Epilepsy – A Window on the Brain

Epilepsy, one of the most common neurological disorders, is an umbrella of 40 syndromes known as the epilepsies. Since the early 20th century, epilepsy has provided researchers with unparalleled avenues to discover how the brain is structured and how it functions: a true ‘window on the brain.’

Rapidly emerging technologies and novel imaging techniques, coupled with the identification of new genes, have given researchers and clinicians an extraordinary ability to explore the brain at the cellular, genetic and neural levels. While current epilepsy research may seem like it’s ripped from the pages of a science fiction novel, it’s real—and even pretty cool. Most importantly, revelations arising from this work have given new hope to the 2.3 million Americans living with the condition.

Today’s epilepsy research is unfolding at a time when the U.S. and European governments are investing unprecedented funds in understanding brain function. When announcing support under the Federal BRAIN Initiative, Francis Collins, M.D., Ph.D., NIH Director said, “The human brain is the most complicated biological structure in the known universe. We’ve only just scratched the surface in understanding how it works – or, unfortunately, doesn’t quite work – when disorders and disease occur.”

The amazing work underway by researchers around the globe is not only informing our understanding of epilepsy, but it is helping shed light on other disorders with similar underlying mechanisms. Autism, cerebral palsy, tuberous sclerosis, neurofibromatosis and Alzheimer’s disease are just a few of the conditions that benefit from epilepsy research.

To celebrate Epilepsy Awareness Month, AES will highlight groundbreaking developments made within the last 10-50 years, made possible by the tens of thousands of people who have dedicated their life’s work to eradicating epilepsy and its consequences.
Advances in Antiepileptic Drugs

Antiepileptic drugs, or AEDs, are the primary form of treatment for people with epilepsy. Up to 70% of people with this condition rely on AEDs to control their seizures.

Just as epilepsy can take many different forms, AEDs come in a variety of formulations. The specific mechanism of each drug may differ, but most AEDs share a common goal: calming the excessive electrical activity of neurons that cause seizures. Increasingly, these drugs are being recognized for their usefulness in non-epileptic neurological disorders as well, such as neuropathic pain, migraine, bipolar disorder and fibromyalgia.

More than 15 new AEDs have been approved in the last 25 years, and epilepsy research continues to unveil versions that are more effective, better tolerated, safer and/or have improved drug interaction profiles. These advances have made it easier for patients to take consistently and have raised the quality of life for numerous people with epilepsy.

Despite this exciting progress, however, more than 400,000 Americans continue to live with treatment-resistant epilepsy. Since 1975, this problem has been tackled by thousands of researchers at universities, biotech companies, and traditional pharmaceutical companies around the globe through collaboration in the National Institutes of Health Federal Anticonvulsant Screening Program, a remarkably effective public-private partnership.

Researchers in this program screen an average of 800 new chemical entities annually using a series of laboratory or live cell (in vitro or in vivo) models. The research in this program goes two ways -- new compounds are developed to impact the behavior of different types of neurons known to be active in many types of epilepsy and scientists take drugs that are found to have antiepileptic properties and break them down to better understand what makes them work. The results of these studies can be evaluated against a global database of other research findings and existing AEDs, enhancing global collaboration and shaving years from the lengthy process of drug development.

These new discoveries -- and many others in progress-- are providing much-needed hope for people suffering from the side effects of current AEDs and those afflicted with poorly controlled or drug-resistant seizures.

Sources:
Mapping the Brain – A Window with a View

Google Earth and GPS offer maps with varying levels of detail – from continents and countries down to cities, highways and individual buildings. Each layer, sector and structure on a map plays a specific role in the function or dysfunction of our planet.

Brain mapping works in much the same way. It illustrates the brain’s structures; its channels and functions. In other words, it reveals the parts of the brain responsible for certain abilities. Brain mapping uses images and data points to create internal and external representations of the brain, ranging from broad views of the whole brain, brain regions and more precise views of specialized centers, neuron "bundles," neuron circuits and even single neurons.

Scientists have been working for nearly a century on this massive map, and epilepsy researchers have played a key role since the very beginning.

An Early Look
In the 1930s, Wilder Penfield began to create the first maps of the brain’s sensory and motor cortices after treating patients with epilepsy. Penfield’s sketch and notes on various functioning areas are displayed upside down as viewed by a surgeon, with the frontal lobe to the left and the occipital lobe to the right.

Electroencephalography (EEG) emerged during this period, allowing scientists to record brain waves and rhythms for the first time – and to explore changes to these patterns in people with epilepsy. This technology allowed Penfield and Herbert Jasper to be the first to use direct cortical recording and brain stimulation in a systematic way in people with epilepsy.

A New Light on Brain Mapping
Young people weren’t the only ones lighting up in the 1970s. Two imaging tools – proton emission tomography (PET) invented by M.E. Phelps and computerized tomography (CT) invented by Godfrey Hounsfield – allowed researchers to light up the brain and visualize it at work. To this day, PET and CT scans remain important tools to reveal abnormalities in the brain and detect regions responsible for seizures.

The last 30 years have seen an explosion of new technologies. The invention of magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI) offer researchers a way to see specific elements of tissue and monitor changes in the brain during various activities. The newest technologies allow researchers to see all the connections between neurons in an intact brain.

So Why Map the Brain?
The answer is simple: A complete brain map will show us where we’re going, and reveal the research and treatment tools needed to get us there. Researchers are using brain maps to understand how the brain functions and how to correct malfunctions in conditions like epilepsy. Brain mapping is also a practical tool for doctors. Neurosurgeons use brain mapping to plan safer surgeries and to develop better treatments. Epilepsy surgery is the most effective and one of the most underutilized treatments for the many people for whom medications are not effective. Epilepsy surgery requires precise mapping to distinguish the extent of the seizure generating brain regions and the areas critical for functions like movement, speech, sensation and memory.

