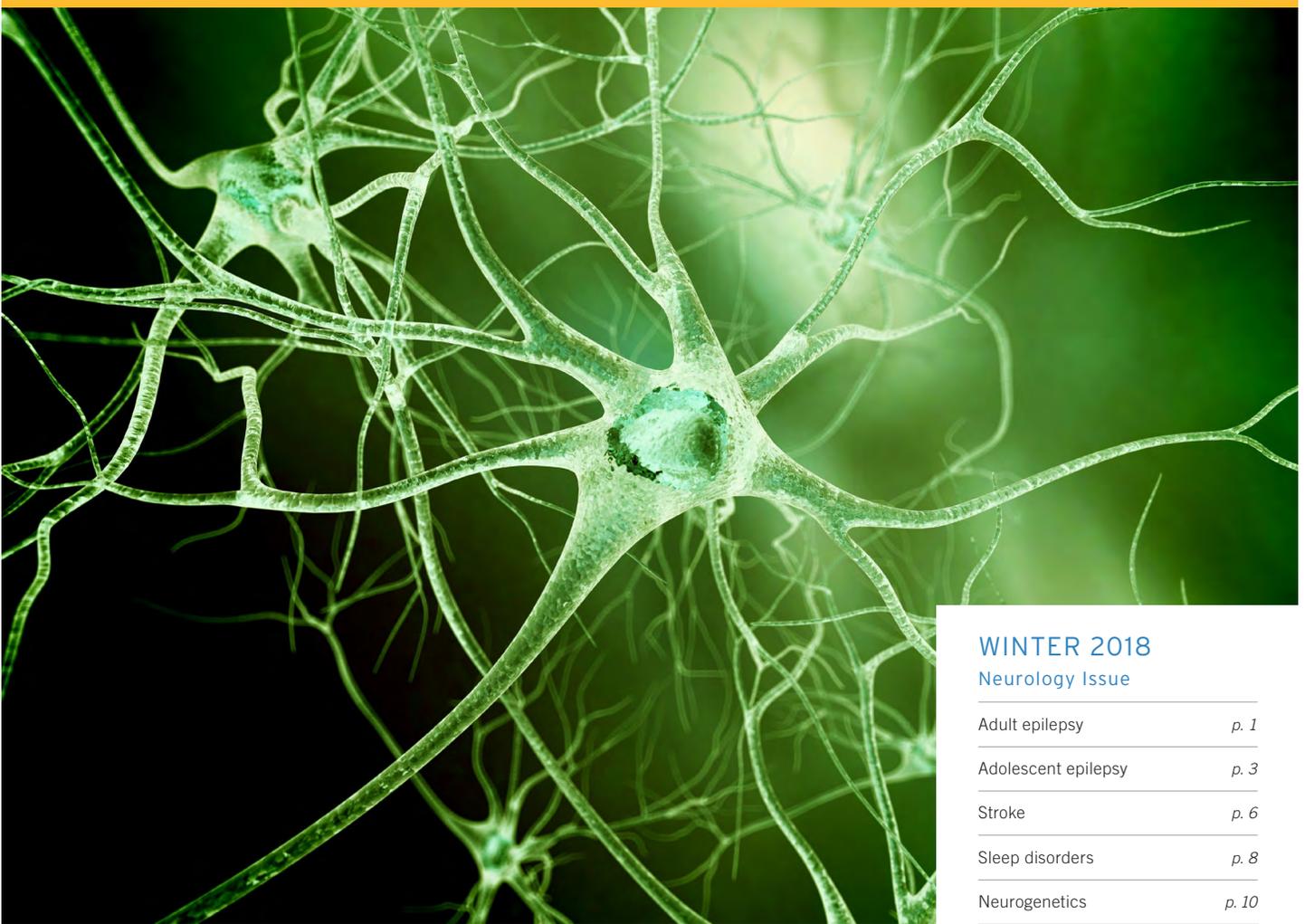


# Physicians Update



**WINTER 2018**  
Neurology Issue

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**ADULT EPILEPSY**

**Specialized epilepsy center offers potential remedies to patients with uncontrolled seizures**

For adults with epilepsy whose seizures are not controlled by medication, a specialized center can ensure proper diagnosis and offer multiple options for effective treatment, dramatically improving patients' quality of life and decreasing their risk for premature mortality. Experts at the UCLA Seizure Disorder Center work in collaboration

with referring physicians to formulate an effective plan that can involve non-surgical approaches, new minimally invasive procedures or, when appropriate, traditional surgery.

The risk of sudden unexplained death in epilepsy (SUDEP) is significant. Patients

*continued on p. 4*

# UCLA Clinical Updates

Learn about the latest advances from UCLA

## Community pain clinics

UCLA has established a growing network of community-based pain centers staffed by physicians who are board-certified in anesthesiology and pain medicine. With more than 100 million Americans suffering from acute and chronic pain, there is a need for cost-effective and convenient strategies to help reduce pain while minimizing reliance on narcotics.

## HIPEC offers regional treatment for abdominal cancers

Hyperthermic intraperitoneal chemoperfusion (HIPEC) is a regional chemotherapy that is paired with cytoreductive surgery to eliminate cancer cells that remain in the abdominal cavity after visible cancer cells have been removed. Because the chemotherapy agent does not circulate through the bloodstream, higher doses can safely be used without the side effects usually associated with systemic chemotherapy.

