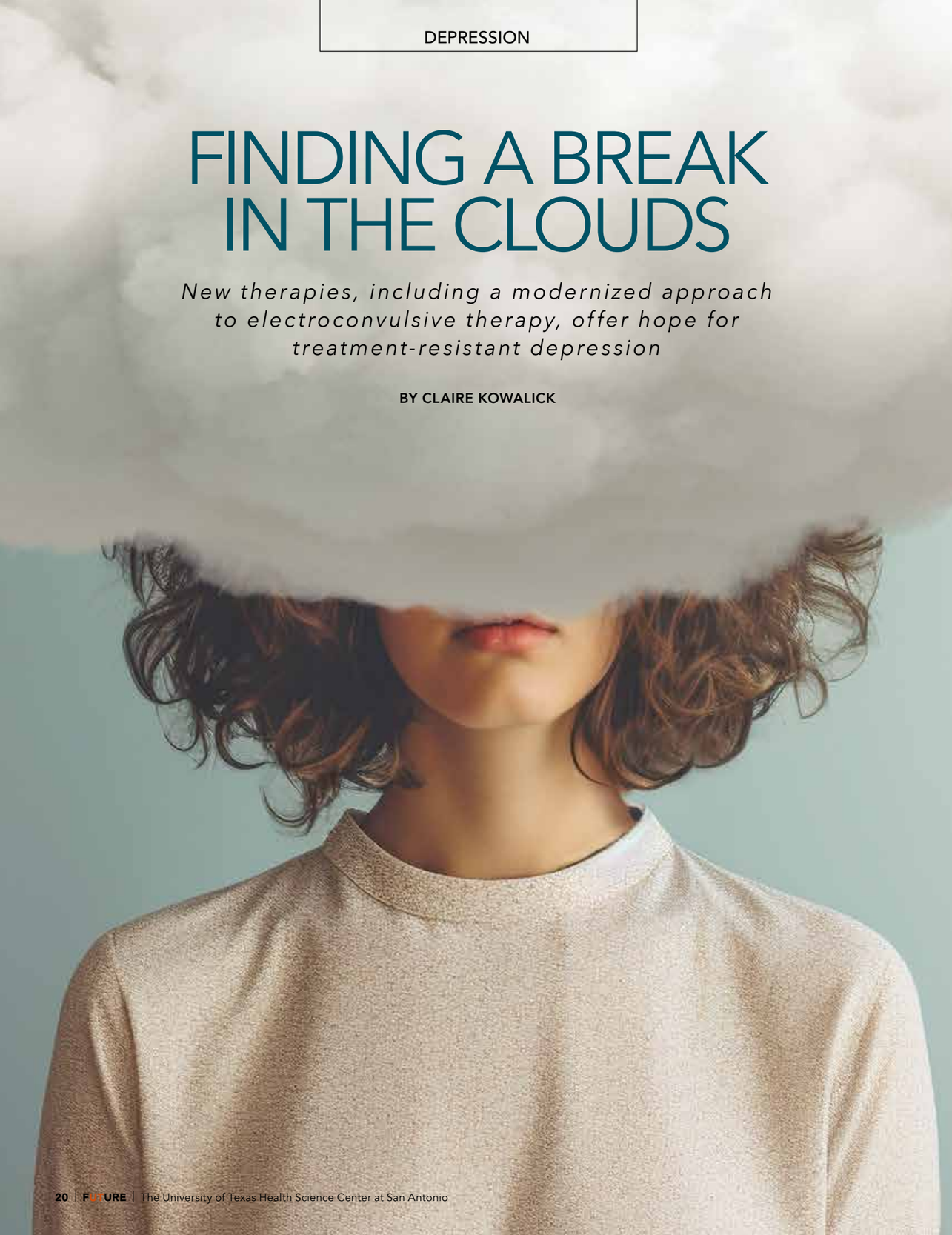
"We don't know if lecanemab works at this stage, but if it does work in the preclinical stage of the disease — if we find that it can delay or prevent the development of cognitive symptoms — that will be a very remarkable achievement," Seshadri said. "We'd actually be preventing Alzheimer's, which is a huge step."

DEPRESSION

FINDING A BREAK IN THE CLOUDS

New therapies, including a modernized approach to electroconvulsive therapy, offer hope for treatment-resistant depression

BY CLAIRE KOWALICK



For some people struggling with their mental health, available treatments can be ineffective, effective for only a short time or cause insufferable side effects. About 30% of people with depression are treatment resistant, meaning they have tried two or more medications or therapies and are still experiencing significant symptoms.

Melissa Martinez, MD, professor of psychiatry and behavioral sciences at the Joe R. and Teresa Lozano Long School of Medicine, specializes in treatment-resistant major depressive disorders, bipolar disorder and schizoaffective disorders. She also sees patients at UT Health San Antonio's Behavioral Health and Wellness Center.

"By the time they get to me, I am going to add something with a completely different mechanism of action and treat the condition from a different angle. The hope is that the new treatment added will work synergistically with other treatments, like different branches of the military fighting together, to attack the illness and win the battle against suffering."

Now within her treatment arsenal are three interventional methods that are safe, fast-acting and highly effective for people diagnosed with treatment-resistant depression. Along with conventional talk therapy and medications, two new interventional psychiatry methods are available at the center, as well as one long-standing treatment with a history of success that is being revisited with a modern approach.

Intranasal esketamine

Ketamine, a compound of the anesthetic and recreational drug phencyclidine, was originally used as an anesthetic that produced less delirium than phencyclidine. An intranasal spray containing esketamine, sold under the brand name SPRAVATO and used for the treatment of depression, was approved by the Food and Drug Administration in 2019.

The drug works by blocking the N-methyl-D-aspartate (NMDA) receptor, which is different from how most antidepressants work, as they usually block the reuptake of serotonin and norepinephrine. The drug decreases symptoms of depression in 60% to 70% of individuals and provides complete remission for up to half of people.

Another plus is that it does all this much faster than other treatments. Regularly available antidepressant medications can take eight to 12 weeks to begin working, whereas esketamine users can begin to see relief in as little as 24 hours after their first treatment.

For treatment, patients come to the clinic where they self-administer a dose of nasal spray under the watch of a health provider. They remain under observation for a couple of hours and then must be driven home.

Martinez said that as soon as she saw this treatment was FDA-approved in March 2019, she sent a message to her department chair about making it available at the center. UT Health San Antonio became one of the first locations in the community to offer intranasal esketamine.

"You can see people who have not responded to other treatments respond to this very quickly. They feel a 'break in the clouds,'" Martinez said.

The treatment is also approved for people with suicidal thoughts, and Martinez said she has patients experiencing relief on this front. She notes that success for mental health treatment can vary greatly from person to person. For one person, progress might mean experiencing suicidal thoughts only a couple times a week instead of daily. For another person, success means getting out of bed and going to work or taking care of their family.