Sources:

Epilepsy Devices – A New Window to Seizure Control

Researchers and doctors began their quest to end seizures in the early 20th century and, in the process, gave birth to the field of neuroengineering. Today this field offers new hope for people with epilepsy, especially for the nearly 400,000 Americans who live with uncontrolled seizures. Since the 1970s, a growing number of researchers in neurology, neurosurgery and neuroscience have focused their efforts on actively modulating neuron functions, networks and behaviors. Knowing when a seizure might happen — or stopping it before it happens — could dramatically improve the quality of life and increase the independence of people with epilepsy.

Neuroengineering, while still a relatively young field, is a rapidly emerging avenue for collaboration among clinicians, neuroengineers and others in the technology industry. These collaborations continue to uncover novel strategies for the treatment and continued study of epilepsy and other neurological diseases.

Major Advances in the Past 15 Years
Implantable devices have garnered widespread attention in recent years. These innovative devices are designed to predict, detect, prevent and abort seizures. Clinical trials of these technologies are yielding exciting results and, once FDA approved, these tools could potentially change the lives of people with uncontrolled epilepsy as part of standard clinical care.

Vagus nerve stimulation (VNS) therapy involves implanting a small device, similar to a heart pacemaker, in the upper chest and connecting it to the left vagus nerve in the patient’s neck. The device, approved by the Food and Drug Administration (FDA), sends regular electrical stimulation via the vagus nerve into the brain. Some patients find that this reduces the number, length or severity of their seizures. Often, VNS is used in conjunction with anti-epileptic drugs (AEDs).

Responsive Neurostimulation System (RNS) was approved by the Food and Drug Administration in 2013. Electrodes are placed on the surface of the brain or deep inside the brain at the site where the seizures are thought to originate. The device is trained, through a process known as ‘machine learning,’ to detect the patient’s specific abnormal electroencephalography (EEG) patterns. It then delivers a burst of stimulation to the area to abort the seizure.

Deep brain stimulation (DBS) therapy involves implanting electrodes into specific areas of the brain. These electrodes give direct electrical stimulation to the part of the brain that modulates seizure activity and seizure spread. Like VNS therapy, DBS aims to reduce the number, length or severity of seizures and is usually used alongside anti-epileptic drugs. This device also helps treat Parkinson’s disease, anorexia and some sleep disorders.

Work on the Horizon
Scientists are working on a device that can be implanted between the skull and brain surface to monitor electrical signals in the brain via EEG. A second device, implanted under the chest, transmits signals from electrodes in the brain to a hand-held device, providing a series of lights that warn patients of a high (red), moderate (white), or low (blue), likelihood of a seizure in the hours ahead.

Another device is worn in the ear canal, similar to a hearing aid, and measures the brain’s electric signals over several days using a process called EEG. This device is currently in development and may lead to applications for people with epilepsy.

In addition to these devices, scientists are applying findings from epilepsy research to the development of computer-brain interfaces that allow for artificial speech or for the development of treatments for certain speech disorders and face blindness, a condition that prevents a person from distinguishing one face from another.

The technologies underlying these devices are improving every day. To advance neuroengineering in epilepsy, the American Epilepsy Society (AES) has teamed with the National Institute of Neurological Disorders and Stroke, and Epilepsy Foundation to launch the Seizure Detection Challenge. This international competition is challenging the best minds in the field of machine learning to develop and improve devices to track and treat epilepsy. The winners of the competition will be announced in December at the 68th AES Annual Meeting.

**Sources:**


Optogenetics – Emerging Technology Bringing New Light to Epilepsy

Scientists estimate that the human brain contains upwards of 86 billion neurons, neatly assembled into channels of a complex communication network. It is the role of neuroscience to unravel the mysteries of these intricate channels—but when one of the channels is damaged or misfiring, it becomes that much more complicated to unravel.

One of the hottest research tools in neuroscience today is optogenetics, a technique that uses gene therapy to deliver light-sensitive proteins to specific cells. Optogenetics combined with imaging techniques such as functional Magnetic Resonance Imaging, or fMRI, will help reveal how the brain works and deliver new treatments.

What’s radical and novel about optogenetics is that it allows scientists to interact with a single cell, or a network of cells, with exquisite precision. Imaging and other technologies allow researchers to watch the brain in action; optogenetics enables them to influence that action, tinkering with specific parts of the brain at specific times to study the response.

Over the past 10 years, neuroscience has been transformed by optogenetics. The speed of discovery and its application to human conditions is running at a pace rarely seen in science. This relatively new technique already has second-generation applications and technologies in development.

Researchers now use optogenetics to target—and control—specific sections of the brain related to seizures. Some scientists liken this new tool to flipping a light switch within the brain. With this innovative technique, it is now possible not only to record neuronal activity during and between seizures, but also to test causality and identify potential new therapeutic approaches.

AES member and University of California researcher Ivan Soltesz, Ph.D., received one of the first NIH BRAIN awards for his work with optogenetics and epilepsy. “Seizures occur when brain cells start firing abnormally and rapidly, like a car speeding out of control,” said Soltesz. “Using optogenetics, we can deliver a pulse of light that activates the brain’s own system for slowing down runaway cells. We either decreased the activity of the gas pedal or increased the activity of the brake. In this way, we succeeded in making the seizures stop when the light came on.”

Sources: