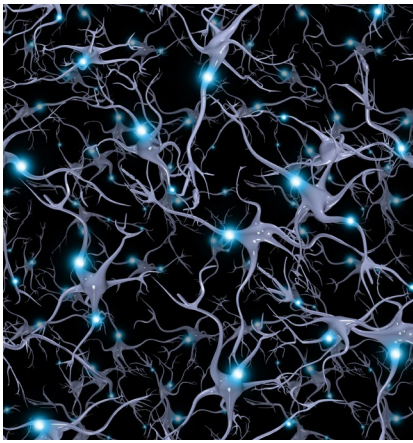
The Epilepsies and Seizures

Hope Through Research

National Institute of Neurological Disorders and Stroke
National Institutes of Health

Table of Contents

What are the epilepsies?



Clusters of brain cells (neurons) sometimes fire or signal faster than normal—as many as 500 times a second. This surge of excessive electrical activity causes seizures.

The epilepsies are chronic neurological disorders in which clusters of nerve cells, or neurons, in the brain sometimes signal abnormally and cause seizures. During a seizure, many neurons fire (signal) at the same time – as many as 500 times a second, much faster than normal. This surge of excessive electrical activity happening at the same time causes involuntary movements, sensations, emotions, and behaviors and may cause a temporary loss of awareness.

Epilepsy has many different causes, different seizure types, and can vary in severity and impact from person to person. Some people may have *convulsions*[1] (sudden onset of repetitive general contraction of muscles) and lose consciousness. Others may simply stop what they are doing, have a brief lapse of awareness, and stare blankly into space for a short period. Some people have seizures very infrequently, while others may have hundreds of seizures each day.

Having a single seizure doesn't mean someone has epilepsy. In general, a person is considered to have epilepsy when he or she has had two or more unprovoked seizures separated by at least

[1] Terms in italics appear in a Glossary found at the end of this document.

24 hours. A provoked seizure is one caused by a known precipitating factor such as a high fever, nervous system infections, acute traumatic brain injury, or fluctuations in blood sugar or electrolyte levels.

Anyone can develop epilepsy. About 2.3 million adults and more than 450,000 children and adolescents in the United States currently live with epilepsy. Each year, an estimated 150,000 people are diagnosed with epilepsy. Most people with epilepsy have seizures that can be controlled with drug therapies and surgery. However, as much as 30 to 40 percent of people with epilepsy continue to have seizures because available treatments do not completely control their seizures (called *intractable* or medication resistant epilepsy).

While some people with epilepsy require lifelong treatment to control their seizures, for others the seizures eventually go away. The odds of becoming seizure-free are not as good for adults or for children with severe epilepsy syndromes, but it is possible that seizures may decrease or even stop over time.

What causes the epilepsies?

The epilepsies have many possible causes, but for up to half of people with epilepsy that cause is unknown. Some epilepsies are clearly linked to genetic factors. The brain's attempts to repair itself after a traumatic head injury, stroke, infection, brain tumor, or other identifiable problem may inadvertently generate abnormal

nerve connections that lead to epilepsy. Brain malformations and abnormalities in brain wiring that occur during brain development also may disturb neuronal activity and lead to epilepsy. Anything that disturbs the normal pattern of neuronal activity can lead to seizures.

Genetics

Genetic mutations may play a key role in the development of certain epilepsies. Many types of epilepsy affect multiple blood-related family members, pointing to a strong inherited genetic component, but gene mutations may occur spontaneously and contribute to development of epilepsy in people with no family history of the disorder (called "*de novo*" mutations). Overall, researchers estimate that hundreds of genes could play a role in the disorders.

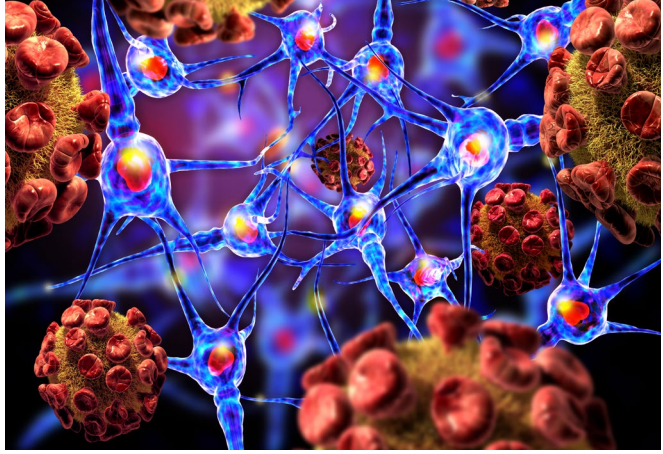
Researchers have linked some genes to specific types of epilepsy. Other genetic mutations may not cause epilepsy but may influence the disorder in other ways. For example, genes may control a person's susceptibility to seizures (seizure threshold) by affecting brain development.