Because esketamine treatment is new, the center continues to monitor how long each person needs treatment and at what dose. Some patients come in, complete the protocol and discharge from the program, said Martinez. For others, a maintenance protocol is needed where the person returns every four to six weeks.

"We continue to use esketamine with caution, as we are still trying to figure out where it lies in the treatment algorithm and how it is best used," Martinez said.

For patients receiving maintenance esketamine, Martinez works with them to try to decrease treatment frequency by suggesting other approaches such as exercise, a change in medications or more intense therapy to avoid the possibility of esketamine dependency.

Transcranial magnetic stimulation

During repetitive transcranial magnetic stimulation (TMS), an individual lies on a table while a TMS device is strategically placed near their head. TMS is believed to work for depression by stimulating the lateral prefrontal cortex, which is thought to be underactive in people with depression. Martinez describes the sensation for most people as a tapping that is perhaps annoying, but not painful. Treatment takes about 20-30 minutes daily for about a month. The treatment does not affect a person's ability to drive, so a patient can leave directly afterward.

"People come every day, but it is only for 30 minutes. They could come over their lunch break or before work. The key is the repetition — that they come every day to get that area of the brain firing," Martinez said.

TMS is a drug-free treatment, so it will not interfere with medications a person is taking. After a full protocol, about 60% of people see some positive response from TMS, and 30% to 40% have full remission of their depression.

Electroconvulsive therapy (ECT)

The image of patients strapped to a table, fitted with electrodes on their temples and delivered painful, high-voltage shocks is what many people imagine when they think about electroconvulsive therapy (ECT). This image, however, is a thing of the distant past, as modernized, evidence-based approaches to ECT are implemented with highly efficacious results.

"It has been around for 100 years, and it has a historically negative association with it. However, things have changed over the years, and new techniques minimize cognitive side effects," Martinez said.

ECT involves the introduction of a controlled electric current to the individual's brain. According to Martinez, one of the reasons ECT has been around for so long is that it is highly effective, with 80% of people reporting some response and up to 50% of people going into full remission from their depressive condition.

INTERVENTIONAL PSYCHIATRY TREATMENTS AVAILABLE AT UT HEALTH SAN ANTONIO

TREATMENT	PROCEDURE	USES	BEFORE/ AFTER TREATMENT	SIDE EFFECTS	RESPONSE RATE	REMISSION RATE
INTRANASAL ESKETAMINE	Self-administered nasal spray under the direction of health provider at center	Treatment-resistant depression	Process is 2-2.5 hours and requires someone to drive patient home	Sleepiness, dizziness, nausea, increased blood pressure	60-70%	40-50%
TRANSCRANIAL MAGNETIC STIMULATION (TMS)	20- to 30-minute treatment, five times a week for 6-9 weeks	Treatment-resistant unipolar depression	20-30 minutes each day; can drive self home	Headache, scalp discomfort, fatigue, lightheadedness	60%	30-40%
ELECTRO-CONVULSIVE THERAPY (ECT)	Sedated with anesthesia, muscle relaxant. Treatment twice weekly for 3-6 weeks then tapered depending on response rate	Treatment-resistant depressions and hallucinations	Requires clearance from primary-care provider and labs. Two- to three-hour process; need a ride home. No driving during therapy	Nausea, headache, fatigue, confusion, slight short-term memory loss	80%	50%

> "ECT has been around for 100 years, and it has a historically negative association with it. However, things have changed over the years, and new techniques minimize cognitive side effects."
>
> **Melissa Martinez**, MD, professor of psychiatry and behavioral sciences

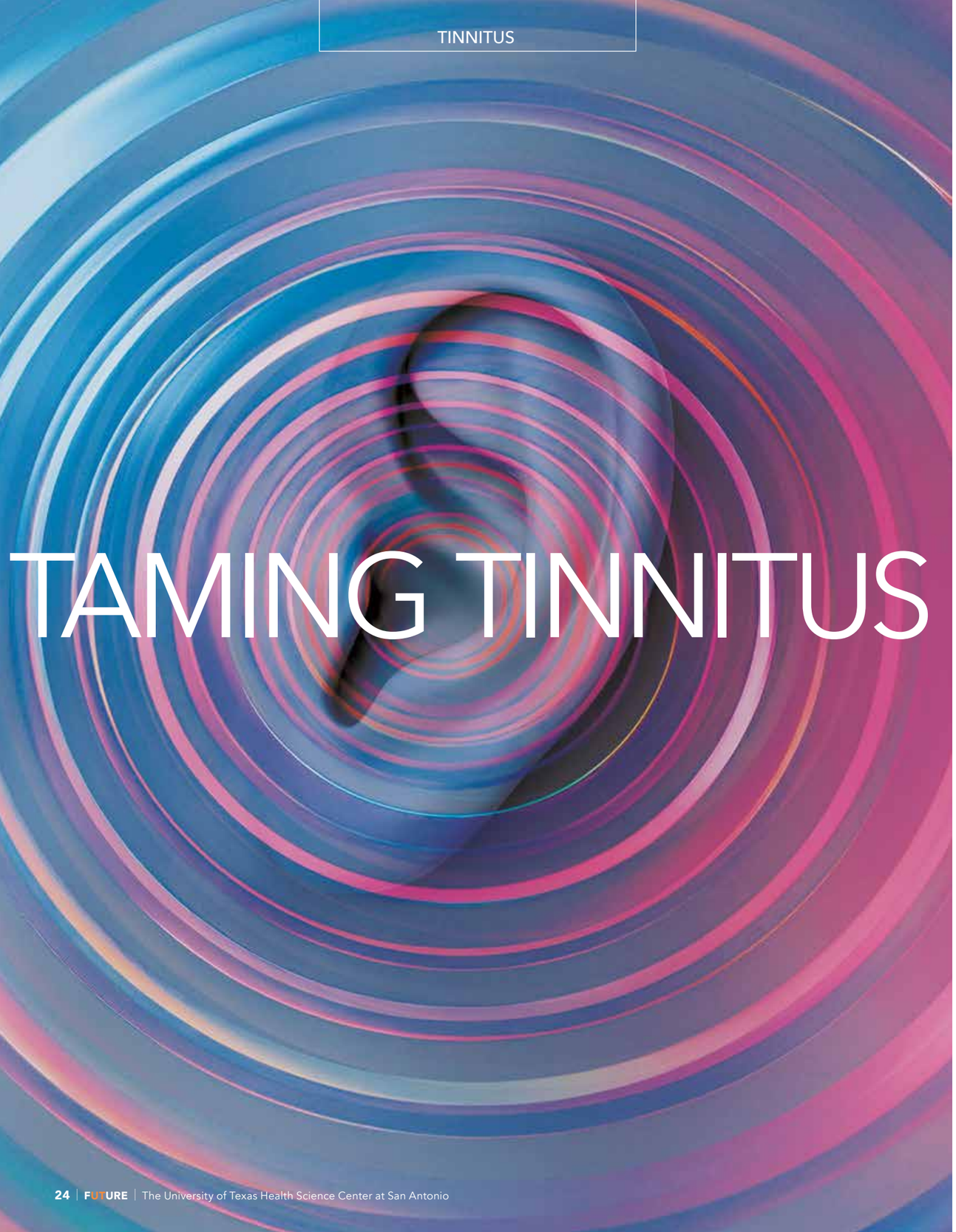
The updated program of treatment used at UT Health San Antonio uses ultra-brief bursts of electric charge and a unilateral stimulation approach rather than the historical bilateral approach to minimize side effects like confusion and short-term memory loss. The procedure itself takes about 30 minutes, including preparation before the procedure and waking up afterward.

