FOR THE

1 IN 26

RESEARCHING FOR A CURE

2024

CURE EPILEPSY

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1 IN 26 AMERICANS WILL BE DIAGNOSED WITH EPILEPSY IN THEIR LIFETIME.

WE RESEARCH FOR THEM.

In CURE Epilepsy's 26th year, it is fitting that we reflect on one of the epilepsy community's most powerful statistics. For many reading this letter, that statistic is all too personal. But for the broader public, the number can serve to raise awareness that epilepsy likely impacts someone they know.

We play a critical role in the research landscape and help scientists generate data so that they can secure larger grants from the National Institutes of Health (NIH), the largest funder of epilepsy research in the world. Unfortunately, NIH's budget took a big hit this year and is at risk in 2025. Now more than ever it is imperative that CURE Epilepsy invests in young researchers and fills gaps to make sure that progress continues unimpeded.

Last year, our organization undertook a strategic planning process to analyze our priorities, our portfolio, and the research areas where scientists can most use our support. This process lays the foundation for us to build initiatives and a grant-making strategy that will have the greatest impact going forward.

Additionally, conversations with stakeholders throughout our community helped us refine the language that guides us. I am pleased to share CURE Epilepsy's new mission statement: **to fund breakthrough research that will transform the lives of people with epilepsy as we lead the search for a cure**. Our fundamental work and vision remain the same, but we've evolved our language to better reflect who we are and the impact that we aim to have on people's day-to-day lives as we march together toward a cure.

Finally, we have been hard at work on a new and improved website with a more modern look and feel and educational information that is easier to find and search. Check out **CUREepilepsy.org** and let us know what you think.

We are excited, emboldened, and confident that our continued leadership will spur scientific advancements and breakthroughs in understanding how and why epilepsy occurs so that we can target and develop cures.

Thank you for joining us on this journey. Our research benefits all of our community, but our community is made up of many, many individuals, each one with a unique story and need. We strive to keep each individual in mind as we pursue our shared vision: to live in a world without epilepsy.

With Gratitude,

Beth Lewin Dean

VOICES FROM THE CURE EPILEPSY COMMUNITY

CURE Epilepsy surveyed our epilepsy community in Spring 2023 to better understand the unique needs and priorities of people living with epilepsy and those who love and care for them — caregivers and healthcare providers among them. To the more than 1,200 people who participated: thank you!

OUR COMMUNITY RELIES ON ADVOCACY GROUPS LIKE OURS FOR INFORMATION **EVEN MORE THAN THEIR HEALTHCARE PROVIDERS.**

75% of researchers surveyed consider **CURE EPILEPSY'S ROLE** in the epilepsy research community to be **EXTREMELY OR VERY IMPORTANT**

DONORS said they're drawn to CURE Epilepsy because of the **ADVANCEMENTS IN UNDERSTANDING** epilepsy and seeing young **RESEARCHERS ATTACKING PROBLEMS.**

ONLY **50%** OF RESPONDENTS LIVING WITH EPILEPSY HAVE SEIZURE CONTROL

3 MOST IMPORTANT RESEARCH PRIORITIES for people living with epilepsy

TREATMENTS AND THERAPIES

PEDIATRICS

GENETICS

MAKE A DIFFERENCE

FOR THE 1
WHO'S BEEN MISDIAGNOSED

Nora Allen
AGE 17, MADISON, WISCONSIN

Nora woke up early on the morning of July 5, 2020. While Nora's mom, Michele, only vaguely remembers hearing her get up, she can still vividly recall the noise that came from her room moments later.

"I quickly shot out of bed and went into her room to see her having a full-blown seizure on her bed," Michele says. "It was the most horrifying thing to witness as a parent."

Michele and her husband rushed Nora to the emergency room, where they faced a barrage of tests and paperwork that would soon become their new normal, including electroencephalograms (EEG) to measure brain activity and meetings with the attending pediatric neurologist.

"At the time, I did not know [the neurologist] was an epileptologist, nor did I know there were neurologists who specialized in epilepsy and were called epileptologists," Michele says. "My worst fear was she had a brain tumor. Never did epilepsy cross my mind."

The epileptologist asked questions about Nora's medical history, and the EEG results came back: Nora was diagnosed with juvenile myoclonic epilepsy (JME) — a type of epilepsy Michele had never heard of. As the epileptologist prescribed a "rescue" medication and recommended Nora revisit the clinic in a month, Michele's mind spun with everything she didn't know about epilepsy.

"I am a (slightly) educated person who has some (minimal) knowledge of medical terminology, and I had no idea what my daughter's diagnosis was or what it meant," Michele says. "I was confused. I was exhausted. I could not comprehend information."

During that month, Nora experienced eye-rolling beyond what you would expect from a young teen, daily absence seizures, and tonic-clonic seizures. At their follow-up appointment, the epileptologist said there was a rare type of epilepsy that involved the eyes and eyelids, but Nora would need to stay in the epilepsy monitoring unit (EMU) for 24 hours to determine whether or not she had it.

Another month and a half passed before Nora's EMU stay, when the epileptologist handed down a new diagnosis. Nora did not have JME; she had Epilepsy with Eyelid Myoclonia (EEM), formerly known as Jeavons syndrome, a rare form of epilepsy that is notoriously difficult to treat.

"When [Nora's epileptologist] left the room, I looked at Nora and cried," Michele says. "I knew we could do this, but my heart ached for my child who would have to live it."

Three years on from her diagnosis, Nora has had many seizures, tried many medications that haven't worked or have made her seizures worse, and experienced all manner of devastating side effects, from immense fatigue to memory issues.

Now, as a more experienced parent of a child with epilepsy, Michele pushes new treatment options, reading peer-reviewed research articles and poking holes in the standard treatment protocol before agreeing to put Nora on a new medication. Nora's care team now expects and appreciates that involvement from her.

"I read every medication package insert before Nora is put on a drug, and I ask a dozen questions," Michele says.

Though Nora has received quality care since her diagnosis, EEM remains poorly understood, intensifying the challenges that all people with epilepsy know all too well.

MORE THAN 70%
OF PEOPLE WITH EPILEPSY WITH EYELID MYOCLONIA (EEM) ARE DIAGNOSED WITH ANOTHER EPILEPSY SYNDROME FIRST

"Epilepsy is hard. It is brutal. It is a relentless and ever-changing disorder," Michele says. "It often feels like it is one step ahead, and it always lurks in the background. You never know when or where it will strike."

Despite the many sleepless nights and what Michele describes as the gut-wrenching, helpless feeling of watching Nora suffer, she's learned to look for the silver lining.

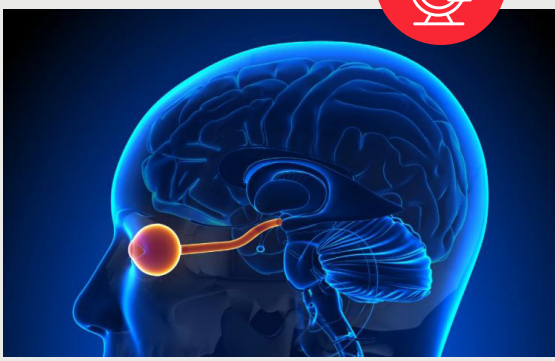
"I have found that the good always has a way of showing up," Michele says. "It shows up in the kindness of a nurse who says, 'Yay!' when Nora is doing well or an EEG tech who takes extra gentle care because getting EEG electrodes placed hurts."

It's that upward momentum that has transformed Michele from an overwhelmed, fearful parent into a relentless advocate for a cure.

"I cannot stop the seizures, I cannot control the side effects, I cannot protect her from epilepsy – but oh yeah, I can be a voice," Michele says. "I can share my story as a parent, I can do what I can to raise funds. I can advocate for her."

And yet, the worry and the sleepless nights persist.

"The fear is not entirely gone. I am not sure it ever will be," Michele says. " I still check on Nora every night because Sudden Unexpected Death in Epilepsy is too real. But the degree of fear has softened, which opens up more room for the good. We welcome the good."



TAKE A CLOSER LOOK: DRIVING RESEARCH INTO THE UNDER-RESEARCHED EPILEPSIES

CURE Epilepsy is committed to finding unique ways to fill research gaps and address the needs of all people living with epilepsy — especially people like Nora, whose under-researched diagnoses have left them with more questions than answers.

When Jon Mugar's daughter was diagnosed with EEM, he reached out to leading epilepsy experts around the world to further explore this misunderstood condition. From his daughter's original misdiagnosis of childhood absence epilepsy to a lack of information about symptoms online, Jon was frustrated that there was so little known and shared about this condition. He was determined to change that. Through Jon's unrelenting advocacy and the philanthropy of his family foundation, CURE Epilepsy established the EEM Initiative to further our collective knowledge of the condition (read more on p. 4) and spark new research.

With our **donor-accelerated research program**, we're also directing resources into other under-funded areas like epileptic spasms. Every project we invest in affirms CURE Epilepsy's commitment to improving our understanding of all forms of epilepsy so that no person is forgotten in our search for a cure.

UNCOVERING ANSWERS THROUGH THE EPILEPSY WITH EYELID MYOCLONIA (EEM) (FORMERLY KNOWN AS JEAVONS SYNDROME) INITIATIVE

As a convener of experts and an umbrella organization encompassing all types of epilepsy, CURE Epilepsy has a unique ability to focus needed attention and resources on under-researched epilepsies. With the Epilepsy with Eyelid Myoclonia (EEM) (formerly known as Jeavons syndrome) Initiative, we created a framework for engaging thought leaders across the field and catalyzing interest in a new area.

