ISSUE 13: MARCH 2020

EPILEPSY HEROES

RARE EPILEPSY NETWORK
SUDEP BIOMARKER CHALLENGE
LIFETIME ACCELERATOR Awardee Mary Ann Brodie
INNOVATOR SPOTLIGHT ON DOC.AI

*This is the 2nd of 3 paintings in the “Brainstorm” series created for our END EPILEPSY campaign in 2018.
IN THIS ISSUE, we celebrate the many heroes working to improve treatment and diagnosis of the epilepsies. From parents and patient participants in the trenches willing to share their lived experience in natural history studies and take part in clinical trials, to research coordinators who make the nuts and bolts of those trials work, to academic and industry scientists seeking new directions for therapies, these heroes bring passion, skills and courage to the fight to END EPILEPSY®. At the Foundation, we strive to be your loyal companions on the journey.

In this issue, we celebrate those that have given their life’s work to something bigger than themselves.

■ The cover art is by artist and activist SABER (also known as Ryan Weston Shook) who has epilepsy. In October 2018, SABER helped launch the Epilepsy Foundation’s first ever nationwide, multi-year campaign, Let’s Use Our Brains to END EPILEPSY, with a live, public art performance. His massive art installation brings attention to this brain disease and the need to find cures.

■ Lifetime Accelerator Awardee Mary Ann Brodie, Executive Director of the Epilepsy Study Consortium, has spent over thirty years in service of testing new anti-seizure medicines, learn more about her journey on page 8.

■ Doc.Ai co-founders Walter and Sam DeBrouwer were inspired to build an artificial intelligence platform to close the healthcare data loop and transform research, learn more about their journey on page 10.

■ In an op-ed piece on page 12, we celebrate the epilepsy volunteers who are contributing to the advancement of knowledge for epilepsy and the broader scientific community.

■ In our Think Big column on page 13, we highlight the founder of the Epilepsy Therapy Project, Warren Lammert, a father of a daughter with Dravet syndrome who was determined to bring new urgency to the search for therapies that would make a difference “in a timeframe that matters.”

These heroes, and so many others, are part of what makes this community great. Joseph Campbell, author of The Hero’s Journey, spent a lot of time writing about what it means to be a hero. He wrote that, “Opportunities to find deeper powers within ourselves come when life seems most challenging.” His call is also our call to arms. Join the movement to END EPILEPSY and find your deeper power to help yourself and others living with the epilepsies through supporting research.

Kind regards,

Brandy Fureman, Ph.D.
Vice President, Epilepsy Foundation
The earliest notion of surgery for epilepsy dates to ancient times. Hippocrates who lived in 400 BC postulated *trephination*, making a hole in the skull, could provide relief from seizures in people who had suffered traumatic head injuries. Fast forward to the early 1500s and well into the 1800s when a growing number of reports of trephination for epilepsy emerged. The success of the surgery was uncertain at best, given the frequent complication of infection and the lack of reported long-term seizure freedom. However, as surgeons moved from creating holes in the skull to dipping beneath the skull, case reports began to emerge detailing descriptions of the removal of tumors, scars and abscesses which led to the relief of seizures.

The late 19th century brought significant advances aided by the work of Hughlings Jackson. Jackson studied patients with focal seizures to better understand localized function in the human brain. Working alongside Jackson was Sir Victor Horsely, who early in his career was able to show positive outcomes of brain surgery for epilepsy in patients with identified brain lesions. The combined efforts of Jackson and Horsely brought the medical community to accept epilepsy surgery as a feasible treatment which merited further exploration.

In the early 20th century, Wilder Penfield and Herbert Jasper led the charge to refine surgical techniques for epilepsy. Their methodical approach combined EEG recording, brain stimulation and available imaging (cerebral angiography, pneumoencephalography) with neuropsychology testing and aided in localizing both lesions responsible for seizures and also seizure foci that were independent of lesions. In the years that followed, scientists and clinicians were able to realize the critical step of implanting surgical electrodes deep in the brain to identify epileptogenic brain tissue.

Further advances in surgery emerged with the arrival of modern three-dimensional brain imaging. Computed tomography (CT) scans in the 1970s aided in the visualization of lesions that declared themselves through seizure activity. Magnetic resonance imaging (MRI) with its high-resolution capabilities eventually became the choice pre-operative imaging technique in epilepsy. Functional imaging with positron emission tomography (PET) and fluorodeoxyglucose (FDG) further aided localization of lesions during surgical evaluations with its ability to identify epileptogenic brain.

The 21st century continues to deliver opportunities for innovative epilepsy surgical care. The refined use of diagnostics (magnetoencephalography, functional MRI, diffusion tensor imaging) and surgical advances (stereotactic radiosurgery, laser interstitial thermal therapy (LITT)) allow for more patients with refractory epilepsy to be identified as surgical candidates and treated with safe, and when possible, minimally invasive image guided surgical techniques that have the potential to bring seizure freedom and improve quality of life.

**Did you know?** Through the Epilepsy Therapy Project, the foundation provides seed funds to accelerate therapeutic options for epilepsy. For example, the Epilepsy Foundation supported the early exploratory studies for LITT in epilepsy to improve surgery safety. The company, known as Visualase®, was acquired by Medtronic and is now in phase 3 clinical trials! The Epilepsy Foundation also recently gave pilot funds to Advanced Scanners to develop better imaging techniques to ensure that surgeons have a more accurate brain map during the surgery to ensure that the removal of tissue is more precise.
The diagnosis of epilepsy carries the weight of much more beyond having seizures. It is the fearful period between seizures, not knowing when the next one will happen. It is the sometimes difficult conversations with peers, colleagues, new partners or employers when disclosing having epilepsy. It is the ongoing struggle to get prescription medications in the right formulation and at the right time. It is the meticulous planning and communication around pregnancy and having a family, balancing the complications of certain medications against the risk of seizures themselves since both can possibly harm fetal health. It is the endless preparations made and precautions taken to protect one’s self or loved one in the event of a seizure while sleeping, playing a sport, swimming, traveling, etc. – and the fact that there is never a good time to have a seizure.

Epilepsy impacts every facet of life, and not only for the person with epilepsy. Parents, siblings, partners, spouses – lives and dynamics on the periphery are touched as well, and all involved have a place in clinical and research priorities.

The Epilepsy Foundation has long recognized this fact and over the past five years has endeavored to shine a light on the need to address epilepsy holistically. We were a founding partner of the Rare Epilepsy Network (REN), a coalition of over thirty rare epilepsy organizations, which originated as a natural history registry in 2014. Over three years, data was shared by over 1,400 individuals, the majority being caregivers enrolling on behalf of a child impacted by one of over 40 rare, often devastating, epilepsy diagnoses.

Comorbidities, developmental milestones, medications and side effects and countless more elements can be studied to gather deeper insight into what it is like to live with or care for someone with epilepsy. In the affected people enrolled in REN, cognitive comorbidities are reported in approximately 40%, non-verbal status in 16%, and autism in approximately 20%. These comorbidities certainly impact the level of care and multidisciplinary inputs a person living with epilepsy already needs and can profoundly impact the affected person’s quality of life if barriers to management exist.

Family members and caregivers are also impacted. The University of Washington Caregiver Stress Scale (UW-CSS) was designed to assess stress levels of caregivers of children with epileptic encephalopathy (EE) with input from the REN. An analysis demonstrated that caregivers of children with EE reported significantly higher stress than caregivers of children with other conditions such as Muscular Dystrophy and Down Syndrome. Further study is critically needed for the creation and validation of Patient Reported Outcome Measures for people with epilepsy, as well as tools for earlier detection of non-seizure related issues that can be intervened upon. A dashboard to preview a subset of REN data, comparing across diagnoses and the full dataset is available. Researchers can also make data requests.

A priority of the Epilepsy Foundation is to improve outcomes for people living with epilepsy. This commitment grew out of our initial support for REN and transformed into the Epilepsy Learning Healthcare System (ELHS), a network dedicated to leading change in the way epilepsy care is provided – centered on targeted quality improvement and committed to incorporating patient and family partner perspectives at every step.

Data is captured in an organized way at every clinical encounter and real-time improvements are adopted by providers in the pediatric and adult practices. Areas of focus are identified by people affected by epilepsy, and it is known that seizures are only part of the puzzle when living with epilepsy.

Learn more at epilepsy.com/elhs and become a partner in the mission: all people living with epilepsy will live at their highest quality of life, striving for freedom from seizures and side effects, and we won’t stop until we get there.
Know the stats:

- Each year, about 1 in 1,000 people with epilepsy die from SUDEP.
- If seizures are uncontrolled, the risk of SUDEP increases to more than 1 out of 150 people living with epilepsy.

Determined to bring an end to Sudden Unexpected Death in Epilepsy (SUDEP) and help people with seizures live to their fullest potential, the Epilepsy Foundation SUDEP Institute actively supports research to understand the causes of SUDEP with the ultimate goal of creating SUDEP prevention and intervention strategies.