"[Patients] do not feel like they are checking into a psychiatric hospital. They do not feel stigmatized. They check in with all the other patients and they are in and out within a few hours," Martinez said.

Treatments are spaced apart two times a week for approximately six weeks to minimize side effects.

Patients recommended for ECT have depression that has failed to respond to multiple antidepressants, usually four or more kinds. Of the three treatments, Martinez said ECT has the highest response and remission rate and is extremely safe.

Choosing the right treatment for a person suffering with major depression comes down to a decision between that person and their health care provider, said Martinez. Of these three treatments, Martinez said her patients are more likely to choose intranasal esketamine or transcranial magnetic stimulation due to lingering fears surrounding ECT. But as education improves about the modernized approach, more people are considering ECT among these innovative approaches to mental health treatment.



TAMING TINNITUS

New insights find connection between this common condition and PTSD

BY CLAIRE KOWALICK

It can manifest as a low- or high-pitched tone — a squeal, buzz, roar, chirp or click seemingly coming from one or both ears or in the head. It can dissipate within seconds or be continually present; barely discernable or as loud as a freight train.

Many people live with tinnitus and consider it to be a minor annoyance, but for up to 20% of sufferers, the condition can be bothersome enough to impair daily function.

John Moring, PhD, assistant research professor in the Department of Psychiatry and Behavioral Sciences at The University of Texas Health Science Center at San Antonio, has lived with tinnitus for as long as he can remember. Moring was a gymnast while growing up and thinks his tinnitus could be related to head or neck injuries he received during that time. While he is lucky enough to be part of the 80% of people only mildly hindered by the condition, he wondered if there was a way to help others who are truly suffering.

PTSD could affect perceived impact

"Tinnitus could manifest as a result of acoustic trauma, but neurobiologically, we're not seeing main alterations within the auditory cortex," Moring said. "It's not necessarily a dysfunction within a person's auditory pathways. Some theories suggest that tinnitus is a dysfunction related to gating mechanisms, resulting in the brain's lack of ability to appropriately screen out information you otherwise would not be attending to. If this gating mechanism fails, we have more information coming in, and the brain doesn't know how to process that, so it is interpreted as tinnitus, potentially."

In a research study, Moring used an Implicit Association Test to determine participants' responses to positively or negatively valenced words paired with tinnitus-related words. A quicker response time to tinnitus-related words, when paired with negative words, was observed when individuals were primed to think about their own tinnitus. This finding suggests an automatic and negative view that individuals often have toward their own tinnitus. A separate outcome from the same study indicated that acceptance of tinnitus can help alleviate tinnitus-related distress.

"If you are less willing to accept your tinnitus as it is, then the more distressed you are going to be," Moring said.

During his clinical internship, Moring treated veterans suffering from post-traumatic stress disorder (PTSD), and he observed that among veterans with PTSD, those who concurrently had tinnitus were more hyper-reactive and had elevated PTSD symptoms compared to those with PTSD only.

"I wondered if there was a connection between tinnitus and PTSD, in particular, and whether this particular combination serves to negatively impact functional outcomes among veterans," Moring said.

When Moring began working at the health science center 11 years ago, there were only three studies that considered the connection between tinnitus and PTSD. One study looked at Cambodian refugees from the Khmer Rouge rule and found a strong connection between PTSD and increased tinnitus distress. This study demonstrated that flashbacks of participants' trauma were very often associated with prominent tinnitus and that those with tinnitus had heightened levels of catastrophic thoughts, compared to those with PTSD without tinnitus.

Not better together

A separate study examining U.S. veterans found that individuals with tinnitus and PTSD fared worse functionally than individuals with PTSD and any other psychological health comorbidities, such as depression or anxiety.

"There is something about these two conditions that serves to limit individuals' functioning in life. Those with co-occurring PTSD and tinnitus may not be as happy or engaged in everyday sorts of activities, may find it more difficult to relax and engage in social activities and can find themselves angrier and more irritable. This combination really does impact their quality of life," Moring said.

Understanding more about brain functioning

9 FACTS ABOUT TINNITUS

1. According to the National Institute for Deafness and Other Communication Disorders, tinnitus is the perception of a sound in the ears that does not have an external source. It is common, affecting between 10% to 25% of the population.
2. Tinnitus can affect children and adults, can be transient or intermittent and can be an unrelenting chronic condition.
3. There are multiple possible causes of tinnitus, including exposure to loud noises, hearing loss, head or neck injuries, or taking certain medications. In some cases, the cause of tinnitus is unknown.
4. Tinnitus sounds and duration manifest differently for each person. It can be perceived as a ringing, buzzing, roaring, hissing, high- or low-pitch tone, blowing, whistling, humming or sizzling. Some describe it like the buzz of cicadas, musical notes or the wave-like woosh when you put your ear to a seashell. Those more affected by tinnitus tend to have a variety of sounds that change day to day.
5. Up to 33% of military personnel experience tinnitus, especially those exposed to acoustic trauma from weaponry and explosive devices like IEDs and RPGs or proximity to aircraft carriers.
6. Up to 90% of those with tinnitus have some form of hearing degradation.
7. Hearing aids for those with hearing loss can mitigate tinnitus by boosting the ability to capture sound in the area, thereby drowning out the tinnitus.
8. Certain medications, or withdrawal from them, can exacerbate tinnitus.
9. Comorbidities like PTSD could prevent habituation to tinnitus sounds, possibly due to auditory-based hypervigilance.

among those with both PTSD and tinnitus can help clarify why these two conditions are particularly deleterious. Moring applied for and was granted a Mentored Research Career Development (K12) award to work with his mentor, Peter Fox, MD, director of the university's Research Imaging Institute, to learn about neuroimaging methods and techniques (read more about the pioneering brain imaging project Fox created on page 29).

Moring also learned how to conduct neuroimaging coordinate-based meta-analyses based on all available data from published findings. While tinnitus seems like an auditory condition, it stems from a neurological dysfunction. Through a tinnitus neuroimaging meta-analysis, Moring learned the auditory cortex is not the primary region involved in the disorder. Instead, main regions associated with tinnitus are located within the default mode network, an area of the brain that is more active when a person is at rest.