We first assembled a steering committee to perform a literature review into the state of EEM diagnosis and treatment. Then, we convened an international panel of 25 physicians and five patients and caregivers with lived experience. They used the modified Delphi method to systematically review expert opinions and evidence. The panel completed three rounds of surveys to gather knowledge and reach consensus where possible on diagnostic criteria and optimal treatment. The consensus represents the field's collective knowledge about EEM and the best ways to treat it and the resulting publications are already helping clinicians and patients make decisions about care.

SEVERAL AREAS OF CONSENSUS INCLUDED:

AN EEG IS A CRITICAL TOOL FOR DIAGNOSIS

EEM AFFECTS PREDOMINANTLY FEMALES, WITH AN AVERAGE ONSET AT 3 TO 12 YEARS OF AGE

EXPERTS RECOMMEND GENETIC TESTING IF THE PATIENT HAS A FAMILY HISTORY OF EPILEPSY, HAS AN INTELLECTUAL DISABILITY, OR THEIR SEIZURES ARE DRUG-RESISTANT

VALPROIC ACID SHOULD BE USED AS A FIRST-LINE TREATMENT, WITH TWO ALTERNATIVES FOR WOMEN OF CHILDBEARING AGE

While a consensus isn't a cure, it helps the research community home in on key points of understanding as well as research gaps. More effective diagnosis and treatment protocols will help move people toward seizure freedom.

INSIDE THE EEM INITIATIVE

Goals

- Decrease time to diagnosis
- Find consensus on and share most promising treatments
- Raise awareness across the epilepsy community

What Are the Main Symptoms of EEM?

- Eyelid myoclonia (brief jerks of the eyelids)
- Sensitivity to light
- Eye-closure induced by bright or blinking lights
- Absence or generalized tonic-clonic seizures

Why Is Diagnosis Often Delayed?

- Clinicians don't always recognize eyelid myoclonia as a type of seizure
- Parents may mistake EEM for a tic or other behavioral issue and take their child to a psychologist instead of a neurologist

Jeavons Syndrome Awareness Day
November 13th

Utilizing the Same Method Across Different Research Areas

Many people with epilepsy experience brief and uncontrollable arm, leg, and head extensions or spasms that last seconds or minutes and leave people with epilepsy and loved ones in constant fear of their next spasm. Driven by the Cunneen family, CURE Epilepsy has engaged a committee of experts to once again use a modified Delphi process to review extensive literature on epileptic spasms to discern the best treatment options. The initiative aims to raise awareness around epileptic spasms and drive more research into the field.

Helping People With Other Underexplored Epilepsies

CURE Epilepsy is spearheading research and scientific advances to help people living with understudied epilepsies like EEM.

Keeping Patients at the Center of Diagnosis and Treatment

CURE Epilepsy conducts a rigorous grant review process engaging both scientific and lived experience reviewers who either live with epilepsy or love someone who does. Lived experience reviewers look for projects that would make the biggest difference in the lives of people with epilepsy.

TAKING FLIGHT AWARD*

Reducing the Need for Invasive Monitoring

Rachel June Smith, PhD
University of Alabama at Birmingham

Clinicians typically rely on invasive, expensive, and time-consuming methods to identify hyperexcitability in the brain. After a lived experience reviewer saw the potential for new monitoring methods to reduce the time patients spend in the epilepsy monitoring unit (EMU), CURE Epilepsy awarded Dr. Rachel June Smith a *Taking Flight* Award, catalyzing her exploration into using datasets from patients who underwent invasive and non-invasive monitoring to build computational models of the brain. Her team will test whether these models can be used to identify hyperexcitable brain regions, potentially reducing the need for invasive monitoring in the future.

* For more information on the CURE Epilepsy *Taking Flight* Award, see p. 8

> "Through the work with CURE Epilepsy, we were able to put together consensus recommendations with international experts for the diagnosis and treatment of EEM. This work has increased the knowledge and recognition of this disorder and has had a positive impact on moving the field forward."
>
> KELSEY M. SMITH, MD
> ASSISTANT PROFESSOR
> DEPARTMENT OF NEUROLOGY,
> MAYO CLINIC, ROCHESTER, MN

SHARING PATIENT HEALTH DATA TO ACCELERATE RESEARCH

RARE X
A Research Program of Global Genes

CURE Epilepsy partnered with Rare-X to accelerate the research of clinicians and investigators worldwide through the EEM Data Collection Program. Add your data at **rare-x.org/jeavons-syndrome.**

MAKE A DIFFERENCE

Help CURE Epilepsy advance our understanding of underresearched conditions like EEM.

FOR THE 1
FACING A RARE CASE OF LATE-ONSET INFANTILE SPASMS

Charlotte Kostolansky
AGE 4, EXETER, NEW HAMPSHIRE

Charlotte was an energetic, joyful, and typically developing toddler when the Kostolansky family's world was turned upside down.

"She was walking and talking at the time," says doting first-time mom Kate Kostolansky.

But in August 2022, right before Charlotte — who her dad, Brett, lovingly called Char Bear — turned two, Kate noticed a change. Charlotte started displaying strange, subtle movements.

Kate says, "She started to develop spasms, very similar to Moro reflex, the thing that happens in babies, often called a startle reflex."

As someone working in healthcare administration herself, Kate knew Moro reflex was nothing to fear. But, as any concerned parent would, she continued to observe her daughter closely.

"She would be doing normal things, and it would just happen," Kate says. "At her age, we knew it was not right."

APPROXIMATELY 90%
OF CASES OF INFANTILE SPASMS ARE DIAGNOSED WITHIN THE FIRST YEAR OF LIFE

Feeling instinctually that Charlotte's increasingly frequent arm-raising and head bobs were atypical, she started Googling the symptoms and recording the movements. Though Charlotte's pediatricians believed she was still developing normally, Kate was already a fierce advocate for her daughter; she requested a referral to a neurologist.

When the neurologist watched videos of Charlotte's movements, one thing came to mind: infantile spasms (IS), a rare and particularly severe form of epilepsy. After an EEG confirmed the diagnosis with the presence of a **hypsarrhythmia**, the neurologist referred them to Boston Children's Hospital and urged them to go quickly. But Kate didn't just have Charlotte's diagnosis to contend with; she was also far along in a pregnancy with her second child.

"I asked if I could wait until after my due date (September 12) and he said, 'No, go right away. This constitues a medical emergency,'" Kate says. "We went in August."

That referral changed their lives in ways they couldn't have imagined.

"In a whirlwind 24 hours, we went from casually exploring a seemingly benign body movement to being admitted to an inpatient neurology service unit," Kate says.

Brett stayed with Charlotte at the hospital while Kate went to her parents' house nearby. All she could think about was her daughter's diagnosis.

"I spent the entire night reading everything I possibly could," she says. "Reading about the unpredictable future and the possible coinciding developmental impact was terrifying."

Equally startling, according to Kate, was the realization that Charlotte's delayed language development may have pointed to IS all along.

"It feels like you're overreacting," she says. "You feel like you sound crazy when you bring it up as a concern."

Charlotte underwent further testing in Boston Children's EMU, which revealed her IS was caused by focal cortical dysplasia, which means the cells in the top of her brain developed abnormally.

For the rest of 2022 and into 2023, steroids failed to reduce Charlotte's seizures. Having initially been hesitant to begin certain medications and discuss surgery, we quickly became eager to explore those options.

"If this failed, we might have been looking at brain surgery," Kate says.

EPILEPSY 101*

HYPSARRHYTHMIA:

ABNORMAL INTERICTAL HIGH AMPLITUDE WAVES AND A BACKGROUND OF IRREGULAR SPIKES

*All Epilepsy 101 definitions are sourced from the National Library of Medicine website at www.nlm.nih.gov

Though the steroids she tried didn't work, Vigabatrin — an anti-seizure medication — did. Charlotte has been seizure free since early 2023.

"Boston Children's did such a great job of balancing the facts of her condition with weighing what was best for Charlotte," Kate says.

Charlotte is now weaning off medication, and Kate and Brett can see their sweet and joyful Char Bear coming back to them.

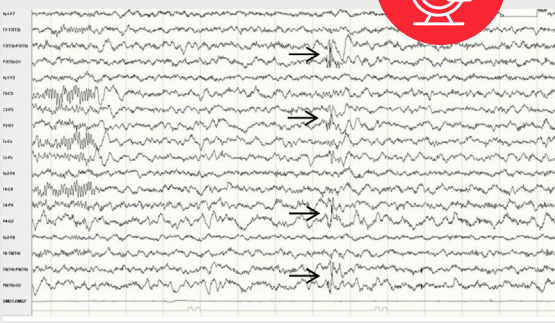
"Her development completely took off," Kate says. "With her spasms gone, we saw such a difference in her language and vocabulary."

As grateful as Kate and Brett are, they know many kids living with infantile spasms don't experience the positive outcome Charlotte did.

Kate wrote a children's book, "Char Bear Keeps Dancing," to raise awareness about IS since there was little information available.

Kate says. "I wanted to capture what we've learned and share it with others. I want them to know there is hope."

CURE Epilepsy continues to advance important research on IS like that of Dr. John Swann (see p. 9) so more children can live free from seizures and side effects.



A sample EEG showing a hypsarrhythmia

TAKE A CLOSER LOOK: IDENTIFYING HYPSARRHYTHMIA

A diagnosis of infantile spasms is usually (however, not always) accompanied by the identification of a hypsarrhythmia on the electroencephalogram (EEG) test. This abnormal pattern of brain activity is characterized by:

- High-amplitude waves and irregular spikes
- Slow waves mixed with sharp and spike waves
- Random spikes that vary in time and location
- A lack of an organized background

Hypsarrhythmia usually appears in early infancy and typically resolves by the age of two. It's caused by a diffuse insult to the developing brain, which can be due to a number of factors, including:

- Acquired brain injury, such as meningitis or a stroke
- Genetic mutation
- Brain development problems
- Medical conditions, such as Down syndrome

Medications that can help manage hypsarrhythmia include: anti-seizure medications, hormone-based monotherapy (ACTH or prednisolone) or vigabatrin.