## Flow diversion stents for unruptured cerebral aneurysms

Flow diversion is a newer endovascular treatment for brain aneurysm in which a metallic mesh tube is placed across the neck of the aneurysm to divert blood flow. The endothelium then grows onto the stent, sealing off the opening of the aneurysm and healing the blood vessel wall.

## Study of noninvasive ventricular tachycardia treatment

UCLA is among the centers studying the use of stereotactic ablative radiotherapy (SABR) to treat ventricular tachycardia without surgery. The use of SABR could present a treatment alternative for cardiac patients too sick for invasive treatments or for whom conventional therapies have been unsuccessful.

## Pediatric Heart Transplant/Heart Failure Program

UCLA pediatric cardiologists often offer treatments that aren't available in other centers, including multi-organ pediatric transplants. Yet despite the higher level of medical complexity of these patients, success rates at UCLA are among the best in the nation.

## UCLA opens diabetes center in Santa Monica

Along with the Gonda Diabetes Center in Westwood, the new Santa Monica office is dedicated exclusively to the care and education of adults with type 1 diabetes, type 2 diabetes and gestational mellitus diabetes.

## New endocrine center offers a streamlined approach to care

The UCLA Endocrine Center is one of only a handful of centers nationwide offering a full range of consultative, diagnostic and therapeutic endocrinology care — including all diseases of the thyroid, parathyroids and adrenal glands — in a single-visit, one-location setting.

## UCLA Scar Treatment Program offers personalized outpatient care

The UCLA Scar Treatment Program offers treatment for symptomatic or asymptomatic scars from any cause, as well as care for burn injuries.



To download these and other clinical advances at UCLA Health, go to: [uclahealth.org/clinicalupdates](http://uclahealth.org/clinicalupdates)

# News from UCLA Health

## Researchers find potential path to repair nerves damaged by multiple sclerosis

A UCLA study finds that gene expression in specific cells and in specific regions of the body can provide a more precise, neuroprotective approach than traditional treatments for neurological diseases.

[uclahealth.org/nerverepair](http://uclahealth.org/nerverepair)

## Researchers map genetic 'switches' behind human brain evolution

UCLA researchers have developed the first map of gene regulation in human neurogenesis, the process by which neural stem cells turn into brain cells and the cerebral cortex expands in size. The scientists identified factors that govern the growth of our brains and, in some cases, set the stage for several brain disorders that appear later in life.

[uclahealth.org/geneticswitches](http://uclahealth.org/geneticswitches)

## Just 4,000 steps a day can lead to better brain health

Walking 4,000 steps or more a day can improve attention and mental skills in adults 60 and older.

[uclahealth.org/4000steps](http://uclahealth.org/4000steps)

## In recovery from sports concussions, state of mind really does matter

Researchers at UCLA have been taking a closer look at the psychological aspects of recovery from head injuries and have recently begun a program that integrates a common type of talk therapy as part of their treatment for athletes with lingering emotional impacts after their injuries.

[uclahealth.org/talktherapy](http://uclahealth.org/talktherapy)

### UCLA's new Endocrine Center offers a streamlined approach to comprehensive and innovative care

The UCLA Endocrine Center, launched in December 2013, is one of only a handful of centers nationwide offering a full range of consultative, diagnostic and therapeutic endocrinology care — including all diseases of the thyroid, parathyroids and adrenal glands — in a single-visit, one-location setting.

**Specialty, accessibility and expertise**

The streamlined approach allows patients and their families an expedient treatment pathway to the highest level of care. Endocrinology is a highly specialized field, and the center's multidisciplinary approach ensures that patients receive the most comprehensive and innovative care available. The center's location in the heart of Westwood, near the UCLA Medical Center, provides easy access to other UCLA departments and services.

**Endocrine care opportunities**

UCLA's Endocrine Center is a leading center for the treatment of thyroid and adrenal disorders. The center's location in the heart of Westwood, near the UCLA Medical Center, provides easy access to other UCLA departments and services.

### Surgery with HIPEC offers effective regional treatment for select metastatic abdominal cancers

Hyperthermic intraperitoneal chemoperfusion (HIPEC) is a regional chemotherapy that is paired with cytoreductive surgery to eliminate cancer cells that remain in the abdominal cavity after visible cancer cells have been removed. Because the chemotherapy agent does not circulate through the bloodstream, higher doses can safely be used without the side effects usually associated with systemic chemotherapy.

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### Clinical trial offers first non-invasive ventricular tachycardia treatment

UCLA is one of a handful of centers worldwide, pioneering the use of stereotactic ablative radiotherapy (SABR) to treat ventricular tachycardia without surgery. The use of SABR could present a treatment alternative for cardiac patients too sick for invasive treatments or for whom conventional therapies have been unsuccessful.

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# New center offers comprehensive care for teens with epilepsy

During the course of his training in pediatric neurology, Jason T. Lerner, MD, sat in on a support group his wife was running for teens with epilepsy. “Hearing about their struggles was eye-opening,” says Dr. Lerner, a UCLA pediatric neurologist. “I came to appreciate how much these patients could benefit from a center that broadly addressed their needs — focusing not just on the underlying epilepsy, but also on comorbidities and the stigma associated with the diagnosis.”