The region is also partially involved in self-generated thoughts such as daydreaming, autobiographical information and future planning. When he relaxed the statistical threshold of the tinnitus meta-analysis, Moring found additional brain regions involved with tinnitus, some of which are also involved in PTSD.

One treatment for both?

Another goal of Moring's K12 study aimed to test whether treatment of PTSD would also improve tinnitus-related stress. Findings demonstrated that while PTSD symptoms declined significantly due to treatment, declines in tinnitus-related distress did not reach statistical significance. However, he observed large effect sizes, indicating a relationship between PTSD treatment and improvement in tinnitus distress. These findings also provide justification for additional research regarding the treatment of both conditions simultaneously.

Moring is now collecting neuroimaging and audiometric data from individuals with both tinnitus and PTSD, healthy controls without either condition and veterans and active-duty service members with either tinnitus or PTSD. With funding from the National Institute of Mental Health, Moring aims to find the neurobiological similarities and differences between these groups. Data from those with both PTSD and tinnitus and those with only tinnitus was entered into a spatial parametric map to show brain activation specific to each condition, as well as regions that share similar activation.

"With tinnitus you have the psychological sequalae like concentration problems, sleep issues, maybe anger and irritability that are overlapping with PTSD," Moring said. "We can now see this overlap neurobiologically, which may result in additive psychological effects and may explain worse functional outcomes among individuals with co-occurring disorders."

Testing crossover effects

Also in the works is a new randomized, crossover clinical trial looking at veterans with tinnitus and PTSD. The study will treat veterans with PTSD using cognitive processing therapy, followed by cognitive behavioral therapy for tinnitus.

Alternatively, participants may be randomized to receive cognitive behavioral therapy for tinnitus followed by cognitive processing therapy for PTSD. Moring said they aim to determine if PTSD treatment could improve tinnitus, possibly to the extent that the second protocol is unnecessary.

"When these symptoms co-occur, and we see that in the brain, that could be the reason these individuals are more impaired. It is an additive effect," he said.

Moring hypothesizes a calming of the system for PTSD could also relieve some tinnitus-related distress.

"I'm thinking it is a unidirectional relationship where PTSD, the psychiatric distress, is serving to inflame the annoyance and perceived loudness of the tinnitus," Moring said.

Because tinnitus is closely tied to individuals with hearing loss, Moring said audiologists that screen for tinnitus should also consider checking for mental health conditions like depression, anxiety and PTSD.

"If that is also contributing to the tinnitus-related distress, maybe it's going to be more efficient to address the psychological side of things first, and in doing so, some of those skills automatically apply to help reduce tinnitus-related distress," he said.

Moring uses the biopsychosocial model to help conceptualize how these disorders are interacting specific to each person. By doing so, he aims to provide individuals with the skills and techniques to promote a more balanced way of thinking about stressful situations and to experience natural emotions.

Moring also aims to change the relationship individuals have with their tinnitus, so that eventually, instead of tinnitus feeling like a large rock in their shoe that impairs functioning, it is a tiny pebble that they notice only occasionally.

> "Some theories suggest that tinnitus is a dysfunction related to gating mechanisms, resulting in the brain's lack of ability to appropriately screen out information you otherwise would not be attending to. If this gating mechanism fails, we have more information coming in, and the brain doesn't know how to process that, so it is interpreted as tinnitus, potentially."
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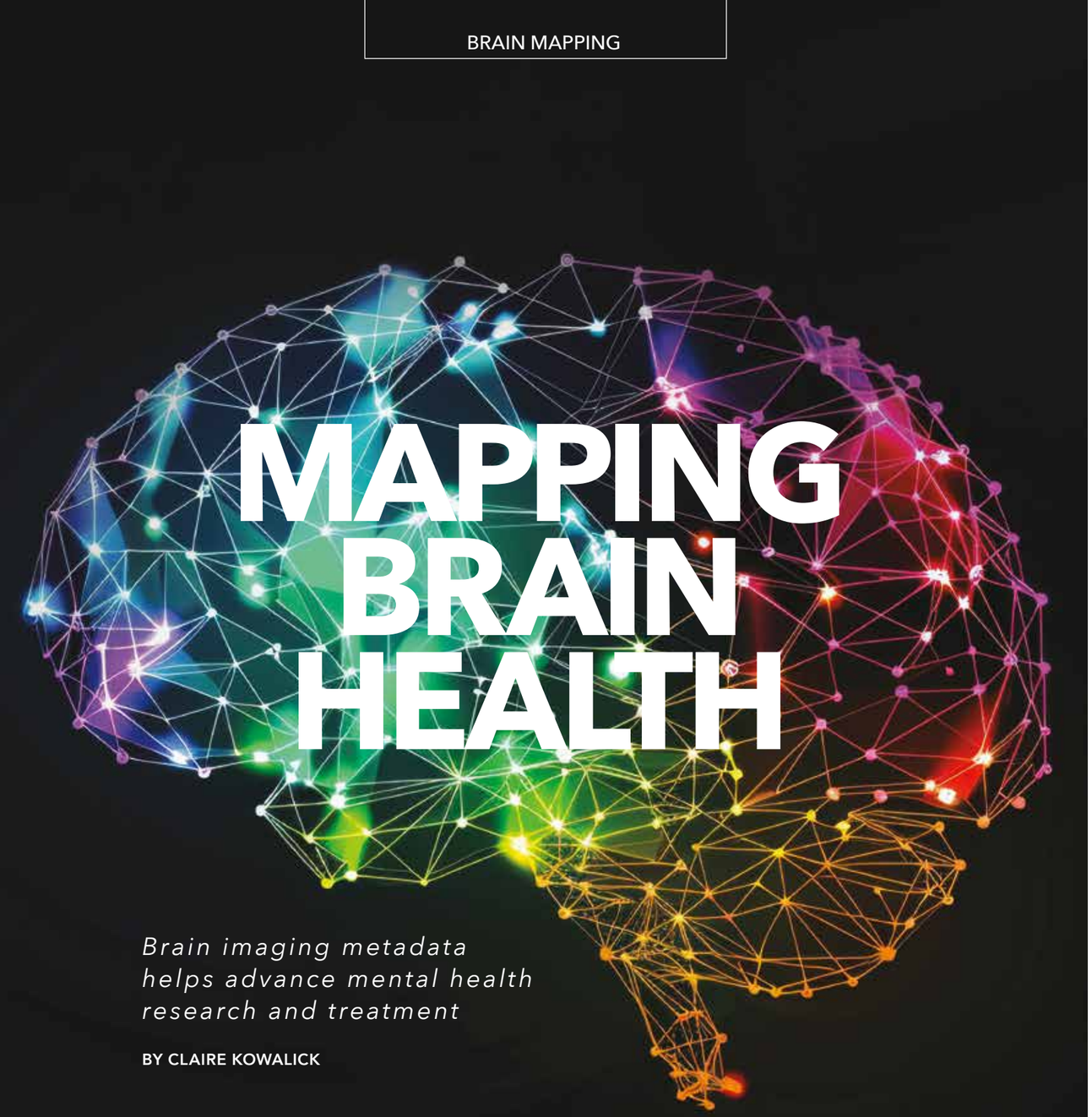


MAPPING BRAIN HEALTH

Brain imaging metadata helps advance mental health research and treatment

BY CLAIRE KOWALICK

BRAIN MAPPING

While most people focus on what they see during brain imaging, Peter Fox, MD, director of the Research Imaging Institute at The University of Texas Health Science Center at San Antonio, will tell you that the real value is in the mathematics and quantitative assessments behind those pictures.