Researchers estimate that hundreds of genes may play a role in the epilepsies.

Other Disorders

Epilepsies may develop as a result of brain damage associated with many types of conditions that disrupt normal brain activity, including:

- brain tumors, including those associated with neurofibromatosis or tuberous sclerosis complex, two inherited conditions that cause benign tumors called hamartomas to grow in the brain
- head trauma resulting from an accident or other traumatic injury
- alcoholism or alcohol withdrawal
- Alzheimer's disease
- strokes, heart attacks, and other conditions that deprive the brain of oxygen (a significant portion of new-onset epilepsy in elderly people is due to stroke or other cerebrovascular disease)
- abnormal blood vessel formation (arteriovenous malformations) or bleeding in the brain (hemorrhage)
- inflammation of the brain
- infections such as meningitis, HIV, and viral encephalitis
- abnormalities of brain development or other neurodevelopmental disorders. Seizures are more common, for example, among individuals with cerebral palsy, autism spectrum disorder, or intellectual impairment.



Many conditions—including infections such as meningitis and viral encephalitis—that disrupt normal brain activity can lead to epilepsy. This illustration depicts a virus attacking brain cells.

Seizure Triggers

Seizure triggers (phenomena that trigger seizures in some people) do not cause epilepsy but can provoke first seizures in those who are susceptible or can cause seizures in people with epilepsy who otherwise experience good seizure control with their medication. Seizure triggers include:

- alcohol consumption or alcohol withdrawal
- dehydration or missing meals
- stress
- hormonal changes associated with the menstrual cycle
- exposure to toxins or poisons such as lead or carbon monoxide
- excessively large doses of antidepressants or other prescribed medications
- sleep deprivation
- visual stimulation, such as flashing lights or moving patterns (a symptom of a condition known as photosensitive epilepsy)

What are the different kinds of seizures?

Seizures are divided into two major categories – *focal seizures* and *generalized seizures*. However, there are many different types of seizures in each of these categories. In fact, doctors have described more than 30 different types of seizures.

Focal Seizures

Focal seizures originate in just one part of the brain. About 60 percent of people with epilepsy have focal seizures. These seizures are frequently described by the area of the brain in which they originate. Many people are diagnosed with focal frontal lobe or medial temporal lobe seizures.

In some focal seizures, the person remains conscious but may experience motor, sensory, or psychic feelings (for example, intense dejà vu or memories) or sensations that can take many forms. The seizure may affect emotions or cause the person to hear, smell, taste, see, or feel things that are not real. There may be movement of just one part of the body, for example, just one hand.

In other focal seizures, a change in consciousness can produce a dreamlike experience, where an individual may display strange, repetitious behaviors such as blinks, twitches, and mouth movements (often like chewing or swallowing, or even walking in a circle). These repetitious movements are called automatisms. These seizures usually last just a minute or two.

Some people with focal seizures may experience *auras* – unusual sensations that warn of an impending seizure. Auras are usually focal seizures without interruption of awareness but some people experience a true warning before an actual seizure. Other people with epilepsy report experiencing a *prodrome*, a feeling that a seizure is imminent lasting hours or days.

Absence seizures—a type of generalized seizure—can cause a person to appear to be staring into space.

The symptoms of focal seizures can easily be confused with other disorders such as narcolepsy, fainting, or even mental illness. Several tests and careful monitoring are needed to diagnose epilepsy from other disorders.

Generalized Seizures

Generalized seizures result from abnormal neuronal activity that rapidly emerges on both sides of the brain. These seizures may cause loss of consciousness, falls, or a muscle's massive contractions. The many kinds of generalized seizures include:

- *Absence seizures*, previously called petit mal seizures, may cause the person to appear to be staring into space with or without slight twitching of the muscles.