The new Adolescent Epilepsy Center at UCLA brings together a team of providers to focus on all aspects of health for adolescents with epilepsy. The center, under the direction of Dr. Lerner, also aims to help adolescent patients make a smooth transition from pediatric to adult providers.

Too often, Dr. Lerner says, care for pediatric epilepsy patients focuses on seizure control while paying insufficient attention to comorbidities and psychosocial concerns. An estimated 30-to-40 percent of adolescents with epilepsy have comorbidities, such as depression, anxiety, attention deficit hyperactivity disorder, learning disabilities, sleep disorders and autism spectrum disorder. In some patients, Dr. Lerner notes, successfully bringing the seizures under control can heighten the severity of any comorbidities — even bringing out previously dormant psychotic symptoms, a phenomenon referred to as forced normalization.

Dr. Lerner says the value of a center that would holistically treat adolescents with epilepsy was brought home by his experience with a patient whose quality of life plummeted after her seizures were finally controlled. “I had followed this patient for a number of years, and when we finally were able to control her seizures and improve her EEG, her underlying anxiety came to the forefront and she could barely leave the house,” Dr. Lerner says. “Often it’s these comorbidities that are the most impactful for patients.”

Treating conditions such as depression and anxiety in patients with epilepsy requires special expertise to ensure, for example, that medications don’t adversely interact with anti-seizure drugs. Dr. Lerner notes that there is a shortage of child

psychiatrists and psychologists in general, and fewer still with expertise in seeing patients with epilepsy. Compounding matters, these providers may not accept insurance. “For many epilepsy patients, we might suspect depression but have trouble referring them for diagnosis and treatment,” Dr. Lerner says. “With our center, if we have a concern, we will be able to refer patients internally to a mental health professional who is experienced in seeing adolescents with epilepsy.”

Many adolescent epilepsy patients see multiple practitioners at different clinics, which is both inconvenient and leads to uncoordinated care, Dr. Lerner notes. The Adolescent Epilepsy Center at UCLA will allow patients to see all of their providers in a single appointment. The center includes pediatric neurologists and epileptologists, nurse practitioners, a psychiatrist, a psychologist, a dietitian, an occupational therapist and a social worker. The center treats any patient ages 12 to 20 who has epilepsy. Some will be treated on a regular basis; others may remain with their community physician for regular care while being referred to the center on a periodic basis to ensure that all of their needs are being met.

In addition to clinical services, the center will include a research component. Plans are already afoot to partner with UCLA’s Mindful Awareness Research Center to examine the potential benefits of incorporating mindfulness for adolescent epilepsy patients, in light of research suggesting that adults with epilepsy can benefit from the practice. Monthly support groups also will be offered to both adolescent epilepsy patients and their caregivers. The center will develop a network of community-based neurologists, psychiatrists and other practitioners with whom it will partner in providing patient care. Finally, there will be a focus on community education. “More than most chronic diseases, there is a stigma associated with epilepsy,” Dr. Lerner says. “Part of improving our patients’ quality of life is educating the community to begin to remove that stigma.”



To learn more about pediatric neurology at UCLA, go to: [uclahealth.org/mattel/pediatric-neurology](https://uclahealth.org/mattel/pediatric-neurology)



The Adolescent Epilepsy Center at UCLA brings together a team of providers to focus on all aspects of health for teens with epilepsy.

Photo: Superstock

“More than most chronic diseases, there is a stigma associated with epilepsy. Part of improving our patients’ quality of life is educating the community to begin to remove that stigma.”

## COVER STORY

# Specialized epilepsy center offers potential remedies to patients with uncontrolled seizures

*(continued from cover)*

with uncontrolled seizures are at five-to-10 times greater risk of dying, and also are at higher risk for depression and suicide. “Every patient who has tried one or two antiseizure medications and is not seizure-free should be referred to a specialized epilepsy center for an evaluation,” says Dawn Eliashiv, MD, codirector of the UCLA Seizure Disorder Center.

Dr. Eliashiv notes that only a small percentage of patients who could be helped by a specialized center are referred. In the U.S., of the 3 million people who have epilepsy, approximately one-third continue to experience seizures even on medication. It’s estimated that 150,000 of these patients are surgical candidates, but only about 2,500 epilepsy surgeries are performed each year. Dr. Eliashiv says one of the main reasons many patients aren’t referred is the widely held misconception among physicians that epilepsy centers only perform surgery, and that their patients either wouldn’t want an operation or wouldn’t be a candidate.

In fact, although surgery can be life changing for patients who need it, many who are referred to the UCLA Seizure Disorder Center can have their epilepsy controlled through medication or nonsurgical procedures. John Stern, MD, codirector of the UCLA Seizure Disorder Center, notes that as many as one-third of patients who undergo a comprehensive epilepsy evaluation are discovered not to have epilepsy. “There is a range of conditions that can mimic epileptic seizures,” Dr. Stern says. “If such patients are being given antiepileptic medications, it’s not going to control those seizures.” At UCLA, patients having nuanced episodes are evaluated to confirm the epilepsy diagnosis, as well as to characterize the condition through MRI, EEG or, when necessary, diagnostic admissions.