Fox has worked for decades to understand the brain and its interconnected processes and networks of disease. As Fox explained, the brain is an information processing engine. It takes in information through our senses, synthesizing it to compute our experience of the world, interpreting the events unfolding around us, making plans and executing actions through neuronal signals to the muscles and other organs.

Just as scientists and engineers express many complex processes with network models, the brain is best understood as a multiscale hierarchy of networks. Diseases can be modeled as disruptions of these healthy networks.

Instead of specializing in any one disorder, Fox focuses on mathematical approaches that can be applied to normal brain functions and to a host of mental, neurological and development disorders.

In the 1980s, Fox introduced a system for standardizing brain imaging analyses and later created a way to share the data created by this strategy online. BrainMap, the standardized strategy he introduced decades ago, has been used by tens of thousands of published studies. Today, BrainMap shares published brain-imaging data from more than 250,000 research study participants' scans. This is critical, since for conditions like mental health disorders, analysis of data on a massive scale is essential.

How it works

Data from a published work is inputted in a standardized way, created by Fox, and expressed in coordinates of x, y and z to pinpoint locations in the brain. Standardization means information from all over the world is mergeable into this treasure trove of data.

Fox explains that brain effects in psychiatric disorders are subtle and may hardly be visible with one person's information. However, when there are data and metadata from 50 studies of 50 patients each and 50 controls, the disease effects come into focus.

At this point, there is no psychiatric disorder that can be diagnosed through imaging, and the neurobiology of mental health disorders is not well understood. Meta-analysis is the only way to get reliable results when associating specific brain areas with mental health disorders.

"We take those massive meta-analytic models to characterize disorders, to design new treatments for them and test them out through clinical trials," Fox said.

Current research is exploring what cognitive areas to focus treatment on, the strength of connections within the networks, and how treatment administered in easier-to-reach areas of the brain affects the deeper regions of the brain.

Potential for targeted therapies

The imaging bank is also used to support work in interventional psychiatry treatments like transcranial magnetic stimulation, or TMS. During TMS treatment, a device is placed near a person's head and magnetic impulses are strategically delivered to target specific portions of the brain.

"In neuromodulation, we've shown that when you stimulate one area, it spreads through the whole network," Fox said.

A first-of-its-kind tool created by Fox's lab and currently in the process of FDA approval is a robotic-driven, MRI-informed TMS system that promises unprecedented gains in therapeutic precision and personalization.

With his system, MRI brain modeling is completed for each individual and mapped to a model of the condition the person is experiencing. The model is used to compute the optimal pose for the robotic arm to deliver treatment. For each day's treatments, the patient is precisely registered to their treatment plan. The robot then solves the path and applies the TMS treatment at a precision within one millimeter.

"This approach is more precise than anything that is being done elsewhere," Fox said.

The BrainMap database makes it possible to catalog data from thousands of images and compare them to see what they have in common. Models are then adapted for each subject and modified frequently to create personalized, targeted treatments.

"We are at that level of trying to discover what the underlying mechanisms are and how we might want to treat them," Fox said.

Through the power of large numbers, Fox and his team are making novel discoveries and using them to create highly precise treatments based on models of neurological function and disease networks. →

“We take those massive meta-analytic models to characterize disorders, to design new treatments for them and test them out through clinical trials.”

Peter Fox, MD, director of the Research Imaging Institute

Impacts for future treatments

In addition to his own research endeavors, Fox mentors and assists other UT Health San Antonio scientists in the use of brain mapping to expand knowledge in a variety of fields.

According to Sudha Seshadri, MD, director of the health science center’s Glenn Biggs Institute for Alzheimer’s and Neurodegenerative Diseases, the support from the Research Imaging Institute is critical to the success of clinical trials on Alzheimer’s, dementia and other conditions. Seshadri said the institute, directed by Fox, is one of the main reasons she decided to come to UT Health San Antonio.

“Over the past six years, the Research Imaging Institute and Biggs Institute have grown together to attract outstanding faculty, initiate new ventures and attract over $40 million in research funding driven by our research imaging capabilities built over the years by Dr. Fox,” said Seshadri.

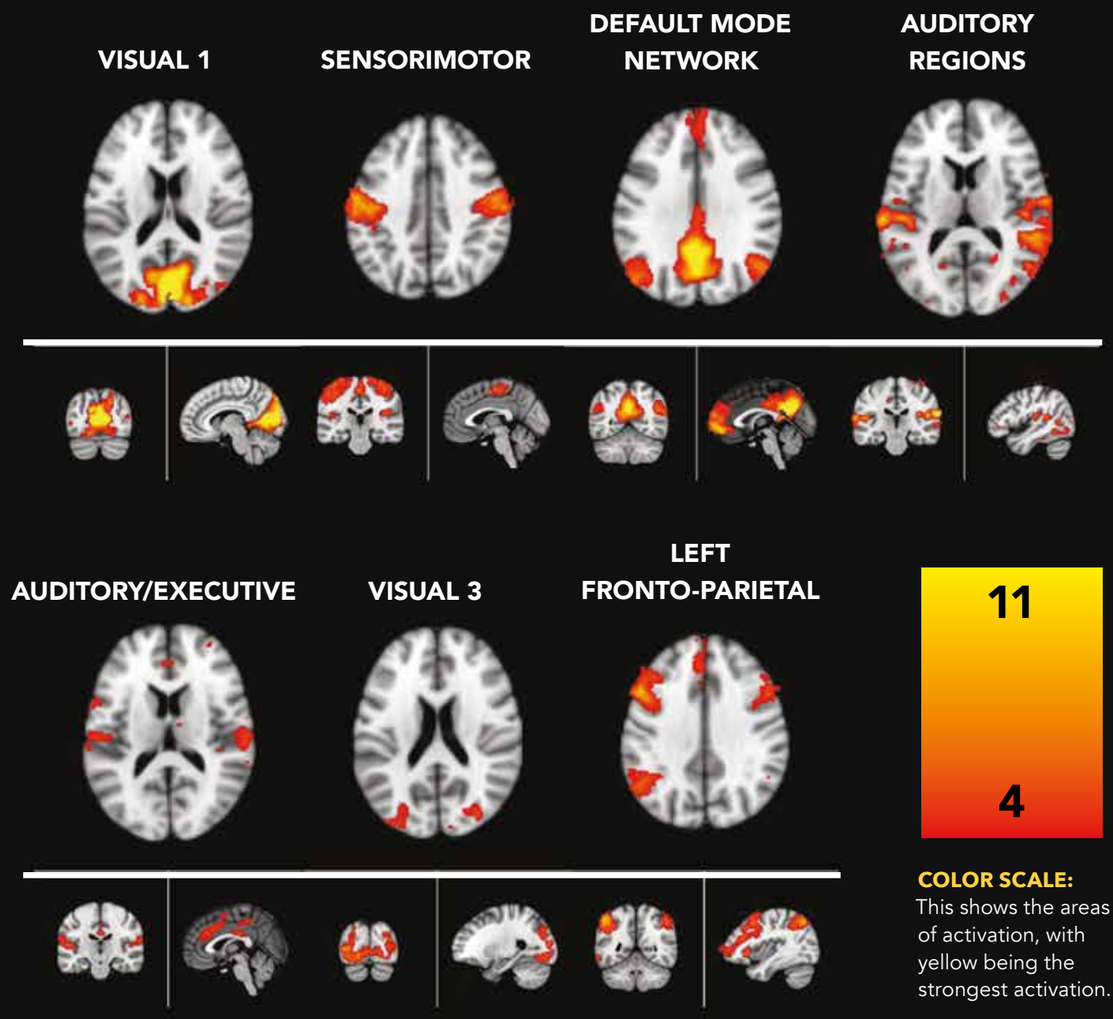
Melissa Martinez, MD, a professor of psychiatry and behavioral sciences, works closely with Fox in the use of repetitive transcranial magnetic stimulation (rTMS) for her patients with treatment-resistant depression. Fox invented an rTMS system that uses brain mapping for extremely precise treatment. The imaging-guided, robotically delivered rTMS at Fox’s lab is being considered for treatment of other conditions including post-traumatic stress disorder (PTSD) and smoking cessation.