SETTING THE STAGE FOR TOMORROW'S DISCOVERIES

Just as research on basic mechanisms lays the foundation for further breakthroughs, our *Taking Flight* Awards have launched careers and uncovered new priorities in epilepsy research. *Taking Flight* Awards are designed for early-career researchers working to develop a research focus independent of their mentors—with many grantees going on to pursue bigger grants and research projects.

TAKING FLIGHT AWARD

This newly expanded one-and-a-half year, $125,000 award supports the next generation of researchers.

Exploring the Causes of Seizures in Focal Cortical Dysplasia

Cathryn Cadwell, MD, PhD
University of California, San Francisco

BASIC MECHANISM STUDIED: CHANGES IN THE CEREBRAL CORTEX

Patients with focal epilepsy have seizures that predominantly affect one half of the brain. Those seizures most commonly arise when the outermost layer of the brain develops abnormally, leading to focal cortical dysplasia (FCD). Dr. Cadwell will study single cells from surgically resected brain tissue from patients to better understand the molecular, anatomical, and electrophysiological changes in cells that lead to seizures in FCD — potentially finding new treatments for patients who don't respond to medication or can't undergo surgery.

Tracing the Link Between the Blood-Brain Barrier and Drug Resistance

Chris Greene, PhD
Trinity College Dublin, Ireland

BASIC MECHANISM STUDIED: THE ROLE OF THE BLOOD-BRAIN BARRIER

The blood–brain barrier (BBB) is comprised of a semipermeable layer of cells in the blood vessels of the brain that orchestrates exchanges between the blood and the brain to maintain optimal neural function. Changes in the BBB have been observed in people with drug-resistant epilepsy, but the link between the two remains unclear. By studying a mouse model of drug-resistant epilepsy, Dr. Greene will seek to identify BBB changes associated with drug resistance and test the therapeutic potential of restoring the BBB to treat drug-resistant epilepsy.

Using Fly Models To Study Sleep Disruptions and Seizures

Vishnu Cuddapah, MD, PhD
Baylor College of Medicine, Houston, TX

BASIC MECHANISM STUDIED: THE RELATIONSHIP BETWEEN SLEEP DISRUPTION AND SEIZURE SEVERITY

It's little understood why sleep disruption increases the likelihood and severity of seizures. Dr. Cuddapah will use a fruit fly model—a model where sleep systems can be manipulated easily—to identify mechanisms that tie sleep disruption to more severe seizures and determine if deactivating brain regions that cause sleepiness decreases seizure risk.

RARE EPILEPSY PARTNERSHIP AWARD*

FUNDED IN PARTNERSHIP WITH TESS RESEARCH FOUNDATION

Connecting Metabolism, Brain Cell Communication, and Seizures

Naomi Dirckx, PhD
Washington University School of Medicine in St. Louis

BASIC MECHANISM STUDIED:
THE EFFECT OF NUTRIENT TRANSPORT ON SEIZURES

Genetic changes in the solute carrier family 13 member 5 (SLC13A5) gene, a protein that transports citrate into cells, can cause seizure development within a day of being born and developmental delays. Dr. Dirckx will study whether SLC13A5 mutations impair how nutrients move between neuronal and supportive brain cells, leading to defective energy production and causing seizures.

*For more information on the *Rare Epilepsy Partnership* Award, see p. 13

Understanding the Causes of Epilepsy

The more we know about how the causes of epilepsy originate, the better we can treat and, eventually, cure them.

In 2013, CURE Epilepsy launched the Infantile Spasms (IS) Initiative with $4 million in funding. We employed a multi-disciplinary, multi-location team consisting of eight research teams led by epilepsy experts from around the U.S. to study the basic mechanisms of IS, search for biomarkers and novel drug targets, and develop better treatments.

Over the past decade, that team has made many breakthroughs and documented findings in 19 publications.

From Bench to Bedside: A Novel Treatment for Infantile Spasms

With funding from CURE Epilepsy, John Swann, PhD of Baylor College of Medicine and his team discovered that treatment with a derivative of the insulin-like growth factor 1 (IGF-1) reduced spasms and irregular wave patterns on the EEG in an animal model of IS.

When the team combined IGF-1 with vigabatrin therapy, an FDA-approved IS treatment, it reduced the dose of vigabatrin required to reduce seizure frequency — and reduced the risk of serious side effects along with it. The Swann lab patented this combination treatment and secured two National Institutes of Health (NIH) grants because of it.

In a subsequent study, Dr. Swann's team found that IGF-1 levels were lower in brain tissue both in a rat model of IS and from infants with IS. The data also indicated that the reduced IGF-1 in the rat model affected the biological pathways critical for neurological development.

The epilepsy community has only continued to reap the rewards of Dr. Swann's work. He's since studied optimal methods for administering IGF-1, discovering that a modified form of IGF-1 could better cross the blood-brain barrier, making it a more effective therapy. When administered to the rats, the modified (1-3) IGF-1 eliminated spasms and hypsarrhythmia, offering hope that children with IS may one day have a treatment from the moment they're diagnosed.

INSIDE THE INFANTILE SPASMS INITIATIVE

$4 MILLION

8 RESEARCH TEAMS

> "As an epilepsy researcher who spends most of my day in the lab, it's been a dream come true to see my years of research in infantile spasms result in a potential life-changing therapy for these children and their families."
>
> JOHN SWANN, PHD

MAKE A DIFFERENCE

Your gift makes it possible for investigators like Dr. Swann to forge ahead toward the cure.

FOR THE 1
WHO DOESN'T KNOW WHY THEY HAVE EPILEPSY

Maggie Loesch

AGE 26, PALATINE, ILLINOIS

For years, Maggie's family and doctors believed she was neurodivergent, explaining gaps in her focus and attention as the result of a relatively common condition.

"Before my epilepsy diagnosis, my family and doctors thought I had attention-deficit/hyperactivity disorder (ADHD)," Maggie says.

Before long, those gaps — which she later learned were absence seizures — became critical.

"I had a tonic-clonic seizure that lasted 20 minutes," Maggie says.

Her parents rushed her to the hospital, where she underwent a battery of bloodwork, electroencephalograms (EEG), and magnetic resonance imaging (MRI). At just eight years old, Maggie was diagnosed with epilepsy.

Though she was relieved to be diagnosed, she was also terrified — of the seizures, the treatments, and the many ways epilepsy might affect her.

50% OF PEOPLE WITH EPILEPSY DON'T KNOW THE CAUSE

Maggie says, "It became clear to my family and me that I was going to be living with epilepsy for the rest of my life."

Once she entered middle school, the reality set in: epilepsy had a hold on virtually every area of her life because of the many ways it changes the brain.

"A person with epilepsy's brain works much harder than a typical brain," Maggie says. "Simple tasks such as being with friends can be very challenging for me."

Academics also proved difficult, no matter how much Maggie wanted to succeed. Her seizures weren't yet under control, leaving her at their mercy.

"I basically missed a year of learning," Maggie says.

But with the support of her family and friends, she not only made it to college but graduated in four years — something she never thought she'd be able to do.

"I learned that having epilepsy has its ways of holding me back, but if I want to succeed and have fun, I have to fight back," Maggie says.

Fourteen years after her diagnosis, she finally feels empowered. Along the way, she also found answers.

"I've learned different ways to cope and manage this challenge," Maggie says. "Through medications, diet, and genetic testing, I have found what is right for me."

Though trial-and-error and medications both helped Maggie improve her quality of life, it's understanding the genetics behind her epilepsy that's given her hope.

"I have a history of seizures on one side of my family, so I was always curious to know," Maggie says. "Maybe [genetics] is the cause of my epilepsy, and maybe there are different treatment options."

She undertook two different genetic panels to answer the question all people with epilepsy have: why me?

"The first one focused on epilepsy genes only," Maggie says. "The results were negative."

It wasn't until the second, more extensive panel that Maggie got her answer. Even then, the results were anything but what she expected.

"I have a duplication of the HCN2 gene," Maggie says. "The gene has been associated with febrile seizures and generalized epilepsy, which are two things I experience."

But Maggie also knows that she's only scratched the surface of what her genetic code holds.

"It's actually a **variant of uncertain significance**," Maggie says. "There hadn't been any reported patients with duplicates of the HCN2 gene until I did my testing."

EPILEPSY 101

A VARIANT OF UNCERTAIN SIGNIFICANCE (VUS):
A CHANGE IN A GENE'S DNA SEQUENCE THAT HAS AN UNKNOWN EFFECT ON A PERSON'S HEALTH

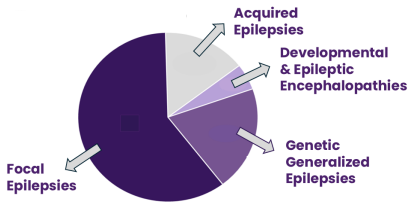
Though she doesn't yet know what her specific genetic variant means or whether it holds the clues to a cure, she believes she's one step closer.

"As of now, science hasn't caught up," Maggie says. "I hope that, one day, it will."

Learn More About Genetic Diagnoses

Watch Maggie Loesch talk more about her genetic diagnosis in our webinar, "Genetic Testing in Epilepsy: Understanding Results and Their Impact on Care" with Drs. Gemma Carvill and Elizabeth Gerard. Read more about their research on p. 13 and visit **CUREepilepsy.org/webinars** to view all of our webinars.

MOST EPILEPSIES HAVE A KNOWN (OR SUSPECTED) GENETIC CAUSE



TAKE A CLOSER LOOK: UNRAVELING THE GENETICS OF EPILEPSY

Epilepsy genetics is a growing field, and advancements are helping clinicians understand epilepsy, tailor specific treatments, and offer more personalized care for those living with this complicated disease.

Epilepsy can be classified into four categories based on its origin and characteristics, each with unique genetic aspects:

1. **Generalized epilepsy** involves seizures that affect both sides of the brain from the onset. Specific genetic mutations have been linked to generalized epilepsy including GABRG2 and SCN1A.
2. **Focal epilepsy** (or partial epilepsy) involves seizures originating in one specific area of the brain. Genetic contributions include DEPDC5 and TSC1 and TSC2.
3. **Developmental and epileptic encephalopathies (DEEs)** are severe epilepsy syndromes that begin in early life and are associated with significant developmental impairments. Genetic factors include SCN2A, CDKL5, and STXBP1.
4. **Acquired epilepsy** develops due to an external cause or injury rather than genetic factors alone. However, genetic predispositions can influence the susceptibility to or severity of acquired epilepsy.

REVEALING THE GENES THAT CAUSE EPILEPSY

As technology has advanced over the past 26 years, so have CURE Epilepsy's efforts to uncover the genes that cause epilepsy — and progress on targeted treatments for those causes. From the discovery of epilepsy-associated genes to our landmark Epilepsy Genetics Initiative (EGI), we continue to push for answers to help people understand and address the underlying causes of their conditions.

Epilepsy Genetics Initiative

CURE Epilepsy created the Epilepsy Genetics Initiative (EGI) in 2014 to establish a centralized database holding the unique genetic blueprint of each contributing individual's particular form of epilepsy. EGI collected genetic data from individuals worldwide for investigators to analyze every six months, underscoring the importance of periodic genetic reanalysis and the value of global data sharing.

1,108
PARTICIPATING PATIENTS AND FAMILY MEMBERS

34 PATIENTS
RECEIVED NEW OR MODIFIED GENETIC DIAGNOSES

CURE Epilepsy Discovery: Funding Research to Investigate Mechanisms of Genetic Epilepsies

Research is progressive; a breakthrough in one study fuels the thesis of another. CURE Epilepsy seeks to support each progression and the emerging investigators behind them.

Dr. Heather Mefford, at St. Jude Children's Hospital, used funding from a 2019 *CURE Epilepsy* Award to explore the causes of treatment-resistant developmental and epileptic encephalopathies (DEE), early-onset epilepsy disorders associated with developmental delay and seizures. Only half of people with DEE have an identifiable genetic cause, but knowing the genetic cause can lead to a better prognosis.

Dr. Mefford set out to identify a non-genetic cause for DEE in individuals without a diagnosis by looking at abnormal methylation, a type of chemical modification in the DNA structure. Her team analyzed a large dataset and found novel methylation changes. Funded by a 2024 *Rare Epilepsy Partnership* Award, Dr. Mefford and her team will now pursue further research that could allow healthcare providers to identify methylation patterns and, in turn, diagnose individuals with DEE.

3 GENERATIONS OF INVESTIGATORS

CURE Epilepsy is committed to supporting generations of researchers. Dr. Mefford mentored Dr. Gemma Carvill, who investigated the genetic causes of epileptic encephalopathy. Dr. Carvill, in turn, mentored Dr. Jeffrey Calhoun, who is researching genetic variants linked to epilepsy risk.

Dr. Heather Mefford
2019 *CURE Epilepsy* Award
2024 *Rare Epilepsy Partnership* Award

Dr. Gemma Carvill
2015 *Taking Flight* Award
2023 *CURE Epilepsy* Award

Dr. Jeffrey Calhoun
2022 *Taking Flight* Award

The Future of Epilepsy Genetics Research

As researchers have identified new genes implicated in epilepsy, CURE Epilepsy has broadened our support for investigators working to unravel the secrets of epilepsy genetics — especially the rare genetic epilepsies.

CURE EPILEPSY AWARD

This two-year, $250,000 award accelerates research that could eventually improve how we diagnose and treat epilepsy.

FUNDED BY
THE JOSEPH GOMOLL FOUNDATION

Novel Diagnostics for Focal Epilepsies

Gemma Carvill, PhD
Northwestern University, Chicago, IL

Collaborators: Elizabeth Gerard, MD (Northwestern University), Alica Goldman, MD, PhD (Baylor College of Medicine), Nuri Ince, PhD (Mayo Clinic)

Most mutations that cause focal cortical dysplasia (FCD) occur within the brain tissue, making it difficult to obtain a genetic diagnosis without surgery. Dr. Carvill's team will study whether DNA from cells attached to depth electrodes can be used to obtain a genetic diagnosis.

RARE EPILEPSY PARTNERSHIP AWARD

This one-year, $100,00 award unites CURE Epilepsy with rare epilepsy advocacy organizations in a partnership to drive research into rare epilepsies.

FUNDED IN PARTNERSHIP WITH CCC COALITION TO CURE CHD2

Investigating Episignatures in CHD2-Related Disorders

Heather Mefford, MD, PhD
St. Jude Children's Hospital, Memphis, TN

People with CHD2-related neurodevelopmental disorders share certain patterns in their DNA, called episignatures, that are used in confirming a CHD2 diagnosis. Dr. Mefford and her collaborator, Dr. Carvill, will explore these episignatures in different cell types to understand how these patterns relate to the problems seen in CHD2-related disorders.

FUNDED IN PARTNERSHIP WITH SLC6A1 Connect

Using Gene Replacement Therapy To Treat SLC6A1-Related Disorders

Hing Lee, PhD
Boston Children's Hospital

SLC6A1 gene mutations interfere with neuronal communication and cause rare pediatric conditions characterized by neurodevelopmental delays, autism, and epilepsy. Dr. Lee and his team will test whether replacing the mutated SLC6A1 gene with a normal copy using a gene therapy approach will reverse symptoms in SLC6A1-lacking mice to understand if gene-replacement therapy is safe, effective, and ready for clinical trials.

FUNDED IN PARTNERSHIP WITH Ring14 USA

Understanding the Genetic Causes of Epilepsy in Ring14 Syndrome

Michael Talkowski, PhD
Harvard University, Cambridge, MA

The cause of epilepsy in Ring14 Syndrome is unknown. Dr. Talkowski and his team propose creating a map of changes in structural genetics, DNA methylation patterns (changes that can turn genes on or off), and gene expression to identify genes, gene networks, and other features that are likely causative for severe seizures and could be used as targets for future therapies.

FOR THE 1
WHOSE DIAGNOSIS TOOK OVER A DECADE

Jack Somers
AGE 39, SANTA MONICA, CALIFORNIA

At 25 years old, Jack Somers was who many people aspire to be: active, well-traveled, and social. Commissioned as a Marine Corps Captain in 2007, Jack spent the following years training in California, deploying on a ship, and eventually putting his feet on the soil of seven different countries, including Afghanistan.

But the day his life changed wasn't in Afghanistan or even in California — it was a Turkey Trot race in his hometown near Chicago. He passed the finish line, and his friends excitedly congratulated him and asked questions about his deployment. Jack didn't know he knew them.

"I had no idea what they were talking about. I really didn't know where I was, what I was doing. I didn't know who the people were that were asking me these questions," Jack says.

Jack knows now what he didn't know then: That lapse was his first seizure. But it wouldn't be his last.

"My next seizure was actually a drop seizure, which was the first of many that I ended up having," Jack says. "I was cooking and just kind of dropped like a sack of potatoes."

After the drop seizures came absence seizures, with one episode quickly turning into a revolving door of seizures he didn't understand and couldn't control.

"All of a sudden, it's just this kind of wave — at least, I experienced this big wave — of more and more of them," he says. "And they started getting more severe, and they started changing in form all the way to two **tonic-clonic seizures**."

Jack medically retired from his beloved career in the Marine Corps because of those seizures, not yet knowing his military service is what caused them. It would take more than a decade from his first seizure to fully understand the ways his brain had permanently changed.

"After my second grand mal seizure, I was diagnosed with generalized seizure disorder, and I thought that was totally different than epilepsy," Jack says.

Not knowing he had epilepsy — or that generalized seizure disorder was epilepsy — put Jack on a painful, decade-long path to his true diagnosis, packed with 40 to 50 different treatment plans, 10 to 12 medications, and excruciating side effects. He also felt more isolated than ever, separated from the Marine Corps, struggling to connect, and still wondering how to manage his seizures.

EPILEPSY 101

TONIC-CLONIC SEIZURE:

FORMERLY CALLED GRAND MAL SEIZURE; A TYPE OF EPILEPTIC SEIZURE THAT CAUSES VIOLENT MUSCLE CONTRACTIONS AND LOSS OF CONSCIOUSNESS

"You can't drive…having that independence taken away is tough to handle, especially when you don't really want to tell the whole world and all your friends that you have a seizure disorder," he says.

Despite his efforts to separate the confident man his friends and family knew him to be from the Jack who needed daily help due to his seizures, they eventually became too much to hide.

"At times, I was having three, four, or five drop seizures where I smashed my head on a sidewalk or a concrete road or on a curb and had to go to the emergency room, get stitches, and have a concussion," Jack says. "People could see it."

Fast forward to 2022, and Jack was lying on a hospital bed, electrodes and wires surrounding his head. His doctor offhandedly said, "We're going to find out what kind of epilepsy you have."

"I just stopped and said, 'Do I have epilepsy?' and [the doctors] said, 'Well, yes, you've had epilepsy for a long time,'" he says. "I just couldn't believe it. I was never told that I had epilepsy."

More specifically, the doctor diagnosed him with post-traumatic epilepsy (PTE), which develops after a traumatic brain injury (TBI). He can still recall the day when his platoon approached a grenade blast and fought bravely through the explosions.

EPILEPSY CAUSED BY A TBI COMPRISES

5% OF ALL EPILEPSIES

"A month and a half after that event, I had my first seizure," Jack says. "[My doctor] kind of looked at me almost like, 'Are you serious? Do you not see the chronological order here?'"

Amid the fear and uncertainty of this new diagnosis, another feeling emerged: relief.

"I felt like for the first time I understood what was going on," he says. "They gave me a whole community, a whole team with a case manager and a coordinator."

Beyond a cure, the one thing Jack wants for all people with epilepsy is the same answers it took him 12 long years to get. He recommends anyone with a TBI reach out for help, whether to CURE Epilepsy, a local support group, or their healthcare provider.

His final piece of advice: Just say "epilepsy." "If you just use generalized seizure disorder…you've got a blindfold on," Jack says. "Use 'epilepsy' and you can take the blindfold off and start to see what you're fighting."

TAKE A CLOSER LOOK: POST-TRAUMATIC EPILEPSY

Currently, there is no known treatment for PTE following TBI. We first need strategies to understand who is at risk for developing PTE and how the brain changes before PTE develops — breakthroughs that could allow us to work toward preventing PTE in patients with TBI.

Through conversations across the epilepsy communitiy, CURE Epilepsy identified gaps in PTE research and, since 2007, has directed nearly **$18 million across 63 research projects** related to TBI and PTE.

Despite the many service members diagnosed with PTE as a consequence of TBIs, the Department of Defense (DOD) Congressionally Directed Medical Research Program (CDMRP) did not have a focus area on this important research area. In 2015, CURE Epilepsy Founder Susan Axelrod worked with members of Congress to establish the Epilepsy Research Program (ERP) within the CDMRP to fill this void. CURE Epilepsy continues to have a seat on the ERP's Programmatic Review Panel, assisting in the development of strategy and funding decisions.

As a result of the significant funding and research efforts of CURE Epilepsy in PTE research, we hosted the first ever International Conference on Post-Traumatic Epilepsy in Milan, Italy this past summer. Read more on p. 16 and 17.

OPENING THE DOOR TO PROGRESS IN POST-TRAUMATIC EPILEPSY (PTE) RESEARCH

PTE can be challenging to study in a laboratory or clinical environment. It can take days or months for the brain to start generating seizures, and while that process — called epileptogenesis — is a unique opportunity for intervention, we currently don't know enough about it to study it effectively.

CURE Epilepsy knew that better understanding how the brain changes before PTE develops would open doors to treating and preventing it. That work also needed to be collaborative, leveraging efforts across the scientific community to accelerate the pace of discoveries.

Team science, which unites researchers of different backgrounds over a common cause, held the key to progress. We pioneered our team science approach for the Infantile Spasms Initiative, then deployed it again to propel PTE research forward.

Breaking Ground on the PTE Initiative

In 2015, CURE Epilepsy launched the PTE Initiative using a $10 million grant from the Department of Defense. Research teams from around the world came together to study PTE from all angles in an effort to overcome research challenges and advance breakthroughs.

Every few months, teams gathered to share their learnings, accelerating the pace of progress across the participating labs. Research teams using similar models continually compared and contrasted their methods and data and sparked new opportunities for investigation.

CURE Epilepsy Discovery: Providing a Foundation for the Development of Novel Therapies

The PTE Initiative has led to many scientific successes to date, all of which have enhanced what we know about PTE and moved us closer to identifying its biomarkers and risk factors.

Uncovering Why Traumatic Brain Injury (TBI) Leads to PTE

Why do some people develop PTE after TBI while others don't? During his tenure at Virginia Tech, Dr. Harald Sontheimer hypothesized that a better animal model would help researchers understand the specific post-TBI brain changes that lead to PTE. Now led by Dr. Michelle Olsen at Virginia Tech, the team worked to develop a newer mouse model of PTE alongside a more established model. They classified how brain changes occur and which changes lead to the development of PTE, which laid the groundwork for identifying new targets for novel therapies.

INSIDE THE PTE INITIATIVE:

Launched in 2015

The PTE Initiative resulted in:

- Over $2.5 million in subsequent funding to further PTE research
- The development and characterization of several different animal models of PTE
- The identification of several potential risk factors and biomarkers for PTE that could reveal who will develop PTE after TBI

Leading the Way to PTE Biomarkers

Biomarkers may one day help us predict who will develop PTE after TBI. To advance that work, Dr. Pavel Klein at the Mid-Atlantic Epilepsy and Sleep Center worked with 10 clinical research teams in the U.S. and Europe to characterize who would be considered high-risk for PTE following TBI. The teams collected blood samples and worked with fellow PTE Investigator Dr. Kevin Wang from Morehouse School of Medicine and others to identify changes in specific biological pathways that lead to PTE.

A New Chapter in PTE Research

Building off the astrocyte findings in the original PTE Initiative, the PTE Astrocyte Biomarker Initiative (PABI) will track how astrocytes change in the brain after TBI and before PTE onset. A collaborative effort across multiple scientific teams and funded by the U.S. Department of Defense's Congressionally-Directed Medical Research Program's (CDMRP) Epilepsy Research Program, PABI will look for a "signature" that distinguishes those who develop PTE from those who do not. PABI is currently studying signs from astrocytes in mouse models and archived blood samples from people post-TBI.

EPILEPSY 101

BIOMARKERS:
A CHARACTERISTIC THAT IS OBJECTIVELY MEASURED AND EVALUATED TO INDICATE NORMAL BIOLOGICAL PROCESSES, DISEASE, OR A RESPONSE TO AN INTERVENTION

ASTROCYTES:
A SUBTYPE OF GLIAL CELLS THAT MAKE UP THE MAJORITY OF CELLS IN THE HUMAN CENTRAL NERVOUS SYSTEM AND PERFORM METABOLIC, STRUCTURAL, HOMEOSTATIC, AND NEUROPROTECTIVE TASKS

Building Community To Take on PTE

In May, CURE Epilepsy partnered with the Mario Negri Institute for Pharmacological Research to host the International Conference on Post-Traumatic Epilepsy (IC-PTE) in Milan, Italy. The event brought together a diverse community of people with epilepsy—Jack Somers among them—and researchers from around the world to discuss scientific advances, explore challenges, and drive the creation of promising new treatments and preventative therapies.





70+
ATTENDEES

4
EARLY CAREER AWARD WINNERS

20+
POSTERS

Financial support for the IC-PTE came from: The National Institute of Neurological Disorders and Stroke (NINDS), The American Epilepsy Society (AES), The International League Against Epilepsy (ILAE), Epilepsy Foundation, Corticale, and Eisai

FOR THE 1
MISSING MILESTONES

Bodie Lance

AGE 12, HENRICO, VIRGINIA

"The first few months [with Bodie] were joyful," Melissa Lance, Bodie's mom, says, "and probably the only time we were a 'normal' family after his birth."

At six months, Bodie developed episodes of staring, hand clenching, and shaking. At eight months and with an electroencephalogram (EEG) and magnetic resonance imaging (MRI) behind him, Bodie awaited a follow-up with a neurologist.

"Five weeks before the appointment, he had a really bad [episode]. His lips were blue and he had been in it for seven minutes when I called 911," Melissa says.

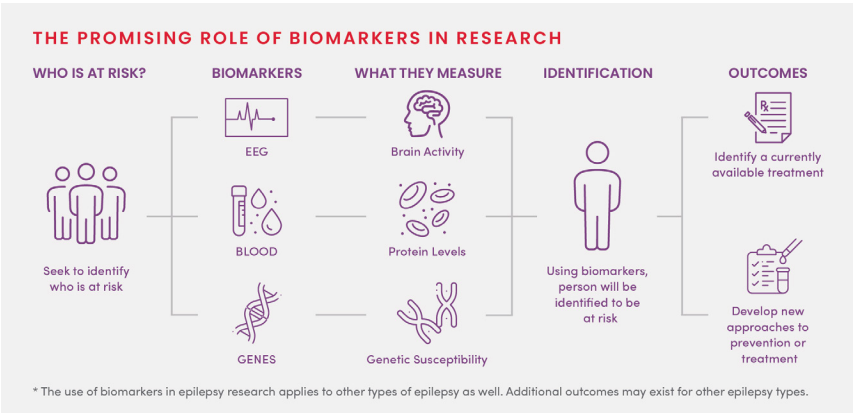
After countless ER visits and another EEG, Bodie's family had an answer: focal epilepsy. They struggled to find an effective treatment, and at age three, he took a turn for the worse. Bodie suffered a 20-minute tonic-clonic seizure.

"After that seizure, he was different," Melissa says. "He lost most of his words and regressed back to diapers. He never recovered those things."

Though cannabidiol (CBD) decreased his seizure duration and vagus nerve stimulation (VNS) therapy helped with the frequency, he's continued to miss milestones and suffered hundreds of seizures. Now, at age 11, Bodie doesn't have complete seizure control. Melissa hopes that one day he will.

"I desperately want a cure. For my son and everyone out there like him," Melissa says.

Identifying Biomarkers as a Future Focus for Epilepsy Research



A biomarker is a biological signal — a molecule in the blood, bodily fluids, or other tissue — that indicates a process, condition, or disease is underway in the body. A biomarker can indicate that epilepsy or a related condition may develop.

The CURE Epilepsy research team and scientific thought leaders have identified biomarkers as a research focus so that, one day, no one has to suffer through seizures or live in fear of Sudden Unexpected Death in Epilepsy (SUDEP).

Biomarker Research in Action

CURE Epilepsy's funding is fueling the work of researchers who are using different types of biomarkers: (1) to help predict and potentially prevent a poorly understood epilepsy type and (2) to develop SUDEP risk prediction tools for those who are at risk.

RARE EPILEPSY PARTNERSHIP AWARD

Exploring Pathways Resulting in Drug-Resistant Epilepsy for Patients With New-Onset Refractory Status Epilepticus (NORSE)

Vincent Navarro, MD, PhD
Sorbonne University

FUNDED IN PARTNERSHIP WITH THE NORSE INSTITUTE

NORSE is a very serious and poorly understood type of epilepsy defined by prolonged seizures without a clear cause, leading to long-term neurological and cognitive disabilities, including drug-resistant epilepsy. With funding from a *Rare Epilepsy Partnership* Award, Dr. Navarro and his team will explore whether there are clinical signs, brain imaging markers, or certain molecules in the blood and cerebrospinal fluid that can help predict who might develop epilepsy after NORSE, which could help in making treatment choices to prevent or delay it. The team also seeks to understand the role of persistent changes in the immune system that may lead to post-NORSE epilepsy.

CURE EPILEPSY AWARD

Comparing Living People With Epilepsy to Those Who Succumbed to SUDEP

Sanjay Sisodiya, PhD, FRCP
University College London

Dr. Sisodiya's team proposes that the summation of multiple subtle changes in an individual's genetic code influences their risk of SUDEP. Through a *CURE Epilepsy* Award, he and his team will compare genetic information from people who succumbed to SUDEP with that from a matched group of living people with epilepsy. If successful, the team will develop SUDEP risk prediction tools using genetic biomarkers.

Standardizing SUDEP Data Collection

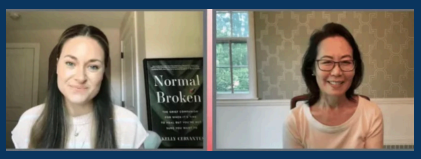
As Dr. Sisodiya's research above aims to use genetic data to develop SUDEP risk prediction tools, advancing our understanding of SUDEP depends on data. CURE Epilepsy launched the SUDEP Data Standardization Project in 2022 to standardize how researchers collect and report on SUDEP data so that all preclinical researchers can characterize SUDEP animal models in the same way.

Using the same data language helps researchers share data and enables greater translation to human studies. Designed for our community, the tools will eventually become public for anyone investigating SUDEP.

DEEPENING OUR EXPLORATION OF RARE EPILEPSIES

CURE Epilepsy is proud to announce a strategic partnership with the NORSE Institute. CURE Epilepsy will serve as the fiscal home for the NORSE Institute, allowing them to receive grants and other gifts restricted to nonprofits. By funding research dedicated to NORSE—like Dr. Navarro's—and through this new partnership, CURE Epilepsy is further broadening its impact in the rare epilepsy space.

NORSE INSTITUTE



LEARN MORE ABOUT NORSE

Nora Wong founded the NORSE Institute to raise awareness and fund research into this devastating form of epilepsy. Listen in to her Seizing Life podcast episode where she shares her son's story and her efforts to catalyze research on this poorly understood condition. Learn more at **CUREepilepsy.org/seizing-life**.

MAKE A DIFFERENCE

Your gift makes it possible for us to find more biomarkers that can predict and one day reduce the risk of developing epilepsy.

FOR THE 1
WHO TRADES SEIZURES FOR SIDE EFFECTS

Francine Ang
AGE 13, SOUTH SAN FRANCISCO, CALIFORNIA

At 7 years old, Francine Ang wanted to do what most kids do: run, learn, play the violin, and spend time with friends. And that's just what she did until she started blacking out so often that she never knew when another episode would strike.

"I couldn't focus," Francine says. "It was really hard for me to learn. I couldn't run. Most physical activity I couldn't do. I had to sit it out."

She even seized in front of her friends.

"Having seizures in front of other people was a problem because I just blacked out in front of them," Francine says. "I was constantly scared of this happening."

The more she seized, the smaller her world became. She knew she could have a seizure at any time and hurt herself.

"I once had a violin recital, and I had a seizure on the stage," Francine says. "I think that's when I started to get really concerned about it."

Now, at 13 years old, Francine understands that her blackouts were characteristic of a specific form of childhood epilepsy.

"I was diagnosed with absence seizures. I had 50 to 100 daily," she says.

Though many people associate absence seizures with stillness, Francine's are different.

"Absence seizures for me and other people aren't like daydreaming," she explains. "It's not always staring off into space. I have action."

Her hands move, her eyelids flutter, and she often hums. But she only knows that because others have told her.

"When I'm having a seizure, it's like a part of my day gets taken out. And when I try to remember what happened while I was having a seizure, I can't. It's like my brain shuts down," Francine says.

Since receiving a diagnosis, Francine has tried at least five medications, each with unpredictable side effects.

"Sometimes, I get a really bad attitude and mood swings. I get really tired, and then I get energetic," she says. "It just doesn't make sense."

Despite their drawbacks, Francine is grateful for antiseizure medications. It's because of medication that she's finally seizure-free.

"For the last year, now that I've been taking medicine daily, I've been seizure-free. I don't feel limited to doing any physical activity. I'm completely good," she says.

Francine has achieved excellent scores in her California Assessment of Student Performance and Progress (CASPP) test, and, according to her mom, has thrived in school.

"She was invited to her school's advanced math program, and a great opportunity introducing her to high school work before she leaves middle school," Francine's mom Ivy Mecano says.

Now in eighth grade, she is well-loved by her teachers and classmates.

Her seventh grade math teacher, Ms. Grace, says, "She has great leadership skills and demonstrates a positive attitude and enthusiasm for learning new things."

Thanks to treatment, Francine can focus and learn and has regained the childhood that epilepsy almost stole from her.

"She was tapered off from her seizure medication last year. Eventually, that medication was discontinued, and she is no longer on any kind of medication for seizures," Ivy says.

Francine knows not all people with epilepsy find treatments that work.

"More treatment and research for absence epilepsy could help me and others reach our goal of no seizures and no side effects," Francine says.

Learn More About Absence Seizures

Watch our recent Treatment Talk, "Diagnosis, Treatment, and Prognosis of Childhood Absence Epilepsy," to hear Francine's conversation with pediatric epilepsy researcher and physician Dr. Juliet Knowles. Visit **CUREepilepsy.org/treatment-talks** to view all our Talks.

TAKE A CLOSER LOOK: IMPROVEMENTS IN TREATMENT TARGETING

Less than a decade ago, treating epilepsy was typically a trial-and-error process. People with epilepsy would try a wide assortment of medications in a variety of dosages to see which drug cocktail might stop, or at least reduce, their seizures. Even now, people like Francine can try numerous medications before finding one that works, grappling with painful and disruptive side effects along the way.

Over the last 25 years, our research into the basic mechanisms of epilepsy has laid the foundation for targeted treatments that seemed all but impossible a generation ago. As we continue to investigate basic mechanisms, we're also building upon that foundation through our research into genes associated with epilepsy, biomarkers that can help predict risk, and therapies that can bring lasting relief to patients and their loved ones.

Our continued push for novel treatments and therapies has given our entire community hope — hope for effective treatments for epilepsy, especially the rarer forms, and hope that we'll one day realize our vision of a seizure-free world.

FINDING CURES FOR ALL THE EPILEPSIES

Every form of epilepsy is different, from the mechanisms that drive it, to the conditions that trigger it, and to the genes behind it. But targeted treatments are a stepping stone to curing this complex condition, especially for people with rare epilepsies. Through our *Catalyst* Award and related initiatives, CURE Epilepsy is leading the charge to uncover safe and effective treatments for more forms of epilepsy.

Launched in 2020, the CURE Epilepsy *Catalyst* Award supports a bold step forward in our work – enabling the science from successful basic research studies to unlock potential new treatments for epilepsy. We created the award in response to a call from our research community for more opportunities to transition research findings into curative therapies. Nine *Catalyst* Awards have been funded to date.

Where there is research, there is hope. With the *Catalyst* Award, we ensure that epilepsy research never loses sight of our ultimate goal: the cure.

CATALYST AWARD

This two-year, $250,000 grant funds research supporting the development of new, transformative therapies.

Using Focused Ultrasound To Modulate Brain Activity And Suppress Seizures

Ellen J. Bubrick, MD
Brigham and Women's Hospital, Boston, MA

Focused ultrasound is a novel technique that is FDA-approved for the treatment of essential tremor. It is being investigated in many neurological disorders as a way to precisely target specific brain regions non-invasively using sound waves. Having obtained initial safety data in a small number of people with epilepsy, Dr. Bubrick and her team will collect additional safety and efficacy data to progress to a larger clinical trial.

Optimizing a Gene Therapy for Human Clinical Trials

Janet Van Eersel, PhD
Macquarie Medical School, Sydney, Australia

Excitotoxicity is a problem linked to epilepsy. It happens when nerve cells in the brain get too much stimulation, which can harm and kill the cells. Dr. Van Eersel's team discovered that a protein called Tau enables excitotoxicity in the brain. They further found that an enzyme known as p38 kinase can modify Tau to stop excitotoxicity. The team developed a gene therapy to boost p38 kinase activity. When this therapy was tested in animals with epilepsy, they found that it reduced abnormal EEG activity and seizure severity. In this study, the team is optimizing this therapy for human clinical studies.

Investigating the Promise of Gene Therapy

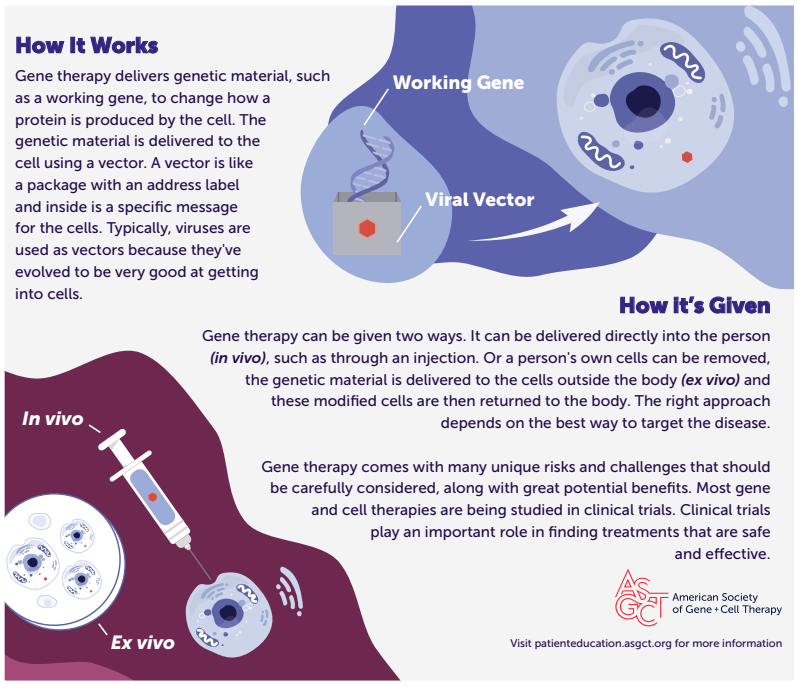
Gene therapy empowers clinicians to treat or prevent a disease by correcting the genetics behind it. Our increased knowledge of epilepsy-associated genes has the potential to enable specific gene therapies.

Gene Therapy for Type 1 Progressive Myoclonus Epilepsy (EPM1)

Berge Minassian, MD
The University of Texas Southwestern Medical Center, Dallas, Texas

In preliminary studies of a genetic mouse model of progressive myoclonus epilepsies, Dr. Minassian and his team showed that replacing the gene cystatin B (CSTB) — the mutations of which cause a type of PME called Unverricht-Lundborg disease — could improve the neurological features and brain pathology associated with the disease. Now funded by a 2023 *CURE Epilepsy* Award, the team aims to complete a full gene therapy study in mice. They hope to eventually use that study to gain regulatory approval to conduct a clinical trial that could reveal a possible PME treatment and pave the way for therapeutic development for related epilepsies.

Exploring the Potential of Gene Therapy



*Graphic sourced to the American Society of Gene & Cell Therapy at asgct.org.

> "Pediatric brain diseases, including most epilepsies, are inherently genetic and in most cases, curing them means directly modifying the gene responsible for their seizures. With the funding provided by CURE Epilepsy, our lab aims to replace the gene responsible for a specific form of pediatric epilepsy and alleviate the suffering from it."
>
> BERGE MINASSIAN, MD

EPILEPSY EXPLAINED

Get answers to your questions about epilepsy medications with Dr. Nathan Fountain. Our NEW video series provides basic information on epilepsy in easy-to-understand language. Learn more at **CUREepilepsy.org/epilepsy-explained**.

MAKE A DIFFERENCE

Your gift makes it possible for researchers to pursue cutting-edge treatments and therapies.

OUR COMMUNITY:
THE REASON BEHIND OUR RESEARCH

While research is the heart of our organization, our reach extends far beyond the lab. Every study we fund, every webinar we host, and every fundraising event our community supports all come back to those living with epilepsy.

From millions of dollars raised in community events to our powerful grassroots programs, our successes in our first 26 years and beyond belong to all people who live with epilepsy and their loved ones. We research for you. With you. Because of you.

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Row 1
2023 NYC Hamilton Unplugged Benefit: Deena Andreola and daughter; Miguel Cervantes and Broadway friend, Andrew Call

Row 2
Expert Panel at 2023 Seattle CARES

Row 3 & 4
Families at 2023 Epilepsy Awareness Day at Disneyland:

Row 5
Participants in 2023 Epilepsy Awareness Day at the Ballpark (Chicago White Sox)

Page 25
2024 Chicago Night of Discovery

Row 1
Former board member Marilynn Gardner and mother, Barbara Kelly (former board member); Board Member Shalee Cunneen and CEO Beth Lewin Dean; Grammy award winning artist Rick Springfield

Row 2
John Corkery and daughter Caitlin; The Walters family

Row 3
Miguel Cervantes and event auctioneer; Founder Susan Axelrod flanked by Founder's Award recipients Gardiner Lapham and Jeanne Donalty

Row 4
Featured guests Erin Gard and mother, Joanne Guthrie-Gard; Board Chair Lisa Cotton

Row 5
Board Member Hannah Whitten, flanked by her parents Reggie and Rachelle Whitten; David Axelrod with Misericordia choir members











FOR THE 1
WHO REMAINS A CHAMPION

Matt Perrone
AGE 47, CHARLOTTE, NORTH CAROLINA

In 1993, 16-year-old Matt Perrone woke up. He swung his feet out of bed and headed for the bathroom to take his daily shower, a routine event on a seemingly normal day.

"The next thing I knew I was having a seizure," Matt says. "I was unconscious, had a tonic-clonic seizure. The door was locked."

He woke up in the hospital, not remembering the panic his mom felt as she ran to the bathroom, unlocked the door, and found him seizing on the floor. It would take a second seizure — a neck seizure — for Matt to receive his epilepsy diagnosis.

With no ability to research online and little information from the doctor, he didn't even know what form of epilepsy he had.

"Speaking to my neurologist as an adult, I think it was juvenile myoclonic epilepsy," Matt says.

He was prescribed medication from the start. Though he experimented with different doses, he found one that controlled his seizures then and now.

"Those two seizures, knock on wood, have been it for me," he says. "I'm extremely fortunate and extremely grateful for that."

Fast forward to 2020, when Matt watched his four-year-old daughter, Abigail, seize for the first time. Matt prompted her to get ready to go to a friend's house, but Abigail ignored him. He quickly realized she was experiencing an absence seizure.

"She started to vomit," Matt says. "And then she started convulsing and having a tonic-clonic seizure."

The seizure stopped when the paramedics came, but Abigail seized again in the ambulance. Yet, she didn't receive a diagnosis or start medication that day.

"They did the same thing, a wait-and-see," he says. "It was extremely scary."

But when she'd go to sleep, she'd seize again, until finally doctors diagnosed her with focal seizures and prescribed medication. She suffered through nine more seizures before finding the right dosage and frequency to control her seizures.

"She's been seizure-free for 18 months," he says. "She had a breakthrough seizure about a year after that, but she's been seizure-free since."

Abigail's diagnosis drove him to build community, specifically as a CURE Epilepsy Champion. He founded EpiPalooza because while he didn't know much about epilepsy, he knew music.

"I called the venue that I've played before, and then I just found some artists that I'd talked to before," he says. "I put on that first show and raised some money and raised awareness because I wanted people to learn about epilepsy."

According to Matt, that message has reached people in unexpected places.

"My own neighbor, I learned through this, her son has epilepsy," Matt says. "That's why I tell people, if they can't donate, spread it. You have no idea how many people are affected by this."

He knows exactly how many because he's one of them. It's for them that he proudly hosts EpiPalooza every year, building community and raising funds for the cure.

CURE Epilepsy Champions

Our Champions host grassroots fundraising events all over the U.S. raising critical funds and awareness for epilepsy research. Events include:

- 10TH ANNUAL STRIDES FOR EPILEPSY 5K
- ELLA'S RACE
- MAFFIE WALK TO CURE EPILEPSY
- REAGAN'S RUN
- DRESSAGE FOR A CAUSE
- DOMINATE EPILEPSY'S PURPLE DAY
- EPIPALOOZA
- EPILEPSY AWARENESS GOLF TOURNAMENT

37
EVENTS HOSTED IN 2023

$430,000+
RAISED

FOR THE 1
WHO WON'T GIVE UP

Daniel Correa, MD
AGE 42, BRONX, NEW YORK

As a child of a person with epilepsy, Dr. Daniel Correa saw first-hand the stigma epilepsy can bring. His mom pushed through discrimination and barriers to opportunity that many people with epilepsy know all too well. Yet, she kept fighting.

"Despite the societal challenges for people living with epilepsy, my mother overcame language barriers and completed two master's degrees while working full time as a communications professional," Daniel says.

Her determination inspired his own.

"Her example helped me prove that my grade school teachers were wrong to write me off because English was my second language," he says.

Now a neurologist and epileptoligst, Daniel has built a personal and professional life around helping people with epilepsy.

"I've dedicated my career to helping people with neurologic disorders find treatments that can support their journey to live better with their conditions," he says.

He is also a passionate CURE Epilepsy Champion.

"In October 2023, I ran the Chicago Marathon raising awareness and funding for CURE Epilepsy, the leading non-governmental funder of epilepsy research in the world," he says.

He ran over 1,200 miles to train for the marathon, all to support the CURE Epilepsy community's tireless pursuit of a cure.

He says, "With each mile I was overjoyed to have the opportunity to raise awareness about epilepsy, contribute to CURE Epilepsy's research programs, and run the Chicago Marathon in honor of my mami and all families living with epilepsy."

He hopes that others will join the epilepsy community in our fight for a future without epilepsy.

FOR MORE INFORMATION ON HOW TO START YOUR OWN NEIGHBORHOOD RUN/WALK EVENT, VISIT

CUREepilepsy.org/ Run-Walk-Series

Team CURE Epilepsy

Our Team CURE Epilepsy participants come from all over the world and have a variety of skill levels and have ran, swam, biked, or climbed to raise critical funds and awareness for epilepsy. Some of our charity partners over the last year include:

BANK OF AMERICA CHICAGO MARATHON

CHICAGO TRIATHLON

TCS NEW YORK CITY MARATHON

MARINE CORPS MARATHON

34
REGISTERED RUNNERS IN 2023

$130,000
RAISED FOR EPILEPSY RESEARCH

FOR THE MANY
FIGHTING FOR A CURE FOR THE 1

This report has highlighted the amazing work CURE Epilepsy is doing to fund breakthrough research that will change lives and, ultimately, lead to the cures we know are possible. The generous support of more than 4,000 individuals, foundations, corporations, and organizations makes our work possible.

Our donors give in different ways and for different reasons. Each and every gift, no matter the size, brings us one step closer to the cure. It is only together that we will accomplish our shared goal of a world without epilepsy. To see our full honor roll of donors, please visit **CUREepilepsy.org/impact-reports**.

Planned Giving

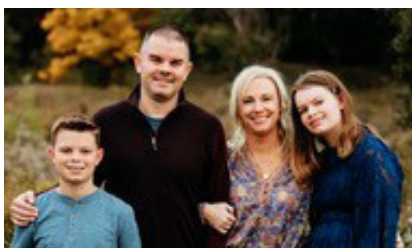
Planned gifts are charitable contributions that are part of a donors financial or estate plans and are typically given to nonprofits once the donor passes away. Remembering CURE Epilepsy in your estate plan is an incredibly meaningful way to leave a lasting legacy.

DON TAYLOR, SAN DIEGO, CA

"We had been giving to CURE Epilepsy for several years but after we lost Mandy to SUDEP, we knew we wanted to do whatever we could to make sure no other families experienced what we did. My wife, Pat, and I had a a quick exchange with a result that we both were on board with: we would increase our annual and include SUDEP research at CURE Epilepsy in our estate. It was quick because we both agreed strongly that this was important. It is great to hear about the progress being made and knowing that we are doing our part to help with that."

Stock Giving

Stock giving, or donating stock to a charity, can be a way to increase the value of a gift and potentially benefit both the donor and the charity. Donating appreciated stock (stock that has increased in value since it was purchased) can provide tax advantages over donating cash.



SHALEE AND BLAKE CUNNEEN, LAGRANGE PARK, IL

"We are proud to support CURE Epilepsy and the amazing research they make possible. Supporting their efforts through gifts of appreciated stock allows us to maximize our impact while minimizing our taxes. Whether we attend an event or participate in a special match day, we know that our funding is helping drive advances that will truly change the lives of people living with epilepsy."

Giving through an IRA

IRA giving, also known as IRA charitable rollovers or Qualified Charitable Distributions, is a tax-efficient way to donate money from an Individual Retirement Account (IRA) to a qualified charity. IRA giving can be a strategic way for individuals 70.5 and older to manage their tax situation while supporting charitable causes.

ELLEN BERNE, MD AND PAUL NEEDLE, PITTSBURGH, PA

"We have chosen to give to CURE Epilepsy since our son Adam was 34 years old. Adam, now 50, has been helped by the excellent physicians here in Pittsburgh, but we still hope new and better treatment options will be available for children and older adults as well."

Giving through a Donor-Advised Fund

A donor-advised fund (DAF) is a charitable investment account that allows individuals to support charities by donating money, stocks, or other assets. DAFs are one of the fastest-growing ways to give to charities because they are tax-advantaged and easy to use.

ELISSA AND MATTHEW MOORE, CHARLOTTE, NC

"We support CURE Epilepsy because 20 years ago, we would not have known that our son Cormac's epilepsy is likely the result of a genetic mutation. It is only because of ongoing support for epilepsy research that knowledge of genetic epilepsy has advanced so significantly. Because we know about the genetic mutations, physicians know what drugs Cormac needs to avoid and what drugs are worthwhile to try. Continuing to support research for genetic epilepsy means that more options will be available to Cormac as he grows up."

Corporate Giving

Demonstrate your organization's commitment to a world without epilepsy by partnering with the leading non-governmental funder of epilepsy research. Corporations, both partner with us on a wide range of engagement opportunities including events, educational activities, communication campaigns, employee matching, and more.

ALEX TAPAS (SALESFORCE)

"We are proud to partner with CURE Epilepsy since our initial employee engagement lunch in Chicago intended to raise awareness and research funds through a company match. The event inspired so many of our employees, even those without a personal connection to epilepsy, that we successfully recruited a large group of volunteers to assist in the CURE Epilepsy Chicago Gala and continue to do so each year. Our reach expanded recently as our colleagues in New York City have started their own educational and fundraising annual event."

Monthly Giving

Monthly giving is a recurring donation program where donors automatically make a gift each month. Monthly donors provide a predictable level of support that helps us plan our work.

JEFF KNUPP, GALENA, OH

"My brother, Tim, and I shared a room growing up and I witnessed his epileptic seizures on a nightly basis. His seizures were never able to be completely controlled, and epilepsy created enormous challenges for him throughout his life. Despite all of this, Tim never lost his zest for life and was a wonderful human being full of love, until we lost him to SUDEP in 2012. We give monthly to honor Tim by doing our part in the quest to find a cure for this disease."

10+ Years Giving

Epilepsy affects many individuals and their loved ones for their entire lives. Some donors choose to make an impact each year over an extended period to support promising research that gives hope to people living with epilepsy.

CHERYL BEIL, PHD AND JEREMY WAYNE, WASHINGTON, DC

“Our son Jeremy has lived with epilepsy for 37 years. We support CURE Epilepsy because we believe research will lead to the answers and cures needed to eliminate epilepsy permanently. No family should have to experience the uncertainty and stress that epilepsy can cause. What I especially appreciate about CURE Epilepsy is the education they provide the community through their monthly summaries of the latest epilepsy research news and the periodic Epilepsy Webinar Series"

New Giving

Every gift, no matter the amount, can make a significant impact on funding transformative research in epilepsy, especially when more and more people join together to help in the search for a cure. We appreciate the more than 2,000 people who made their first gift in 2023.

THE GARCIA FAMILY, ARLINGTON, VA

"As a family we have been dealing with Carina’s epilepsy for more than 25 years. Despite taking three medications and a recent surgery, she continues to experience seizures and many constraints to leading a “normal" life. We now choose to support CURE Epilepsy in hope that their research may lead to our little girl's seizure freedom."

Tribute Giving

Tribute Giving, also known as memorial or honor donations, is a way to recognize and honor people or events by donating to a cause in their name, either in celebration of a special occasion or to honor their life.

CHRISTY SHAKE AND MICHAEL KOLSTER, BRUNSWICK, ME

"We chose to support CURE Epilepsy for my son Calvin's 5th birthday and have continued to direct funds from our network to epilepsy research because although we do have more days free of seizures than we did, 16 year later we continue the daily struggle with seizures and their devastating side effects."

THANK YOU, VOLUNTEERS

CURE Epilepsy's work depends on all of our volunteers. We thank each of you, including those who serve on our committees. CURE Epilepsy scientific researchers and members of our lived experience community kindly volunteer their time and expertise to ensure the science we fund has the highest potential impact in the epilepsy community. We do not list their names to maintain the integrity of our grant review process.

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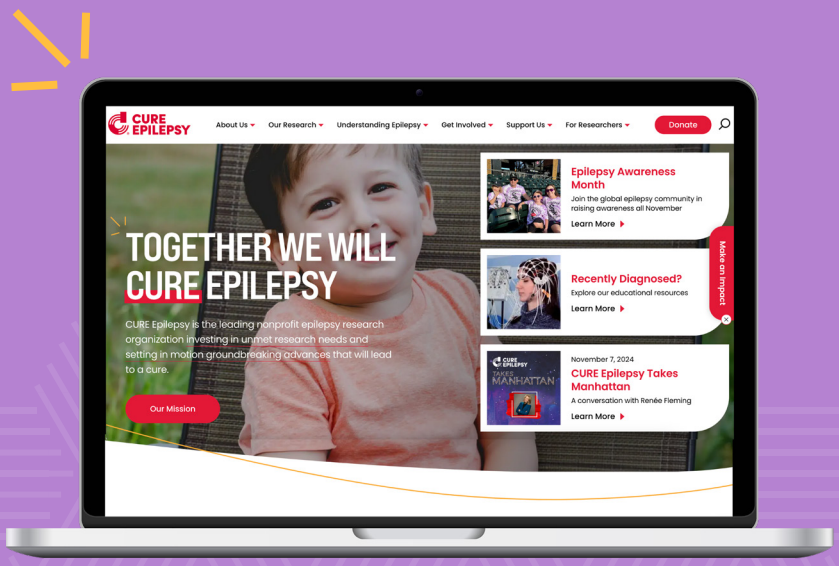
CURE EPILEPSY: NEW MISSION. NEW WEBSITE. SAME AIM.



Our new mission is to fund breakthrough research that will transform the lives of people with epilepsy as we lead the search for a cure. Our fundamental work and vision remain the same, but we've evolved our language to better reflect who we are and the impact that we aim to have on people's day-to-day lives as we march together toward a cure. Learn more about our mission and impact on our newly redesigned website

CUREepilepsy.org

CURE EPILEPSY

CUREEPILEPSY.ORG/IMPACT-REPORTS

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