For patients with a confirmed epilepsy diagnosis, characterizing the condition can lead to the use of a different medication that may be more successful. There are approximately 20 approved epilepsy medications operating through a half-dozen different mechanisms, as well as experimental drugs available through clinical trials. “Consultation in the epilepsy clinic can lead to medication changes that can reduce the seizure burden — or, for some patients who are seizure-free, reduce the side effects of the treatment to improve their quality of life,” Dr. Stern says.

**Although surgery can be life changing for patients who need it, many who are referred to the UCLA Seizure Disorder Center can have their epilepsy controlled through medication or nonsurgical procedures.**

For the one-third of patients found to have medically refractory epilepsy, surgery may be an appropriate option, and the UCLA Seizure Disorder Center is able to stop the disabling seizures in a high percentage of these cases with minimal or no side effects. Because of the significant advances that have been made in surgical approaches in recent years, many more patients are candidates for surgery than in the past.

Beyond resective epilepsy surgery, the UCLA Seizure Disorder Center offers both neurostimulation and MRI-guided laser ablation. Vagus nerve stimulation (VNS)



Patient undergoing an electroencephalogram (EEG) epilepsy screening.

Photo: Medical Images

## STORY HIGHLIGHTS

For adults with epilepsy whose seizures are not controlled by medication, a specialized center can ensure proper diagnosis and offer multiple options for effective treatment.

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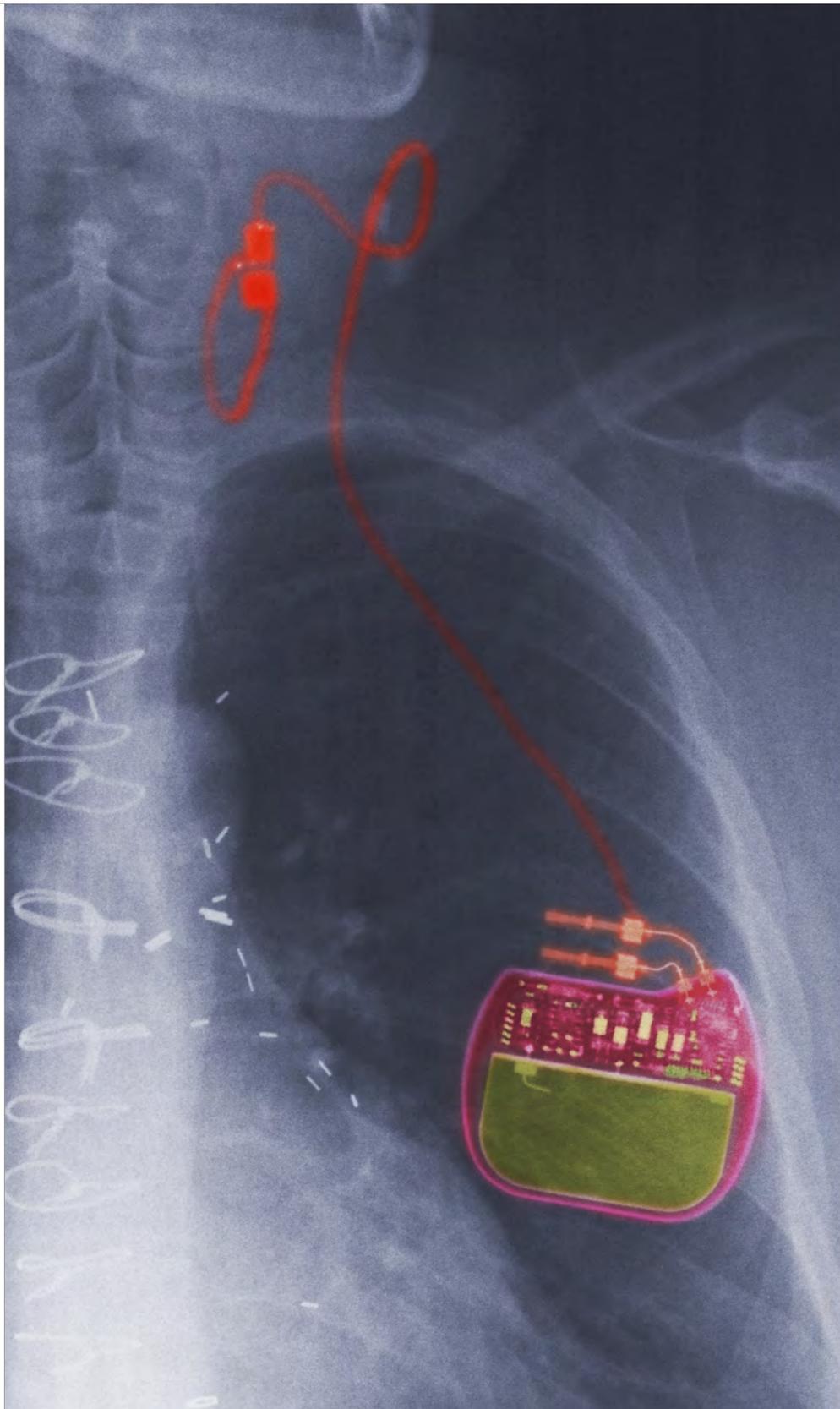
was approved by the FDA in 1997, but recently approved newer generations of the vagus nerve stimulator are able to monitor changes in heart rates as a proxy for seizure activity. This allows the device to deliver additional stimulations during the onset of seizure activity. UCLA also is a leader in the use of responsive neurostimulation, in which a device analogous to a heart defibrillator is implanted into the brain area where the seizures originate. “This device is able to detect the changes that occur when a seizure is about to begin and trigger shock waves that can stop the seizure from occurring,” Dr. Eliashiv explains. “It allows us to successfully treat patients who have seizures coming from both sides of their brain, or patients who have seizures that are close to critical areas of motor and language that we would not want to surgically remove.” The device, approved in 2013, has been shown in multicenter trials to reduce median seizure frequency by approximately 70 percent in medically refractory patients.

Laser thermal ablation, another relatively new minimally invasive technique, is ideal for patients in whom the area of the brain generating the seizures is small but difficult to reach through traditional surgery. “If we don’t need to remove the tissue, we can eliminate the electrical abnormality simply by heating it to the point that it’s no longer capable of producing the seizures,” Dr. Stern says. “In addition to being less invasive, this has allowed patients to benefit from surgery who never would have been candidates in the past.”

The bottom line is that a specialized epilepsy center can offer potential remedies to most patients with uncontrolled seizures. “Too often, the impediment for patients is the sense that although they are having occasional seizures, things aren’t that bad, and they think they should just accept their situation,” Dr. Stern says. “At a minimum, these patients should be referred for an evaluation. Often we can get the seizures under control and vastly improve their quality of life.”



**For more information about epilepsy care at UCLA, go to:**  
[neurology.ucla.edu/clinic/programs/epilepsy](http://neurology.ucla.edu/clinic/programs/epilepsy)



CXR with vagus nerve stimulator for epilepsy

Photo: Alamy



Photo: UCLA

# Hospital on wheels brings immediate care to stroke patients

## STORY HIGHLIGHTS

The UCLA Health Mobile Stroke Unit enables rapid delivery of brain-saving medications to stroke patients who might otherwise face debilitating delays in treatment.

The unit consists of an ambulance equipped with CT scanning technology along with a highly trained team able to perform diagnostic testing and initiate appropriate treatment.

UCLA Health has launched the first mobile stroke unit on the West Coast, enabling rapid delivery of brain-saving medications to stroke patients who might otherwise face debilitating delays in treatment. The unit consists of an ambulance equipped with CT scanning technology along with highly trained personnel who respond to calls involving patients suspected of having a stroke. The team is able to perform diagnostic testing and initiate appropriate treatment before transporting the patient to the hospital for further care.

The UCLA Health Mobile Stroke Unit (MSU) was launched in September 2017, responding to select 911 calls in Santa Monica in coordination with the Santa Monica Fire Department. In January 2018, the unit began a partnership with Los Angeles County that will ultimately involve collaborations with multiple fire departments to

expand the number of patients who are covered by the service.

Roughly every 40 seconds, someone in the United States will have a stroke, and one person every four minutes will die as a result. During the stroke's acute phase, each moment without treatment can lead to the death of additional brain cells. "In most strokes there is either a lack of blood flow to tissue in the brain or bleeding into the tissue in the brain. In either case, getting treatment to the patient fast improves the outcome," says May Nour, MD, PhD, medical director of the UCLA Arline and Henry Gluck Stroke Rescue Program. "This program brings the first minutes of emergency treatment to the patient in the field rather than waiting until the patient arrives at the hospital."

"Time is brain in acute stroke — every minute counts," adds Jeffrey Saver, MD, director of the

UCLA Comprehensive Stroke Center. The MSU brings “the hospital to the patient in order to save as much brain as possible.”

The mobile unit doesn’t replace treatment in the hospital; rather, it expedites care by starting care in the field. Within its jurisdiction, the MSU, along with ambulance paramedics, responds to calls made over the 911 dispatch system for patients who have symptoms indicative of a possible stroke. If the patient is deemed not to have suffered a stroke, the regular ambulance provides usual care. If a stroke is determined to be likely, the mobile unit takes over the case.

Patients undergo CT scanning in the unit and the team can give blood tests to determine whether a stroke is occurring, along with the type of stroke. If the patient is having ischemic blockage, the clot-dissolving drug tPA can be administered; for a hemorrhagic stroke, immediate treatment typically involves reducing any anticlotting medicines the patient is taking and quickly bringing blood pressure under control. Patients are then transported to the most appropriate stroke-receiving hospital. Those who have blockage of a major artery and may not benefit from tPA, for example, are taken to a center where surgical thrombectomy can be performed to open the artery.

In the initial phase of the pilot program, the MSU includes a neurologist specializing in stroke treatment. As the program expands, a neurologist will oversee the care via a live video and voice connection from Ronald Reagan UCLA Medical Center, communicating with a neurocritical care nurse, a CT technologist and a paramedic in the unit.

The MSU is equipped with a mobile CT scanner and a mobile blood-testing laboratory. “The images we have been getting from the CT scans have been very high resolution and rapidly acquired, which allows for confident decisions to be made in the field,” Dr. Saver says.

The idea of an ambulance equipped with a CT scanner has been a dream for the field of stroke neurology dating back 30 years, Dr. Saver notes. Even before the advent of the clot-busting drug tPA, it was known that any treatment for stroke would need to be initiated quickly to be most effective. It also was clear that the treatment would be different depending on the type of a

stroke — be it a blockage, in which the goal is to dissolve clots to restore blood flow, or a bleed, in which clotting is desirable — and that accurate diagnosis would require brain imaging. The development of a CT scanner lightweight enough to be positioned on a moving platform allowed for the dream’s fulfillment. In 2011, the first such unit began running in Germany, and in 2014 Houston became the first city in the U.S. to run a mobile stroke unit. Approximately a dozen cities have followed suit.

By initiating treatment with time-dependent, proven therapies earlier, the mobile stroke unit is sure to improve outcomes, Dr. Nour says. In addition, the unit will ultimately allow for the testing of new therapies in the hyper-acute time frame when they have the best chance to work, making it an ideal platform for future research. “It makes sense that if we’re giving medications that dissolve clots or reverse the bleeding into tissue of the brain faster, clinical outcomes will be better,” Dr. Nour says. “The question is, will this be cost-effective? We know that the morbidity and mortality related to stroke are very high, which has a big drain on the medical system, so we think it will be.”

To find out, the UCLA unit is serving as the West Coast anchor for the first national demonstration project to gather data on the degree of improved patient outcomes and cost-effectiveness with accelerated field treatment. Positive results from the three-year study could lead the federal Centers for Medicare and Medicaid Services and other insurers to reimburse emergency medical service and hospital systems for mobile stroke clinical activities.

The availability of faster treatment underscores the importance of educating older patients and their loved ones about the signs of a stroke and the need to report it immediately, Dr. Nour notes. The acronym FAST — face drooping, arm weakness, speech difficulty, time to call 911 — is commonly used, but other signs are also important, she explains, including sudden-onset weakness, numbness, changes in vision and acute difficulty with balance.



For more information about the UCLA Health Mobile Stroke Unit, go to: [uclahealth.org/mobile-stroke](http://uclahealth.org/mobile-stroke)



Photo: Getty Images

The UCLA Health Mobile Stroke Unit brings the first minutes of emergency treatment to the patient in the field rather than waiting until the patient arrives at the hospital.

# Addressing sleep issues can aid diagnosis of health concerns

## STORY HIGHLIGHTS

A good night's sleep can be as essential to overall health and quality of life as diet and exercise.

Chronic sleep deprivation is associated with mental and physical health issues, impairs one's alertness and can result in memory and other cognitive problems.

During an overnight sleep study, breathing abnormalities (shown in the green boxes) that contribute to sleep disruption and daytime sleepiness can be detected.

Image: Courtesy of Dr. Alon Avidan

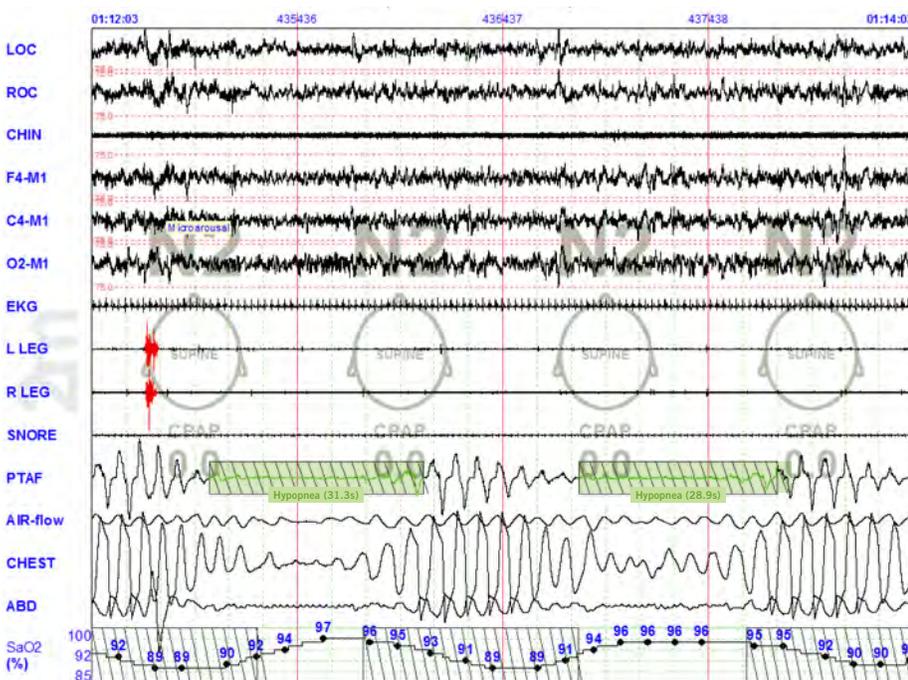
In a fast-paced society in which many people are working longer hours, spending more time on their commutes and trying to fit more activities into their day, the recommended eight hours of sleep each night can seem like a luxury. But the director of the UCLA Sleep Disorders Center points out that regularly getting a good night's sleep can be as essential to overall health and quality of life as diet and exercise. And he recommends that physicians ask their patients about sleep habits and refer them for evaluation and treatment if there are concerns.

“In primary care settings, many patients don't recognize that they may have a serious underlying sleep disorder at night, which might be the root cause of fatigue and sleepiness during the day,” says Alon Avidan, MD, MPH, director of the UCLA Sleep Disorders Center and a professor in the Department of Neurology. “But poor sleep has an enormous impact on health and should be discussed with their physician, even if physicians don't ask their patients about how well they sleep.”

Dr. Avidan notes that chronic sleep deprivation is associated with a myriad of mental and physical health issues. It increases the risk of depression and impairs one's alertness and ability to drive and can result in memory and other cognitive problems. It also can predispose patients to diabetes and obesity. Obstructive sleep apnea, a common but frequently undiagnosed disorder that often is the source of daytime sleepiness, increases the risk of hypertension and stroke when left untreated. Older adults who have poor sleep also are even more prone to developing cognitive and memory difficulties, or to an acceleration of existing neurocognitive problems. Finally, Dr. Avidan says, untreated sleep disorders can exacerbate chronic pain, as well as depression, in a bidirectional manner. Poor pain control and depression may worsen sleep, and poor sleep worsens depression and pain.

The UCLA Sleep Disorders Center provides consultations for patients with sleep disorders, who are treated in the clinics, as well as conducting overnight sleep studies in the UCLA Sleep Disorders Laboratory for patients who require additional diagnostic testing for conditions such as sleep apnea. A team that includes neurologists trained in sleep medicine as well as clinicians from pulmonary and internal medicine, pediatrics, family medicine, head and neck surgery, and dentistry deliver personalized treatment programs to manage a broad spectrum of sleep disorders in adults and children. Disorders may include obstructive sleep apnea, insomnia, restless leg syndrome, parasomnia, excessive daytime sleepiness, narcolepsy, circadian rhythm disorders such as jet lag syndrome and abnormal behaviors during the night. The UCLA Sleep Disorders Center also promotes research and community education, while working collaboratively with referring physicians to ensure exemplary care.

An epidemic of sleep deprivation exists in the United States, Dr. Avidan notes. In part, this can be attributed to the cultural norm that sleep





is like a “bank account” and you can borrow hours to remain awake and repay later. The problem is that this borrowed time is taken at a “very high interest rate,” and it is not possible to always catch up on the weekends. “With the increasing demands of work and school, there are people who experience a great deal of sleep deprivation when over-commitments to a full plate of academic and social activities takes a toll on their sleep” Dr. Avidan says. Two societal trends are providing additional fuel. The epidemic in the U.S. and developing world of overweight and obese individuals has contributed to more patients presenting with symptoms of sleep apnea, which include snoring, daytime sleepiness, problems breathing at night, as well as attention deficit hyperactivity disorder and reduced school performance in pediatric patients, Dr. Avidan notes. In addition, the fastest growing patient population includes patients over age 65, which means that more older adults will present with a host of health problems. “We are seeing more adults who are getting only four or five hours of sleep and

believe that this is normal for their age group,” Dr. Avidan says. In fact, “an 80-year-old man needs as much sleep as a 20-year-old college student, but it is the ability of the older adult to obtain seven-to-eight hours of sleep that is impaired due to the primary sleep disorders, such as abnormal leg movements at night and sleep apnea.

Given sleep’s vital importance to quality of life and overall health, Dr. Avidan urges physicians to make it a central part of every patient visit. “Patients should be asked about snoring, stopping breathing at night, restlessness in the legs, nightmare/terror-like episodes, daytime sleepiness, any difficulties falling asleep or maintaining asleep, and their overall sleep quantity and satisfaction,” he says. “If there is any sleep problem, it shouldn’t be ignored, as there is no substitute for a good night sleep.”



For more information about the  
**UCLA Sleep Disorders Center, go to:**  
[sleepcenter.ucla.edu](http://sleepcenter.ucla.edu)

An overnight sleep study can be beneficial for patients who require additional diagnostic testing.

Photo: Ann Johansson

“With the increasing demands of work and school, there are people who experience a great deal of sleep deprivation when overcommitments to a full plate of academic and social activities takes a toll on their sleep.”

# Advances in neurogenetics opens window to rare neurological conditions

## STORY HIGHLIGHTS

Genomic technology has important implications for patients with genetic disorders that have eluded diagnosis and for those who may have been misdiagnosed in the past.

The evolving technology has led to surprising discoveries of rare diseases that never would have been expected based on how they were originally described.

The advent of genomic technologies, particularly exome sequencing, has vastly improved the ability of neurogeneticists at major centers like UCLA to diagnose patients with extremely rare neurologic conditions, according to Brent L. Fogel, MD, PhD, associate professor of neurology and human genetics and director of UCLA's newly established Clinical Neurogenomics Research Center. This has important implications, both for patients with genetic disorders that have eluded diagnosis and for those who may have been misdiagnosed in the past, Dr. Fogel says.