John Moring, PhD, assistant research professor in the Department of Psychiatry and Behavioral Sciences, knew that to get to the neurological root of connections between tinnitus and PTSD, he needed training in brain mapping. Fox served as Moring’s mentor during his career-development training in neuroimaging. Moring said that because of Fox’s superior tutelage, he was able to conduct coordinate-based meta-analyses that highlight potential connections between the two conditions.

Globally, the surge in brain-mapping research seen today owes much to Fox’s leadership and the groundbreaking BrainMap initiative that he pioneered. His framework now enables the seamless collection and integration of brain data from researchers worldwide, fueling advancements that were once thought impossible and uncovering connections within the brain previously unimagined — offering new insights into these complex functions.

Fox’s work has not only revolutionized neuroscience, but also has catalyzed a shift in how neurological and mental health research is approached, laying the foundation for a future where the diagnosis and treatment of these conditions will be redefined.

Activation maps show how brain regions are interacting while participants are “at rest” during a functional MRI scan. These images, from a study conducted by John Moring, PhD, provide a view of the brain’s resting-state network among a sample of 35 participants, including 24 with tinnitus only and 11 with both tinnitus and post-traumatic stress disorder. These images show several overlapping regions of the brain that are active in both tinnitus and PTSD. Current and future work by Moring will determine if treatments for one disorder could be effective for both disorders. These networks align with a previous study that included approximately 30,000 participants using the BrainMap database created by Peter Fox, PhD.



COLOR SCALE: This shows the areas of activation, with yellow being the strongest activation.

Preventing opioid relapse

Methocinnamox, a novel compound for opioid use disorder treatment, advances toward clinical trials

BY CLAIRE KOWALICK

Drug overdoses happen every day, every hour. "More people die from drug overdose than cars and guns put together. It is a shocking number," said Charles France, PhD, a professor of pharmacology and psychiatry and the Robert A. Welch Distinguished University Chair in Chemistry at the Joe R. and Teresa Lozano Long School of Medicine.

Yet, few Food and Drug Administration-approved medications are available for opioid use disorder. While certain drugs have been around for decades to treat it, the problem persists, compounded in recent years by the explosive growth in the availability of synthetic opioids like fentanyl, said France. The problem, he said, is multifaceted due to the stigma surrounding addiction, lack of access to life-saving medication, inadequate mental health services and poor health care in general in the country.

"Certainly, people are not getting the health care they need for mental health disorders," he said.

Current treatments

The three most common pharmaceutical interventions for opioid use disorder are methadone, buprenorphine and naltrexone, each of which has pros and cons.

Methadone is a full agonist that replaces the drug individuals are currently using. "It keeps people satisfied. They do not feel the need for the opioid, and they do not go into withdrawal," France said.

Buprenorphine is a partial agonist that shares some properties with methadone but is not as strong. "Under the right conditions, it will help people from going into withdrawal and keep them from having cravings," said France.

A drawback to both drugs is the potential for diversion and abuse.

Naltrexone, France said, is more advantageous in many ways because it is an antagonist, meaning it does not stimulate opioid receptors or replace the opioid.

OPIOID USE DISORDER

Rather, it blocks the effects of the administration of opioids. The drug's action is short-lived, however, and if its effects wear off sooner than the effects of the opioid, the adverse effects of the opioid may return.

Vivitrol, an extended-release formula of naltrexone, lasts about a month but it is costly, requires special handling and its effectiveness varies markedly among individuals. It may, however, be an improvement over the shorter-acting formulation of naltrexone because the monthly dosing could increase treatment compliance.

Nalmefene, an opioid-receptor agonist nasal spray, was also approved in 2023 by the FDA.

Exploring a better option

Years of rigorous investigation at The University of Texas Health Science Center at San Antonio has laid the groundwork for an effective novel treatment for opioid use disorder that is safe, long lasting and inexpensive to manufacture.

France, the leading expert in the U.S. on the compound methocinnamox and its use as a treatment for opioid use disorder, has studied opioids for more than 40 years, 24 of those at his lab at the health science center. His work is predominantly funded through grants from the National Institutes of Health and the National Institute on Drug Abuse. Recent NIH UG3/UH3 funding aims to advance methocinnamox for use in a clinical setting.

First discovered in 1988 at the University of Bath, England, methocinnamox is what's called a mu opioid receptor antagonist with a long duration of action that can block and reverse the effects of opioid drugs such as heroin, morphine, oxycodone and the synthetic opioid fentanyl.

France has been studying the drug in his lab for years and is in the process of moving it through drug development for the prevention of relapse and overdose in opioid-experienced individuals who are not currently taking an opioid.

According to France, some of the remarkable qualities of methocinnamox are that it is orally bioavailable, shelf stable and a single administration blocks the effects of opioids for a very long time, despite the rapid clearance of the drug from the plasma. Studies in rats and non-human primates show methocinnamox to be extremely effective, even in small doses, and safe even at massive doses.