- *Tonic seizures* cause stiffening of muscles of the body, generally those in the back, legs, and arms.
- *Clonic seizures* cause repeated jerking movements of muscles on both sides of the body.
- *Myoclonic seizures* cause jerks or twitches of the upper body, arms, or legs.
- *Atonic seizures* cause a loss of normal muscle tone, which often leads the affected person to fall down or drop the head involuntarily.
- *Tonic-clonic seizures*, previously called grand mal seizures, cause a combination of symptoms, including stiffening of the body and repeated jerks of the arms and/or legs as well as loss of consciousness.
- Secondary generalized seizures.

Not all seizures can be easily defined as either focal or generalized. Some people have seizures that begin as focal seizures but then spread to the entire brain. Other people may have both types of seizures but with no clear pattern.

Some people recover immediately after a seizure, while others may take minutes to hours to feel as they did before the seizure. During this time, they may feel tired, sleepy, weak, or confused. After a seizure, some people may experience headache or pain in muscles that contracted.

What are the different kinds of epilepsy?

Just as there are many different kinds of seizures, there are many different kinds of epilepsy. Hundreds of different epilepsy syndromes – disorders characterized by a specific set of symptoms that include epilepsy as a prominent symptom – have been identified. Some of these syndromes appear to be either hereditary or caused by de novo mutations. For other syndromes, the cause is unknown. Epilepsy syndromes are frequently described by their symptoms or by where in the brain they originate.

Absence epilepsy is characterized by repeated seizures that cause momentary lapses of consciousness. These seizures almost always begin in childhood or adolescence and tend to run in families. Individuals may show body movements such as a jerking arm or rapidly blinking eyes, while others appear to be staring off into space. Immediately after a seizure, the person can resume whatever he or she was doing. Absence seizures may occur so frequently (in some cases up to 100 or more a day) that the person cannot concentrate in school or other situations. Childhood absence epilepsy usually stops at puberty. Most children with childhood absence epilepsy have a good prognosis but there may be long-lasting negative consequences and some children will continue to have absence seizures into adulthood and/or go on to develop other seizure types.

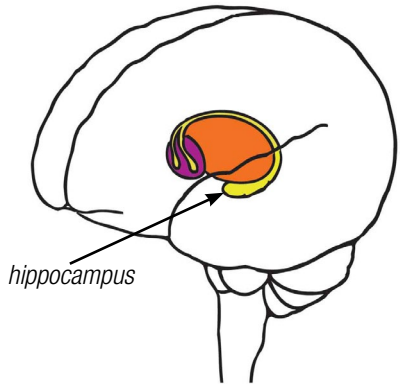
Frontal lobe epilepsy features brief focal seizures that may occur in clusters. It can affect the part of the brain that controls movement. Seizures can cause muscle weakness or abnormal, uncontrolled movement such as twisting, waving the arms or legs, eye deviation to one side, or grimacing, and are usually associated with some loss of awareness. Seizures usually occur when the person is asleep.

Temporal lobe epilepsy, or TLE, is the most common epilepsy syndrome with focal seizures. The seizure itself is a brief period of impaired consciousness, with symptoms that may include auras of nausea, emotions, or unusual smell or taste. TLE often begins in childhood or teenage years.

Neocortical epilepsy is characterized by seizures that originate from the brain's cortex, or outer layer. The seizures can be either focal or generalized. Symptoms may include unusual sensations, visual hallucinations, emotional changes, muscle contractions, convulsions, and a variety of other symptoms, depending on where in the brain the seizures originate.

There are many other types of epilepsy that begin in infancy or childhood. For example, *infantile spasms* are clusters of seizures that usually begin before the age of 6 months. During these seizures infants may drop their head, jerk an arm, bend at the waist and/or cry out. Children with *Lennox-Gastaut syndrome* have several different types of seizures, including atonic seizures, which cause sudden falls and are also called drop attacks. Seizure onset is usually

before age four years. This severe form of epilepsy can be very difficult to treat effectively. *Rasmussen's encephalitis* is a progressive form of epilepsy in which half the brain shows chronic inflammation. Some childhood epilepsy syndromes, such as childhood absence epilepsy, tend to go into remission or stop entirely during adolescence, whereas other syndromes such as *juvenile myoclonic epilepsy* (which features jerk-like motions upon waking) and Lennox-Gastaut syndrome are usually present for life once they develop. *Lafora disease* is a severe, progressive form of myoclonic epilepsy that begins in childhood. Children with *Dravet syndrome* have seizures that start before age one and later in infancy develop into other seizure types.