Exome sequencing is a diagnostic tool that allows physicians to sequence all the protein-coding information of the 20,000 genes in the human genome simultaneously — some

70 million base pairs — in just a few hours. Using that information, a team of scientists and clinicians, including neurogeneticists, can do a complete assessment of what, if any, potential mutations fit the patient's clinical phenotype.

“We've been using this test for more than five years, and it has revolutionized the way genetic testing is performed and our patients are evaluated,” Dr. Fogel says. “Before we started, it was very challenging to diagnose these patients because of the number of potential genes involved. We had to make our best guess as to what gene was the problem, which meant the testing was biased; we were limiting ourselves to a certain small set of genes and if it wasn't there, we never were going to find it. Now that we are looking across the entire genome, if there

Photo: Science Photo Library



is something to find, it's going to rise to the top for us to see. Instead of digging through the haystack, we let the needle come to us."

This has led to a rethinking of many past assumptions. "We have learned an important lesson; these diseases can be variable and don't always look like they're supposed to according to the textbooks. We have had surprising discoveries of rare diseases that we never would have expected to find based on how they were originally described," Dr. Fogel says. "In general, we are learning that there is much more neurogenetic disease out there than we ever fully appreciated before."

The patients Dr. Fogel and his colleagues treat with cerebellar ataxia — a disorder of balance and coordination — illustrate how the new genomic technologies have changed the clinical equation. Because most of these patients are adults, with no family history of disease, the conventional thinking had been that their conditions couldn't be genetic. "Most people thought that these patients had some form of idiopathic late-onset cerebellar ataxia, and that there was nothing that could be done to identify it any better than that," Dr. Fogel says. "But when we started to do this testing, we found a genetic cause in at least one-fifth of them. Most people often envision genetic disease as little kids who have severe developmental phenotypes, but we've learned that adults are also commonly affected, and we can help a lot of them understand why."

Far more patients with rare genetic neurologic disorders are being diagnosed as a result of genomic testing. Previously, Dr. Fogel notes, many patients with neurological symptoms of unknown origin either wouldn't be referred for diagnostic testing or would receive testing that primarily involved guesswork. "Either the test wouldn't show anything and that was the end of it or, more rarely, someone would guess right and the patient would get diagnosed," Dr. Fogel says. "In some cases, a rare inconsequential change would be noted in one of these genes and although a diagnosis would be made, it was the wrong diagnosis." Often, patients would endure what is commonly referred to as a diagnostic odyssey, going from one center to another on a futile quest for a diagnosis spanning many years, at considerable cost.

Even when there are no available cures, capping that odyssey can have an enormous impact on patients' lives. "It makes a big difference to people who are disabled to know why," Dr. Fogel says. Among other things, the knowledge that the cause is genetic ends the nonproductive search for other culprits, which can include a constant array of doctor visits, workups, imaging studies and blood tests. The diagnosis can have an impact on other family members who may or may not be at risk, and can inform family planning decisions by defining the risk of passing on the condition.

For most rare genetic neurologic diseases, there is sadly no specific treatment, Dr. Fogel notes, but a diagnosis can steer clinicians toward therapies that have shown some benefit in patients with the same condition and away from those that have been shown to be of no benefit. Even more important, the ability to diagnose more genetic conditions is a boon to research efforts at finding new therapies. The past year has seen new breakthrough gene therapies for certain genetic neurological diseases coming to the clinic, making it even more important for patients to get a correct diagnosis now.

The UCLA Clinical Neurogenomics Research Center was established in part to ensure access to appropriate state-of-the-art genomic technologies for all neurology patients as an important piece of UCLA's Precision Health Initiative, while also furthering genomic research. Patients are given the opportunity to utilize genomic testing appropriate for their condition, such as exome sequencing, as well as to provide samples for a large biobank the center is creating that will be used by researchers studying these conditions in an effort to improve care for these patients.

These and other new genomic technologies raise the value of sending patients for evaluation and testing, Dr. Fogel says. He recommends referral of patients with neurological symptoms that are unexplainable and getting worse, as well as patients with a previous diagnosis that seems as if it could be inaccurate.



**For more information about neurogenetics at UCLA, go to:**  
[neurology.ucla.edu/clinic/programs/neurogenetics](https://neurology.ucla.edu/clinic/programs/neurogenetics)



Photo: Getty Images

**"Now that we are looking across the entire genome, if there is something to find, it's going to rise to the top for us to see. Instead of digging through the haystack, we let the needle come to us."**

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U.S. News & World Report's Best Hospital Survey ranks UCLA No. 1 in Los Angeles and No. 7 in the nation.

## 6th Annual UCLA Review of Clinical Neurology

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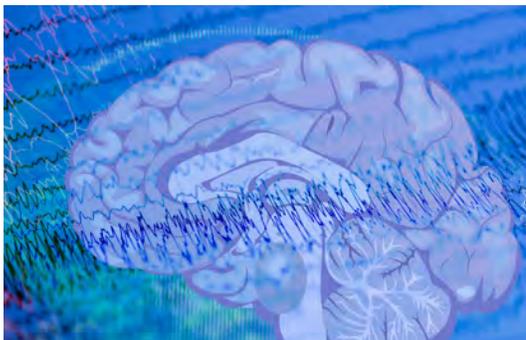


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## Physicians Update

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