While France never thought, as a lifelong professor and researcher, that he would be in the drug-development business, the extraordinary potential of methocinnamox drew him into the process.

Currently, all investigational new drug-enabling studies required by the FDA are complete. If additional funding is secured, and the process moves along with "lightning speed," France said there could potentially be a phase 1 clinical trial in humans by 2025.

If methocinnamox passes through its drug-development hurdles, France hopes it will quickly become readily available to providers with patients who have used opioids or who want to refrain from using opioids.

Few Food and Drug Administration-approved medications are available for opioid use disorder. While certain drugs have been around for decades to treat it, the problem persists, compounded in recent years by the explosive growth in the availability of synthetic opioids like fentanyl.

Charles France, PhD, professor of pharmacology and psychiatry and the Robert A. Welch Distinguished University Chair in Chemistry

UNDERSTANDING AND ADDRESSING ADDICTION

A new university initiative brings clinical care, research, education and community engagement under a comprehensive framework to address substance use, addiction and related conditions

BY CLAIRE KOWALICK

For a health condition as complex as substance use disorder, there are no simple solutions.

But the possibilities for addressing the vexing health crisis stemming from substance use and addiction substantially increase when an intentional strategic model for a system of care is applied to create a scaffold of interlinking functional practices.

That's the aim of the Be Well Institute on Substance Use and Related Disorders, a pioneering initiative established earlier this year at The University of Texas Health Science Center at San Antonio. The novel approach to advance research, education and evidence-based treatments for substance use and addiction was created by Jennifer Sharpe Potter, PhD, MPH, the institute's founding director.

Potter also serves as the university's vice president for research and is a professor in the Department of Psychiatry and Behavioral Sciences. She notes that the health science center has long had a robust track record of innovative research and clinical work in the field of substance use disorder. The Be Well Institute aligns the science emerging from the university with a public health approach to address substance use across Texas.

"As a state university, it is our responsibility to use the science and intellectual gains at the health science center to improve the lives of our fellow Texans," Potter said.

She started working with the Texas Department of Health and Human Services in 2018 to bring evidence-based practices to assist in the statewide opioid use disorder crisis. After that effort, the Centers for Disease Control and Prevention funding aided the Waiver Texas program that increased the number of providers in the state that could prescribe buprenorphine, an opioid agonist used to treat opioid use disorder.

Now, with more than $50 million in National Institutes of Health, state and other federal funding annually, the Be Well Institute operates as a highly integrated and collaborative center of excellence with national scope for research, clinical and public health programs, as well as education and community engagement to advance the field addressing addiction and related conditions.

The institute encompasses a range of projects and initiatives, including its Be Well Clinic, the physical location at the university providing patient treatment services, and Be Well Texas, a statewide in-person and telehealth program that launched prior to the establishment of the Be Well Institute and is supported by the Texas Health and Human Services Commission and other federal funding.

Tara Wright, PhD, associate professor, Department of Psychiatry and Behavioral Sciences

In addition to its in-person and telehealth clinical operation, Be Well Texas coordinates a network of more than 140 community providers treating for opioid and other substance use and providing recovery support services across the state.

Compassionate, low-barrier care

"It is about bringing compassion and treatment to everyone in a way that is low-barrier and evidence-based, and we believe that everyone deserves it," said Tara Wright, PhD, with the Be Well Texas program and associate professor in the Department of Psychiatry and Behavioral Sciences.

Rather than trying to become a new entity that replaces established medical centers, the Be Well Institute aims to encourage a support system for established providers to help them assist their communities.

"We do not want to just come in and take over, because they know their communities the best, and they know what they need," said Wright, who notes that substance use treatment also comes with a unique set of challenges related to governmental regulations.

"Every legislative session brings changes for substance use. It is a very fast-changing, regulatory field and we must keep up with that," Wright said.

Individualized treatment, support

Because Texas is a large state with many rural areas, some people may not have ready access to substance use disorder treatments. The institute's Be Well Clinic uses both in-person and videoconferencing appointments to offer life-saving services to many individuals who would not otherwise have access.

Van L. King, MD, medical director of Be Well Texas, chief of the university's Division of Alcohol and Drug Addiction and professor in the Department of Psychiatry and Behavioral Sciences, said the clinical mission of the Be Well Institute is to be high-quality and high-impact in the San Antonio community and throughout Texas.

The Be Well Clinic does this by offering low-barrier, evidence-based treatment incorporating medications, psychotherapies, contingency management, case management and peer coaching and support. For those who are uninsured, funding is available to supply medications and transportation to clinic appointments to minimize barriers to care.

According to King, recovery from substance use disorder involves significant lifestyle changes. Individuals ideally need a place to live that is drug and alcohol free,

"My vision of the next five to 10 years is that new treatments will come out of the institute that were developed by our scientists and deployed here, and that these treatments are informed by the context of our community and what matters here."

Jennifer Sharpe Potter, PhD, MPH, director of Be Well Institute, and vice president for research, UT Health San Antonio

a stable income, options for enjoyable recreational and social activities that do not involve drugs or alcohol and access to treatment for co-occurring mental and physical illness. Along with treatment at the clinic, clinicians connect clients with programs and services that can address these other aspects so that each person has their best chance at recovery.

The goal is for people to be able to self-manage their condition with minimal or even no formal treatment over time, said King. To bring it into perspective, consider a person who has had a substance addiction for 10 or 20 years and how long it will take that person to restructure a life without their drug of choice, he added.

"Everyone has their own story and needs. We want to support people for as long as they need support," he said.

Van L. King, MD, medical director of Be Well Texas and chief of the university's Division of Alcohol and Drug Addiction

Be Well Clinic patient referrals come from many different avenues. Some are referred by their primary doctor or nurse practitioner, some are self-referred, others come after a visit to the emergency room and some are referred by first responders after an overdose.

"The linkages between Be Well and hospital systems in San Antonio and throughout the state are crucial," King said. "Health care providers can help motivate patients in crisis to establish treatment to help them on their journey of recovery. The key issue is that we can treat acute problems in the hospital and reverse overdoses in the community, but unless patients have an outpatient clinic to establish ongoing care to help change their lives in ways meaningful to them, they frequently continue pursuing high-risk drug and alcohol use."

King said retention rates at the clinic are high, especially for those with severe opioid use problems.

"We are especially encouraged by our retention rates with patients who experience an overdose reversal referred by the San Antonio Fire Department. These results are as good or better than community efforts in other Texas cities," he said. "We plan to continue efforts to connect with other service providers in San Antonio to better integrate services for these highly affected citizens."

Leveraging technology

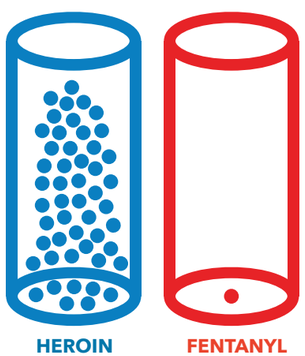
Beyond the Be Well Clinic's use of telemedicine to connect with patients, the institute is using and researching the latest technologies to make treatment more accessible. This includes a contingency management application loaded onto a patient's mobile device to provide positive reinforcement and encouragement to attend important treatment-related activities. Researchers at the Be Well Institute are investigating other mobile applications for effectiveness.