SUDEP is the sudden, unexpected death of someone with epilepsy, who was otherwise healthy. In SUDEP cases, no other cause of death is found when an autopsy is done. The mechanism(s) of SUDEP are still under intense investigation by researchers in the US and across the world. For the past five years, we have launched a series of challenges designed to attract new ideas for why SUDEP happens. Challenges have ranged from developing awareness campaigns, creating tools to assess risk, and submitting ideas on potential causes for SUDEP.

Currently, we are sponsoring the Biomarker Challenge.

The Epilepsy Foundation SUDEP Institute is currently challenging Solvers worldwide to identify specific and sensitive biomarkers of SUDEP to facilitate the development of interventions for people at high risk for SUDEP. A biomarker is a biological molecule that can be found in blood, other body fluids or tissues that signal a normal or abnormal process of a condition or disease. The Epilepsy Foundation SUDEP Institute partnered with InnoCentive to offer the Biomarker Challenge and we are in the final stretch of accepting solutions. If we can understand who is at risk for SUDEP, we can create intervention strategies to prevent SUDEP from happening.

Consider submitting a solution for the Biomarker Challenge

Whether solvers have been involved in any of the previous biomarker milestones, this final milestone is open to anyone, across the world, who has a solution that can address the specific Challenge request. If you or someone you know is doing work the epilepsy community could benefit from, we encourage you to submit your solution by October 10, 2020 and win $800,000! Learn more now through the InnoCentive site.
THE SUDEP INSTITUTE

Biomarker Challenge

Each year, more than 1 out of 1,000 people with epilepsy die from sudden unexpected death in epilepsy (SUDEP). If seizures are uncontrolled, the risk of SUDEP increases to more than 1 out of 150. SUDEP is the leading cause of death in young adults with uncontrolled seizures.

Among the 65 million people worldwide living with epilepsy, nearly one-third have ongoing seizures despite existing therapies.

To accelerate the identification of effective treatments for SUDEP, the Epilepsy Foundation SUDEP Institute is sponsoring a $1 million challenge to develop a predictive biomarker to identify people at risk for SUDEP. If we can know who is at risk, we can develop prevention strategies and intervene before it is too late.

With the help of our partners at InnoCentive, all of the challenges allow us to take advantage of interdisciplinary approaches and alternative perspectives. Through combining and contrasting ideas, the best and most valuable solutions will be identified and financially supported.

PLEASE CONSIDER DONATING to funding the winning solution - it will be a win for ALL who have a loved one living with epilepsy.

CHALLENGES TO DATE:

**Challenge 1: Advocacy Campaign**
Empowering people with epilepsy, $15k awarded

**Challenge 2: Self Management Tools**
Preventing epilepsy seizures, EpSMon (Epilepsy Self-Management) mobile app created

**Challenge 3: Identifying Potential Biomarkers**
Predictive biomarkers of epilepsy seizures, $75k awarded

**Challenge 4: Bringing Biomarkers to Clinical Practice**
Developing predictive biomarkers of SUDEP

- **Milestone 1**: Project plan, $40K awarded
- **Milestone 2**: Proof of concept, $80K awarded
- **Milestone 3**: Validation data in humans of predictive value for SUDEP $800,000 prize

The Final Milestone of our Final Challenge is live now and open until October 10, 2020!

Biomarkers may be genetic, structural within the body, metabolic, physiological, or something else that is quantifiable.

The winning biomarker will be easily and safely measured, cost-efficient to detect, modifiable with intervention (something we can actively treat or prevent), be consistently associated with SUDEP or life-threatening seizures, and will drive human intervention. For example, the biomarker may identify a high-risk patient group to allow testing of existing interventions such as seizure detection devices.

Learn more go to epilepsy.com/sudep

03/2019 880SBC
Over the past two years, we have witnessed nine different epilepsy products successfully complete the needed clinical trials and gain FDA approval. These approvals were for rare epilepsy syndromes, for new rescue therapies, for focal epilepsies and for new seizure monitoring tools. There is a lot of movement in the pipeline and we have a reason to celebrate! Please see below for the quick snapshot.

**FDA approvals for rare epilepsies**
- April 2018, FDA approves Everolimus® for Tuberous Sclerosis
- June 2018, FDA approves Epidiolex® for Lennox-Gastaut syndrome and Dravet syndrome
- November 2018, FDA approves Sympazan® (Clobozam as an oral film to make it easier to give to children who have difficulty swallowing pills) for Lennox-Gastaut syndrome

**FDA approvals for new rescue medication options for those with Acute Repetitive Seizures**
- May 2019, FDA approves Nayzilam® (Midazolam nasal spray) for acute repetitive seizures for those age 12 and older
- January 2020, FDA approves Valtoco® (Diazepam nasal spray) for acute repetitive seizures for those age 6 and over

**FDA approvals for Focal Epilepsies**
- May 2018, FDA approves Deep Brain Stimulation for focal epilepsy
- November 2019, FDA approves Cenobamate (XCOPRI®) for focal onset epilepsy

**FDA approvals of new diagnostic tools**
- January 2018, FDA approves Embrace® as a seizure monitor for generalized tonic-clonic seizures in adults
- May 2018, FDA approves zEEG® by Zeto, a wireless dry headset EEG technology
- January 2019, FDA approves Embrace2® as a seizure monitor for children 6 and up with generalized tonic-clonic seizures

When a medical product has completed the pivotal clinical trials, the company must submit a new drug application (NDA) with the FDA. The submission of the NDA is the formal final step taken by a drug sponsor to get the official approval by the FDA to market a new drug in the United States. It typically takes around 60 days to go through this review process.

Currently, there are two new drug applications for epilepsy under FDA review:
- Fintepla® for Dravet syndrome
- Libervant® (Diazepam oral film) for seizure clusters in those 6 and up

Curious to know what other products are in the epilepsy pipeline? Check out [www.epilepsy.com/pipeline](http://www.epilepsy.com/pipeline) to learn more.

Are there specific innovations that you would like to see in the Pipeline? Email innovation@efa.org and let us know.

Out of an abundance of caution for public health and safety, the Epilepsy Foundation postponed the 2020 Pipeline Conference, and Shark Tank previously scheduled for March 12-13 in Santa Clara, California. We made this difficult decision in light of the many unknowns about the rapidly changing COVID-19 situation in the conference region itself and around the globe. The Pipeline Conference showcases the many different products in the epilepsy pipeline – with over 50 different companies presenting.
The Lifetime Accelerator Award was established in 2012 to honor physicians, scientists, industry leaders, and others who have demonstrated a lifelong commitment to bringing new therapies to people living with epilepsy. Recipients are chosen by an independent committee of global thought leaders and clinical investigators in epilepsy and seizure therapy discovery and development.

Q: How did you get involved with the epilepsy field?
A: In the 1980s, I interviewed to work with Dr. Marc Dichter at the University of Pennsylvania, Graduate Hospital Epilepsy Center as an administrator and later as a clinical coordinator. Knowing nothing about neurology at the time, accepting that job was one of the best decisions I ever made.

Q: What did you do at the center?
A: My initial role was to organize and oversee the daily administrative activities of the Penn Epilepsy Center. Two years later, in addition to managing the Center, I took on the role of study coordinator working with Dr. Jacqueline French. In addition, to the clinical trials, we organized preceptorships and educational activities for industry, investigators and coordinators.

In 1992, we launched our first Antiepileptic Drug Trials Symposium which began as a workshop for coordinators and investigators to learn how to conduct clinical trials. This meeting has continued bi-annually for the last 28 years and now focuses on issues related to antiepileptic drug and device development. This is attended by representatives from academia, industry, the National Institutes of Health and FDA to review what has been learned and to discuss strategies for future AEDD development.

This year’s awardee is Mary Ann Brodie who has devoted more than 30 years of her life towards advancing clinical trials in epilepsy. Mary Ann received her award in March 2020. We sat down with Mary Ann to learn a little bit more about her career and her perspective on epilepsy.
Q: What would be the most important piece of advice that you would give to other clinical coordinators?
A: Always keep an open dialogue with your investigator and ask for guidance if there are any uncertainties. Clinical trials have inclusion and exclusion criteria that are critical to ensure that you are enrolling the right people for the right study. As a clinical coordinator, you should know the ins and outs of what those criteria are and whether your patients qualify. There is a lot of uncertainty and chaos going on in our patients lives, the clinical study should not contribute to that chaos.

Q: What was the first thing that struck you about epilepsy?
A: What struck me was the depth with which seizures can impact people’s lives. One of the first patients with epilepsy that participated in one of our trials was a young gentleman who worked in the court system as a stenographer. Because of his seizures, he was unable to continue to work. It was devastating to think that someone so young had to give up his career. Then there were the adult children of elderly parents who had intractable seizures. Hearing the parents talk and worry about who would care for them long term was distressing. These are only some of the dynamics that pushed us to continue to look for help for these patients.

Q: After being a clinical coordinator and manager for over 20 years, you helped found the Epilepsy Study Consortium. What is the Epilepsy Study Consortium?
A: The Epilepsy Study Consortium is a group of scientific investigators from academic medical research centers who are dedicated to accelerating the development of new therapies in epilepsy to improve the care of people with epilepsy. The organization’s goals include building a partnership between academics, industry and regulatory agencies and optimizing clinical trial methodology in order to responsibly speed new treatments to people with epilepsy.

Q: How did the Epilepsy Study Consortium start and how did it evolve over time?
A: In 2007, as the requests for consulting on clinical trials and drug development increased, Dr. Jacqueline French asked if I would join her in establishing the Epilepsy Study Consortium. This became a team effort including Bree DiVentura, a clinical coordinator also at the Penn Epilepsy Center. In addition to consulting we also focused on educational components for industry. We would set up classes to have industry learn the epilepsy basics and advisory boards to help them develop their drug. We wanted to ensure that those designing clinical trials had the opportunity to meet people with epilepsy, learn from their experiences with epilepsy, and understand the realities that people with epilepsy face.

We then began to provide assistance in writing protocols and establishing source documentation to standardize trials. After recognizing the necessity to have the appropriate participants enrolled in trials, we developed site training tools and conducted review of seizure classification and diagnosis. As a team effort, the consortium has dramatically grown throughout the years and we are constantly adding tools and support.

Q: In your perspective, what is the biggest roadblock for moving epilepsy clinical trials forward?
A: Recruitment. The good news is that there are now a lot more options for individuals to try before considering a trial. But it also means that it is now harder to get the right people into a critical clinical trial to test a new therapy. The problems with recruitment result in more clinical study sites getting involved to ensure that the numbers are met. The more sites complicate the logistics of data coordination and ethical approvals, leading to slower clinical trial starts and increases the overall cost of launching and completing a trial.

Q: How has the epilepsy pipeline changed in the past 5 years?
A: For a while, it seemed like all the companies were leaving epilepsy – especially due to financial constraints and recruitment issues. And although these issues remain, the tide seems to be shifting. This past year alone, we worked with 43 companies on epilepsy trials and within this past year, four new therapies have gotten FDA approval for epilepsy indications: Cenobamate, Deep Brain Stimulation, Nayzilam® (midazolam), and Valtoco® (diazepam nasal spray). It’s an exciting time for the epilepsy field.

As a clinical coordinator, you should know the ins and outs of what those criteria are and whether your patients qualify.
Innovator Spotlight
MEET SAM DE BROUWER CO-FOUNDER OF DOC.AI

Sam De Brouwer is the co-founder of doc.ai. Recently, doc.ai launched an epilepsy digital health trial to test how artificial intelligence (A.I.) might be able to help identify the right treatment for the right person at the right time. We sat down with Sam to learn a little bit more about what inspired her to co-found doc.ai and her own personal connection to epilepsy.

Q: How are you connected to epilepsy?
A: My youngest son, Nelson, had a traumatic brain injury when he was 5. At the time, he was obsessed with superheroes and wanted to fly. I will never forget that Saturday. He jumped out of a three-story window to test his abilities. We rushed to the hospital immediately, but the fall had damaged the left and frontal side of his brain. He has had epilepsy ever since.

Q: How did life change for your family?
A: In the hospital, they put him in a medically induced coma to stabilize his brain on top of the surgery. The doctors told us that his brain was constantly on fire, and he was given anti-seizure drugs right away. When Nelson woke up from his coma half paralyzed and unable to speak, seizures were the last thing on our minds. We focused on intensive rehabilitation therapy. My son is an amazing fighter. After intense months of rehab, he could walk but was a bit unbalanced, and he could begin to speak again. As he began to walk, the falls from the seizures were a huge problem. He wears a helmet to protect his head. As he began to speak, that’s when it really hit us. He spoke of the intense fear, anxiety, and shame that he felt whenever he had a seizure.
Q: What did you decide to do?
A: My husband and I could wrap our heads around rehabilitation – there was a path and we knew what we could do to help. But with the seizures, we felt this big black hole. The trial and error of it all was incredibly scary. We were in an endless loop, constantly testing whether this new medication would get his seizures under control, whether the dosage had to be adjusted, etc. There were also some terrible side effects that we had to work through. Our son was fighting to get better, and we knew that we needed to fight too. Our initial approach was to collect data on everything – that was our lifeline to hope. We decided to devote our lives to improving data collection to inform healthcare outcomes. This was in 2005 and the smartphone hadn’t come out yet. We initially thought about building a research center, but then the smartphone came, and that changed everything.

Q: What do you mean?
A: My husband recognized the potential right away. He is a huge Star Trek fan, and he thought, what if we could put sensors on the phone to get the information necessary for healthcare needs just like the tricorder in Star Trek? We moved to Silicon Valley and began to support hardware sensor development for the medical community. As access to data improved, as the machine learning algorithms became easier to access, and as technology became cheaper, we decided that we would switch our attention to software development. That was when we founded doc.ai.

Q: What is doc.ai?
A: doc.ai is a platform to test digital health trials. We want to enable users to take control of their own health data to develop precise, personalized models that could help them predict and change future health outcomes. When we started this company, we began to hunt for an epilepsy project to take on. When I was talking to my son’s neurologist, he mentioned that his research team at Stanford wanted to develop algorithms that could find optimal drug options for those living with epilepsy. There are over 25 different drug options for epilepsy, and they can be combined in multiple ways to create hundreds and thousands of different strategies. We knew this journey all too well. My son often asks me to “do something for epilepsy” and this was my opportunity to say that I am doing something for epilepsy. I told his neurologist that I don’t know if we can solve the optimal treatment question, but we can certainly try. Learn more at doc.ai

Q: Is there anything else that you would like to add?
A: There are a lot of people living with epilepsy. Use the Epilepsy Foundation and your local community to learn more from each other. Remember that you are not alone. It is going to be a scary journey but don’t ever settle. Hang in there. Sometimes it is going to suck and there are no words that could make it better – but please don’t give up. Also, medical research needs us to volunteer. Whether it is for the doc.ai digital health trial or other trials, please volunteer if you are able. Because only through research can we improve the healthcare options for future generations.

Q: How is your son doing now?
A: My son is 20 now. It has been 15 years, and his brain is still always on fire. His seizures are better managed, we have them down to 8 to 10 a day, and they are smaller than before. He has always been a fighter and is not giving up. He is my superhero.
In 2001, Jesse Sullivan cheated death. He had forgotten to wear rubber gloves when working with an active power supply line, and over 7,000 volts of electricity coursed through his body – the amount used to power between 9 to 10,000 homes. One month later, he awoke from a coma with both arms amputated. Dr. Todd Kuiken of the Chicago Rehabilitation Institute heard of Sullivan’s case. For the past 20 years, he had been developing a new prosthetic limb that utilized neuro-engineering, a technology that connects the nerves in our body to machines. Jesse agreed to try it.

In 2002, Jesse Sullivan became the world’s first bionic man. His mechanical limbs were directed by his brain, bringing about a neuro-prosthetic revolution. We now have neuro-prosthetic limbs for amputees and the paralyzed, cochlear implants for the deaf, and retinal implants being developed for the blind. The scientific community, for the most part, understands how the nerve signaling in our periphery works. But there is still one area of the body left to conquer – the brain.

One of the most efficient ways to understand the brain is through understanding epilepsy. Epilepsy is a neurological condition characterized by unprovoked and recurrent seizures. A seizure is essentially a brain network problem. Anything that can disrupt how the brain works - from genetics to brain injury and inflammation to metabolism - can contribute to a seizure. The severity, manifestation, and frequency of seizures depends on where and how the problem in the brain network occurs. If we can understand this, then we understand the brain. For this reason, those interested in brain mapping and computer-brain interfacing technology have turned to epilepsy patients to advance the technology forward.

In this issue of epilepsy heroes, I wanted to pay tribute to the epilepsy community for volunteering their time to advance knowledge not just for epilepsy but for everyone. One example of their invaluable contributions that the epilepsy community has made is in the data that is gathered before epilepsy surgery.

When seizures don’t respond to medication, it is sometimes possible for brain surgeons to remove an area of the brain that is causing the brain network to seize. Prior to the surgery, doctors evaluate whether someone is a good candidate for surgery by placing electrodes in the brain to record when and where seizures occur. This helps to localize the beginning of a seizure and see if surgery may be possible. For decades, these pre-operative procedures have informed scientists and medicine about what the brain can do.

In the 1950s, Wilder Penfield (a leader in epilepsy research and care) would map out the brain during epilepsy surgery to lessen the risks associated with removing a piece of brain during the surgery. He noticed that if he stimulated a specific area of the brain, different parts of the body would move. For example, one area would trigger a shoulder twitch, an elbow to move, or a hand to shoot up depending on the location of the brain stimulation. Another area elicited hallucinations or other sensations. One patient famously exclaimed, “I can smell burnt toast!” during one of these mapping procedures.

It was those early studies that allowed stories like Jesse Sullivan’s to be possible. In the past few years, new research on memory improvements, language, and computer brain interfacing have cropped up and they were made possible by those living with epilepsy volunteering their time and their brains while undergoing surgical evaluation. We should be very proud of what the epilepsy community has contributed to brain understanding. Thank you for all that you are doing and continue to do as a community to push the envelope forward in scientific discovery.
The History of the Epilepsy Therapy Project

In 2002 Warren Lammert, father of a child with epilepsy and Orrin Devinsky MD, a renowned epileptologist, founded the Epilepsy Therapy Project (ETP). Warren’s motivation derived from his own struggles to find treatment for his daughter Sylvie. It became clear to him that there was a desperate need for new therapies.

The Epilepsy Therapy Project differed from many other research-driven non-profits focused on epilepsy, in that the focus was squarely placed on helping people now living with epilepsy, not 20 or 30 years in the future. The founders understood that the randomized controlled trials and other research needed to shepherd a new therapy from the laboratory through development, all the way to FDA approval, costs 50-100 million dollars. One option would have been to raise millions of dollars, and to put that money towards a single shot of success. But there was another way.

The Epilepsy Therapy Project took on a mission of finding the best therapies and devices that were along the path, but needed a push at a critical inflection point, that would increase the likelihood of the drug receiving major investment from pharmaceutical and device companies and other sources. They developed several strategies to push new therapies forward, including:

• A “New Therapies Commercialization Grant” for academicians or start-up companies

In October of 2012, inspired by the Institute of Medicine report’s suggestion that the two groups would be stronger together, the Epilepsy Foundation merged with ETP. The original spirit and mission of ETP is still at the core of the research agenda that is now being pursued at the Epilepsy Foundation. Over the years, the methods used by ETP (and now the Epilepsy Foundation) have been shown to be very successful.

Investments of one kind or another by ETP/EF have been contributory in bringing a number of novel therapies and devices to the “finish line” of FDA approval, including the Empatica Embrace, a device that can detect convulsive seizures and alert caregivers, and Epidiolex®, the first drug approved for treatment of Dravet syndrome, to name a few. Moreover, during the years from 2002 to 2020 the pipeline of new therapies and devices has expanded substantially. The Pipeline conference has ensured that there are open lines of communication between the drug and device developers.

The work of the Epilepsy Therapy Project continues within the Epilepsy Foundation, and will ensure that the best therapies are brought forward as rapidly and efficiently as possible.
Epilepsy Foundation In the News

FORMER GRANTEE DR. PATRICK FORCELLI was in the news about his work in identifying “choke-points” in animal models that switch off seizure activity regardless of where the seizure originated. Read more about the work here: https://www.sciencedaily.com/releases/2019/12/191216221243.htm

“The Epilepsy Foundation has been pivotal for my career at multiple stages. The support helped me to continue to do science and has reinforced my commitment to epilepsy research. The first grant I received was an Epilepsy Foundation Fellowship as a graduate student, which helped me to secure follow on funding from NIH. As an Assistant Professor, a grant from the Epilepsy Foundation/American Epilepsy Society helped me launch my lab and generate the preliminary data that led to my first funded R01 (a big grant from NIH). Thank you for all the work you do in supporting early careers!”

- Patrick Forcelli, PhD

CONGRATS TO ZETO, which is developing a new way to do EEG with dry electrodes. Goodbye glue! Zeto won the shark tank in 2016 and in 2018 they became FDA approved. This year, they officially went on the market and just closed their series A financing to move forward! Learn more: https://prn.to/33dZnZZ

Upcoming Research Grants

SUDEP BIOMARKER CHALLENGE
> Submissions open now
Prize for $800,000
www.innocentive.com/ar/challenge/9933784

DRAVET SYNDROME FOUNDATION RESEARCH GRANTS FOR POSTDOCTORAL FELLOWS
> Submissions open August 21, 2020
Up to $50,000 for 1 year
https://www.dravetfoundation.org/research-grant-awards/

DRAVET SYNDROME FOUNDATION RESEARCH GRANTS FOR CLINICIANS AND ESTABLISHED INVESTIGATORS
> Submissions open August 21, 2020
Up to $150,000 over 2 years
https://www.dravetfoundation.org/research-grant-awards/

Do you have questions or a research funding opportunity to share? Email GRANTS@EFA.ORG
Want to donate funds to research? Go to: DONATE.EPILEPSY.COM/DONATE-RESEARCH

LEARN MORE ABOUT THE FOUNDATION’S RESEARCH PRIORITIES AT EPILEPSY.COM/RESEARCH
Clinical Trial Portal List

Clinical trials are the way new treatments are tested for safety and effectiveness before being approved and made available to people with epilepsy.

Go to EPILEPSY.COM/clinical_trials to learn more.

Rare Epilepsy Syndrome Trials

CANNABIDIOL AS AN ADD-ON THERAPY IN TUBEROUS SCLEROSIS COMPLEX
This study is looking at how effective and safe cannabidiol (CBD) is in people 1 year to 65 years old living with Tuberous Sclerosis Complex (TSC). CBD is given in addition to their current anti-seizure medications.

PREVENTING EPILEPSY USING VIGABATRIN IN INFANTS WITH TUBEROUS SCLEROSIS COMPLEX
This Phase IIb trial will test whether earlier treatment versus standard treatment with vigabatrin in infants with tuberous sclerosis complex (TSC) will have a positive impact on developmental outcomes at 24 months of age. It also tests whether early treatment prevents or lowers the risk of developing infantile spasms and refractory seizures. It is a randomized, double-blind, placebo-controlled clinical trial design. Infants under the age of 6 months diagnosed with TSC but without history of seizures or infantile spasms may be eligible.

FOCUSED ULTRASOUND FOR TREATMENT OF EPILEPSY
The University of Virginia Comprehensive Epilepsy Program is conducting a research study on the use of focused ultrasound to treat deep lesions in the brain causing intractable epilepsy in adults 18 to 80 years old. The study will evaluate the effectiveness and safety of an investigational device that uses ultrasound or sound waves from outside the head to treat seizures that are not well controlled by medication and are due to a small growth of abnormal cells in the middle of the brain, most commonly hypothalamic hamartomas.

PERAMAPANEL STUDY FOR INFANTS WITH EPILEPSY
This clinical research study is being done to learn more about the safety of Perampanel (E2007), the study drug, and how well it’s tolerated in infants, from 1 month to less than 24 months old (<2 years), who have epilepsy.

Focal (Partial-Onset) Seizures Trials

ESLICARBZEPINE ACETATE (ESL) AS FIRST OR LATER ADD-ON THERAPY FOR THE TREATMENT OF PARTIAL-ONSET SEIZURES
This study is looking at how effective and safe eslicarbazepine acetate (also known as ESL) is in people 18 years of age or older with partial-onset (focal) seizures, when it is added to their current anti-seizure medication(s).

PFIZER A0081096: LOOKING FOR CHANGES IN EYESIGHT FROM USING PREGABALIN
This study will look at people between 18-65 years old, taking their own anti-seizure medications in addition to either the study drug (Pregabalin) or a placebo. The aim is to look for changes in eyesight.

EPILEPSY FOUNDATION’S HUMAN EPILEPSY PROJECT (HEP2): RESISTANT FOCAL SEIZURES STUDY
This study, the Human Epilepsy Project 2: Resistant Focal Seizures (HEP2) is designed to better understand the challenges of living with focal seizures that do not respond to medication and determine biomarkers of epilepsy severity and treatment response.

Focal or Generalized Seizures Trials

STEREOTACTIC LASER ABLATION FOR TEMPORAL LOBE EPILEPSY (SLATE)
This study is looking at the safety and efficacy of MRI-guided laser ablation therapy with Visualase™ (laser ablation may also be called laser interstitial thermal therapy or LITT) for seizures coming from the temporal lobe in people who are taking seizure medicines.

EFFECTIVENESS OF INHALED STACCATO ALPRAZOLAM IN TREATING AN EPISODE OF FOCAL OR GENERALIZED SEIZURES
A new clinical trial is looking at how effective and safe orally-inhaled alprazolam (also known as STAP-001) is in people 18 years of age or older with focal or generalized epilepsy when given at the time of a seizure episode. This study is commonly referred to as StATEs (Staccato Alprazolam Terminates Epilepsy Seizures).
Upcoming Conferences

4TH INTERNATIONAL SLC13A5 DEFICIENCY RESEARCH ROUNDTABLE
March 23, 2020 • Dallas, TX

CURING THE EPILEPSIES: SETTING RESEARCH PRIORITIES
April 13–15, 2020 • Bethesda, MD
Postponed until January 4–6, 2021

PHELAN-MCDERMID SYNDROME FOUNDATION CONFERENCE
July 22–25, 2020 • Kissimmee, FL

GORDON RESEARCH CONFERENCE (GRC) ON MECHANISMS OF EPILEPSY AND NEURONAL SYNCHRONIZATION
August 15–21, 2020 • Barcelona, Spain

Have a conference that you want to share? Email CONTACTUS@EFA.ORG

Mission

Epilepsy Foundation is a nationwide network organization on a mission to lead the fight to overcome the challenges of living with epilepsy and to accelerate therapies to stop seizures, find cures, and save lives.

We’re mobilizing action to END EPILEPSY.