Potter is the primary investigator of a randomized study currently underway to evaluate the effectiveness of a mobile medical application called KIOS. The study

Fentanyl, a powerful synthetic opioid, is

50

times more powerful than heroin and is used to treat severe pain



"Identifying people at risk is one way you can help prevent substance use."

Natalie Maples, DrPH, MA, assistant professor in the Department of Psychiatry and Behavioral Sciences

INTO THE LIGHT

Statewide fentanyl awareness campaign aims to save lives, reduce stigma

Fentanyl, a powerful synthetic opioid, is 50 times more powerful than heroin and is used to treat severe pain. Illegally manufactured fentanyl, however, is especially dangerous because people may be unaware that they are taking the drug when it is added to counterfeit pills and sold as legitimate prescription drugs.

According to the Drug Enforcement Administration, the abundance of illegally manufactured synthetic opioids appears to be the primary driver of the dramatic increase in accidental drug overdose across the nation. Since 2014, fentanyl-poisoning deaths in Texas have increased sharply, with the preliminary data showing 2,293 deaths in 2023, according to the state's Department of Health and Human Services.

For the past several years, Natalie Maples, DrPH, MA, assistant professor in the Department of Psychiatry and Behavioral Sciences, has shaped a statewide awareness campaign about illegally manufactured fentanyl.

"In our campaign, we use a variety of different platforms like social media, within schools, billboards, TV and movie theaters," said Maples.

The campaign aims to bring the idea to the larger community that this problem exists, and that ignoring it will not make it go away. Letting people know this is everyone's concern aids progress in reducing the stigma around substance use disorders and opening access to treatment options, she said.

Maples was chosen for this awareness project due to her expertise in training personnel across Texas and beyond in evidence-based mental health and substance use disorder care. Since 2012, she has led the Centralized Training Infrastructure for Evidence-Based Practices.

After the first year of the fentanyl awareness campaign, Maples said they saw some success and produced more impressions than they predicted. One thing that made a difference was the targeted approach based on areas of the state with comparatively higher numbers of accidental synthetic opioid deaths.

"We were able to look at that county data to target where our campaign was going to be, because Texas is enormous," Maples said.

The project is now funded for a third year. According to Maples, they will reanalyze the data and will sharpen their approach for targeted accuracy in regions of Texas with the highest need. They will also disseminate a wider variety of videos for Spanish speakers.

In addition, research and observational evidence over the years has led to an increased focus on preventing substance use issues before they begin. Programs in schools and a training infrastructure allow for awareness of risk factors that may mean a child or young adult is at risk of substance use, said Maples.

"Identifying people at risk is one way you can help prevent substance use."

MORE SERVICES AND EDUCATION

The programming and services of the Be Well Institute continue to grow, including plans to add an adolescent substance use expert to begin a treatment program in fall 2024 as well as additional training opportunities.

Training programs are essential to spreading interest in and knowledge about treating addiction, said Van L. King, MD, medical director of Be Well Texas.

"Addiction is highly stigmatized, but patients often do well and go on to lead happy and successful lives. For the most severe disorders, most will need professional assistance. We want to ensure that trainees working with us realize that treating these patients is very rewarding and successful," King said.

Medical students, psychiatry and family medicine residents, and nursing students have opportunities to rotate through the Be Well Clinic. The university and the Audie L. Murphy Memorial Veterans' Hospital now have a joint addiction medicine fellowship that provides sub-specialty training to physicians.

"New treatments and treatment approaches are occurring regularly," King said. "It is an exciting time, and young physicians, nurse practitioners and physician assistants appreciate having this training."

Adrienne Lindsey, DBH, director, Be Well Center for Substance Use Training and Telementoring program

examines people in the early recovery phase who are taking buprenorphine for medication-assisted treatment for opioid use disorder. Patients log in daily, rating themselves on variables such as depression, pain, drug craving and other factors that can impact drug use.

The highly individualized, evidence-informed application software tracks changes in patient symptoms over time and encourages patients to increase recovery behaviors that are associated with improvement in symptoms and reach out for appropriate support. King said this kind of support may be beneficial between therapy sessions or at times when the patient cannot reach other support to avoid drug use. An initial study of the app demonstrated very good acceptability and usability.

Another study, led by Wright, examines an application that uses chat-bot style messaging to help the user screen for possible problems with substance use and encourage appropriate follow-up.

Comprehensive training

The capstone of the Be Well Institute is a premiere evidence-based training program — the Be Well Center for Substance Use Training and Telementoring — that provides eight learning communities related to specific aspects of substance use disorder.

Adrienne Lindsey, DBH, director of the training program, said the need for this training was spurred because the time between the establishment of an evidence-based practice and when it is implemented in the field can take more than 17 years. This lag is especially evident in the realm of substance use disorder.

Lindsey said a prime example of this is seen in the deployment and use of treatments for opioid use disorder. The three current medications available — methadone, buprenorphine and naltrexone — are highly efficacious. However, there is a low uptake from providers willing to prescribe the medications as well as reticence of pharmacies to dispense them. She equates the problem to failing to tell a patient with cancer about chemotherapy or radiation treatment.

"It is very similar in terms of the potential reduction in mortality. The fact that we do not offer it at the scale needed, and we are in the midst of this overdose epidemic, is a related crisis and ethical conundrum," Lindsey said.

The training center aims to be a catalyst in the implementation of effective, evidence-based practices and helping providers get the tools they need to begin implementing these practices. The sessions are for anyone who encounters people with substance use disorders, including health care providers and public safety professionals, along with individuals who have lived experience of substance use and can serve as peer recovery-support specialists.

The training program was developed based on Project ECHO, a mentorship and training model created by the University of New Mexico's ECHO Institute. The Be Well Institute also partners with the university's Center for Research to Advance Community Health, which uses the ECHO model.

The goal is to build capacity throughout vast areas through a "hub and spoke" model, where the hub of experts extend knowledge to the various spokes, building capacity until the hub is no longer needed. The spokes then become the new hubs, extending knowledge further, and so on.

New model for needed solutions

Substance use disorders and related illnesses continue to cause devastating consequences to communities, and people are demanding new ways to address the problem, said Potter. The work the Be Well Institute does in partnership with the state helps grow the science at the university by creating an infrastructure for asking more questions and finding more solutions. In turn, the widespread provider training and scientific innovations that emerge through the Be Well Institute benefit the entire state and ensure unprecedented access to care for years to come, she added.

"My vision of the next five to 10 years is that new treatments will come out of the institute that were developed by our scientists and deployed here, and that these treatments are informed by the context of our community and what matters here."

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