According to research, repeated temporal lobe seizures are often associated with shrinkage and scarring of the hippocampus—a part of the brain important for memory and learning.

Hypothalamic hamartoma is a rare form of epilepsy that first occurs during childhood and is associated with malformations of the hypothalamus at the base of the brain. People with hypothalamic hamartoma have seizures that resemble laughing or crying. Such seizures frequently go unrecognized and are difficult to diagnose.

When are seizures not epilepsy?

While any seizure is cause for concern, having a seizure does not by itself mean a person has epilepsy. First seizures, febrile seizures, nonepileptic events, and eclampsia (a life-threatening condition that can occur in pregnant women) are examples of conditions involving seizures that may not be associated with epilepsy. Regardless of the type of seizure, it's important to inform your doctor when one occurs.

First Seizures

Many people have a single seizure at some point in their lives. The seizure can occur with or without any obvious triggering factor. Many people with a first seizure will never have a second seizure.

Physicians often counsel against starting antiseizure drugs after a first seizure. In some cases where additional epilepsy risk factors are present, drug treatment after the first seizure may help prevent future seizures. Evidence suggests that it may be beneficial to begin antiseizure medication once a person has had a second unprovoked seizure, as the chance of future seizures increases significantly after this occurs. A person with a pre-existing brain problem, for example, a prior stroke or traumatic brain injury, will have a higher risk of experiencing a second seizure. In general, the decision to start antiseizure medication is based on the doctor's assessment of many factors that influence how likely it is that another seizure will occur in that person.

Febrile Seizures

Some children have a seizure during an illness with a high fever. These seizures are called *febrile seizures*. Antiseizure medications following a febrile seizure are generally not warranted unless certain other conditions are present: a family history of epilepsy, signs of nervous system impairment prior to the seizure, or a relatively prolonged or complicated seizure. Researchers also have identified several different genes that influence the risks associated with febrile seizures in certain families. The risk of subsequent non-febrile seizures is low unless one of these factors is present.

Febrile seizures, which occur in infants and children, may arise during the course of an illness with a high fever.

Nonepileptic Events

An estimated 5 to 20 percent of people diagnosed with epilepsy actually have non-epileptic seizures (NES), which outwardly resemble epileptic seizures, but are not associated with seizure-like electrical discharge in the brain. Non-epileptic events may be referred to as psychogenic non-epileptic seizures or PNES, which do not respond to antiseizure drugs. Some people with epilepsy have psychogenic seizures in addition to their epileptic seizures.

Other nonepileptic events may be caused by narcolepsy (sudden attacks of sleep), Tourette syndrome (repetitive involuntary movements called tics), irregular heartbeat, and other medical conditions with symptoms that resemble seizures. Because symptoms of these disorders can look very much like epileptic seizures, they are often mistaken for epilepsy.

Are there special risks associated with the epilepsies?

Although most people with epilepsy lead full, active lives, there is an increased risk of death or serious disability associated with epilepsy and some antiseizure medications. Two life-threatening conditions associated with the epilepsies are *status epilepticus* and *sudden unexpected death in epilepsy (SUDEP)*.

Status Epilepticus

A person with status epilepticus either has an abnormally prolonged seizure or does not fully regain consciousness between recurring seizures. Status epilepticus can be convulsive (in which outward signs of a seizure are observed) or nonconvulsive (which has no outward signs and is diagnosed by an abnormal EEG). Nonconvulsive status epilepticus may appear as a sustained episode of confusion, agitation, loss of consciousness, or even coma.

Any seizure lasting longer than 5 minutes should be treated as though it was status epilepticus.

There is some evidence that 5 minutes is sufficient to damage neurons and that seizures are unlikely to end on their own, making it necessary to seek medical care immediately. The mortality rate can be as high as 20 percent if treatment is not initiated promptly.

Sudden Unexpected Death in Epilepsy (SUDEP)

People with epilepsy have an increased risk of sudden unexpected death. Some studies suggest that each year approximately one case of SUDEP occurs for every 1,000 people with the epilepsies. People with more difficult to control seizures tend to have a higher incidence of SUDEP.

SUDEP can occur at any age. Researchers are still unsure why SUDEP occurs. People with epilepsy may be able to reduce the risk of SUDEP by taking all antiseizure medication as prescribed; this is particularly important for individuals who take more than one medication for their epilepsy.

How are the epilepsies diagnosed?

A number of tests are used to determine whether a person has a form of epilepsy and, if so, what kind of seizures the person has.

Medical history. A doctor will ask for details about any past illnesses or other symptoms a person may have had, any warning experience, as well as any family history of seizures. Since people who have suffered a seizure often do not remember what happened, caregiver or other accounts of seizures are vital to this evaluation.

Blood samples may be used to screen for disorders associated with seizures and to check for underlying health conditions.

Blood tests. Blood samples may be taken to screen for metabolic or genetic disorders that may be associated with the seizures. They also may be used to check for underlying health conditions such as infections, lead poisoning, anemia, and diabetes that may be causing or triggering the seizures.

Developmental, neurological, and behavioral tests. These tests that measure motor abilities, behavior, and intellectual ability can help determine how epilepsy is affecting an individual and provide clues about what kind of epilepsy the person has.

Imaging and monitoring. These tests can help record electrical activity and identify brain structures or abnormalities that may lead to seizures.

- An electroencephalogram, or EEG, can assess whether there are any detectable abnormalities in the person's brain waves and may help to determine if antiseizure drugs would be of benefit. This most common diagnostic test for epilepsy records electrical activity detected by electrodes placed on the scalp. Whenever possible, an EEG should be performed within 24 hours of an individual's first seizure.
- A magnetoencephalogram (MEG) detects the magnetic signals generated by neurons to help detect surface abnormalities in brain activity. MEG can be used in planning a surgical strategy

to remove focal areas involved in seizures while minimizing interference with brain function.

- The most commonly used brain scans include CT (computed tomography), PET (positron emission tomography) and MRI (magnetic resonance imaging). CT and MRI scans reveal structural abnormalities of the brain such as tumors and cysts, which may cause seizures. A type of MRI called functional MRI (fMRI) can be used to localize normal brain activity and detect abnormalities in functioning. PET scans can be used to identify brain regions with lower than normal metabolism, a feature of the epileptic focus after the seizure has stopped.
- SPECT (single photon emission computed tomography) is sometimes used to locate seizure foci in the brain.

Can the epilepsies be prevented?

Currently there are no medications or other therapies that have been shown to prevent epilepsy. In some cases, the risk factors that lead to epilepsy can be modified. Good prenatal care may prevent brain injury in the developing fetus that may lead to epilepsy and other neurological problems. Treating cardiovascular disease, high blood pressure, infections such as meningitis in high-risk populations, and other disorders that can affect the brain during adulthood and aging also may prevent some cases of epilepsy. Wearing seatbelts and bicycle helmets, and correctly securing children in car seats, may avert some cases of epilepsy associated with head trauma.

How can epilepsy be treated?

Once epilepsy is diagnosed, it is important to begin treatment as soon as possible. Research suggests that medication and other treatments may be less successful once seizures and their consequences become established. Several treatment approaches can be used depending on the individual and the type of epilepsy. If seizures are not controlled quickly, referral to an epileptologist at a specialized epilepsy center should be considered, so that careful consideration of treatment options, including dietary approaches, medication, devices, and surgery, can be performed in order to gain optimal seizure treatment. An epileptologist is someone who has completed advanced training and specializes in treating the epilepsies.

Medications

The most common approach to treating the epilepsies is with medication. More than 20 different antiseizure medications are available today, all with different benefits and side effects. Most seizures can be controlled with one drug (called *monotherapy*).

Antiseizure medications are the most common treatment for epilepsy. There are more than 20 different such medications available today—all with different benefits and side effects.

Deciding on which drug to prescribe, and at what dosage, depends on many different factors, including seizure type, lifestyle and age, seizure frequency, drug side effects, medicines for other conditions, and, for a woman, whether she is pregnant or will become pregnant. It may take several months to determine the best drug and dosage, and the effectiveness of a medication can diminish over time, which can increase the risk of seizures. If one treatment is unsuccessful, another may work better.

Seizure Medications include:

Generic	Brand Name (United States)
Carbamazepine	Carbatrol, Tegretol
Clobazam	Frisium, Onfi
Clonazepam	Klonopin
Diazepam	Diastat, Diazepam, Valium
Divalproex Sodium	Depakote, Depakote ER
Eslicarbazepine Acetate	Aptiom
Ezogabine	Potiga
Felbamate	Felbatol
Gabapentin	Neurontin
Lacosimide	Vimpat
Lamotrigine	Lamictal
Levetiracetam	Keppra, Keppra XR
Lorazepam	Ativan
Oxcarbazepine	Oxtellar, Oxtellar XR, Trileptal
Perampanel	Fycompa
Phenobarbital	
Phenytoin	Dilantin, Phenytek,
Pregabalin	Lyrica
Primidone	Mysoline
Rufinamide	Banzel
Tiagabine Hydrochloride	Gabitril
Topiramate	Topamax, Topamax XR
Valproic Acid	Depakene
Vigabatrin	Sabril

In June 2018, the U.S. Food and Drug Administration approved cannabidiol (Epidolex) for the treatment of seizures associated with Lennox-Gastaut and Dravet syndromes for people ages 2 and older. The drug contains only a small amount of the psychoactive element in marijuana and does not induce euphoria associated with the drug.

Some people with epilepsy may need a combination of drugs to control or reduce the frequency of their seizures. However, combining medications may amplify side effects such as fatigue and dizziness or interact with many other drugs in potentially harmful ways.

The chance that someone will eventually be able to discontinue antiseizure medication varies depending on the person's age and type of epilepsy. Some people with epilepsy may be advised to discontinue their antiseizure drugs after 2-3 years have passed without a seizure. Others may be advised to wait for 4 to 5 years, and others may need to continue their medications. More than half of children who go into remission with medication can eventually stop their medication without having new seizures. The odds of successfully stopping medication are not as good for people with a family history of epilepsy, those who need multiple medications, those with focal seizures, and those who continue to have abnormal EEG results while on medication. Discontinuing medication should always be done with supervision of a health care professional

There are specific syndromes in which certain antiseizure medications should not be used because they may make the seizures worse. For example, carbamazepine can worsen epilepsy in children diagnosed with Dravet syndrome.

Surgery

Surgery is generally recommended only when focal seizures persist after the person has tried at least two well-tolerated medications, or if there is an identifiable brain lesion (a dysfunctional part of the brain) believed to cause the seizures. When someone is considered to be a good candidate for surgery experts generally agree that it should be performed as early as possible.

Surgical evaluation takes into account the seizure type, the brain region involved, and the importance of the area of the brain where seizures originate (called the focus) for everyday behavior. In general, people have a better chance of becoming seizure-free after surgery if they have a small, well-defined seizure focus. Surgeons usually avoid operating in areas of the brain that are necessary for speech, movement, sensation, memory and thinking, or other important abilities.

Surgery for epilepsy does not always successfully reduce seizures and can result in cognitive or personality changes as well as physical disability. Nonetheless, when medications fail, several studies have shown that surgery is much more likely to make someone seizure-free compared to attempts to use other medications. Even when surgery completely ends a person's seizures, it is important to continue taking

Surgery can significantly reduce or even halt seizures in some people, although it involves some level of risk.

antiseizure medication for some time. Doctors generally recommend continuing medication for at least two years after a successful operation to avoid recurrence of seizures.

Surgical procedures for treating epilepsy disorders include:

- Lobectomy or lesionectomy involve removing the defined area of the brain that cause focal seizures. The most common type of lobectomy is a temporal lobe resection (in which all or part of the affected temporal lobe of the brain is removed), which is performed for people with medial temporal lobe epilepsy.
- Multiple subpial transection may be performed when seizures originate in part of the brain that cannot be removed. It involves making a series of cuts that are designed to prevent seizures from spreading into other parts of the brain while leaving the person's normal abilities intact.
- Corpus callosotomy, or severing the network of neural connections between the right and left halves (hemispheres) of the brain, is done primarily in children with severe seizures that start in one half of the brain and spread to the other side. Corpus callosotomy can end drop attacks and other generalized seizures. However, the procedure does not stop seizures in the side of the brain where they originate, and these focal seizures may even worsen after surgery.
- Hemispherectomy (surgery to remove or disable of one hemisphere of the brain) and hemispherotomy (surgery to remove half of the brain's cortex, or outer layer) are used predominantly in children

who have seizures that do not respond to medication because of damage that involves only half the brain, as occurs with conditions such as Rasmussen's encephalitis. This type of surgery is performed only when other therapies have failed. With intense rehabilitation, children can recover many abilities.

Possible therapies for treating epilepsy either than through medications or surgery include:

Diet

A high-fat, very low carbohydrate ketogenic diet is often used to treat medication-resistant epilepsies. The diet induces a state known as ketosis, which means that the body shifts to breaking down fats instead of carbohydrates to survive. A ketogenic diet effectively reduces seizures for some people, especially children with certain forms of epilepsy. Studies have shown that more than 50 percent of people who try the ketogenic diet have a greater than 50 percent improvement in seizure control and 10 percent experience seizure freedom. Some children can discontinue the ketogenic diet after several years and remain seizure-free, but this is done with strict supervision and monitoring by a physician. The ketogenic diet is not easy to maintain, as it requires strict adherence to a limited range of foods. Researchers are looking at modified versions of and alternatives to the ketogenic diet.

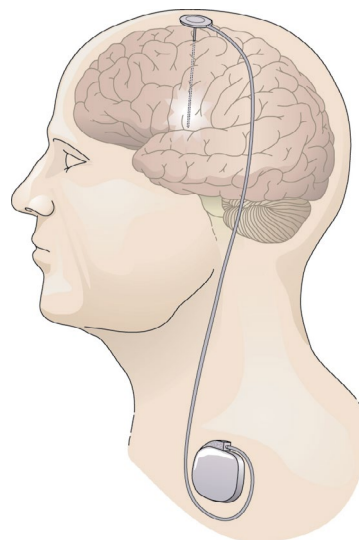
Devices

Electrical stimulation of the brain may help people with medication-resistant forms of epilepsy who are not candidates for surgery.

- Vagus nerve stimulation involves surgically implanting a device under the skin of the chest that is attached to the vagus nerve in the lower neck. The device delivers short bursts of electrical energy to the brain via the vagus nerve. On average, this stimulation reduces seizures by about 20 - 40 percent. Individuals usually continue to take epilepsy medication but often experience fewer seizures and may be able to reduce the dosage of their medication.

- Responsive stimulation involves the use of an implanted device that analyzes brain activity patterns to detect a forthcoming seizure. Once detected, the device administers an intervention, such as electrical stimulation or a fast-acting drug to prevent the seizure from occurring. These devices also are known as closed-loop systems. One such device is available for adults with refractory epilepsy (hard to treat epilepsy that does not respond well to trials of at least two medicines).

- Deep brain stimulation is an add-on treatment for people age 18 and older with drug-resistant focal epilepsy. It involves surgically implanting an electrode connected to a pulse generator – similar to a heart pacemaker – to deliver electrical stimulation



Deep brain stimulation, which uses mild electrical impulses to stimulate the brain, has been tried as a treatment for epilepsy in several different brain areas.

to specific areas in the brain to regulate electrical signals in neural circuits. Stimulation of an area called the anterior thalamic nucleus has been particularly helpful in providing at least partial relief from seizures in people who had medication-resistant forms of the disorder.

Experimental devices that may offer new treatment options include:

- Trigeminal nerve stimulation uses electrical signals to stimulate parts of the trigeminal nerve and affected brain regions. Its efficacy rate is similar to those for vagal nerve stimulation. Freedom from seizures, although reported, remains rare for both methods.
- Transcutaneous magnetic stimulation involves a device being placed outside the head to produce a magnetic field to induce an electrical current in nearby areas of the brain. It has been shown to reduce cortical activity associated with specific epilepsy syndromes.

What is the impact of the epilepsies on daily life?

Most people with epilepsy can do the same things as people without the disorder and have successful and productive lives. In most cases epilepsy does not affect job choice or performance. One-third or more of people with epilepsy, however, may have cognitive or neuropsychiatric co-concurring symptoms that can negatively impact their quality of life.

Mental health and stigmatization

Depression is common among people with epilepsy, often with accompanying symptoms of anxiety disorder. People with epilepsy should not simply accept that depression is part of having epilepsy and should discuss symptoms and feelings with health care professionals.

Children with epilepsy have a higher risk of developing depression and/or attention deficit hyperactivity disorder than their peers.

Children are especially vulnerable to the emotional problems caused by ignorance or the lack of knowledge among others about epilepsy. Children with epilepsy have a higher risk of developing depression and/or attention deficit hyperactivity disorder compared with their peers. Behavioral problems may precede the onset of seizures in some children. This often results in stigmatization, bullying, or teasing of a child who has epilepsy. Depression or anxiety in people with epilepsy can be treated with counseling or most of the same medications used in people who don't have epilepsy. Counseling services and support groups can help families cope with epilepsy in a positive manner.

Driving and recreation

Most states and the District of Columbia will not issue a driver's license to someone with epilepsy unless the person can document that she/he has

been seizure-free for a specific amount of time (the waiting period varies from a few months to several years). Some states make exceptions for this policy when seizures don't impair consciousness, occur only during sleep, or have long auras or other warning signs that allow the person to avoid driving when a seizure is likely to occur. Studies show that the risk of having a seizure-related accident decreases as the length of time since the last seizure increases. Commercial drivers' licenses have additional restrictions. People with epilepsy should take extra care if a job involves operation of machinery or vehicles.

The risk of seizures also limits people's recreational choices. Individuals may need to take precautions with activities such as climbing, sailing, swimming, or working on ladders. There is some evidence that regular exercise may improve seizure control in some people, but this should be done under a doctor's supervision.

Education and employment

By law, people with epilepsy (or disabilities) in the United States cannot be denied employment or access to any educational, recreational, or other activity because of their epilepsy. However, significant barriers still exist for people with epilepsy in school and work. Antiseizure drugs may cause side effects that interfere with concentration and memory. Children with epilepsy may need extra time to complete schoolwork, and they sometimes may need to have instructions or other information repeated for them. Teachers should be told what to do if a child in their classroom has a seizure, and

parents should work with the school system to find reasonable ways to accommodate any special needs their child may have.

Pregnancy and motherhood

Most women with epilepsy can become pregnant, have a healthy pregnancy, and have a healthy baby.

Potential risks to the developing child of a woman with epilepsy or on antiseizure medication include increased risk for major congenital malformations (also known as birth defects) and adverse effects on the developing brain. Birth defects that have been commonly reported with antiseizure medications include cleft lip or cleft palate, heart problems, abnormal spinal cord development (spina bifida), urogenital defects, and limb-skeletal defects. Some antiseizure medications, particularly valproate, are known to increase the risk of having a child with birth defects and/or neurodevelopmental problems, including learning disabilities, general intellectual disabilities, and autism spectrum disorder. It is important that a woman work with a team of providers that includes her neurologist and her obstetrician to learn about any special risks associated with her epilepsy and the medications she may be taking.

It is important for pregnant women with epilepsy to work with a team of health care providers to learn about any special risks associated with the medicines they may be taking.

The use of antiseizure medications is considered safe for women who choose to breastfeed their child. On very rare occasions, the baby may become excessively drowsy or feed poorly, and these problems should be closely monitored.

What research is being done on the epilepsies by the NINDS?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use the knowledge to reduce the burden of neurological disease. The NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world. The NINDS conducts and supports research to better understand and diagnose epilepsy, develop new treatments, and ultimately, prevent epilepsy. Researchers hope to learn the epileptogenesis of these disorders—how the epilepsies develop, and how, where, and why neurons begin to display the abnormal firing patterns that cause epileptic seizures.

Mechanisms

Researchers are learning more about the fundamental processes – known as mechanisms – that lead to epileptogenesis. Basic science studies are investigating the biology that contributes to epilepsy, including how brain cells communicate with one another and the role of various brain chemicals in epilepsy. Scientists are investigating how neurotransmitters (chemicals which carry signals from one nerve cell to another) interact with brain cells to control nerve firing and how non-neuronal cells in the brain contribute to seizures. For example, studies are focusing on the role of various neurotransmitters in inhibiting activity in the central nervous system.

The blood-brain barrier plays in important protective role between the circulatory systems and the fluid surrounding the brain, as it keeps toxins in the blood from reaching the brain. However, this protective layer of cells and other components can also block potentially beneficial medications from reaching the brain. NINDS-funded research projects aim to identify ways to overcome this barrier and lead to new treatments for the epilepsies and other neurological disorders.

Research has shown that the cell membrane that surrounds each neuron plays an important role in epilepsy because it allows neurons to generate electrical impulses. Scientists are studying details of the membrane structure, how molecules move in and out of membranes, and how the cell nourishes and repairs the membrane. A disruption in any of these processes may lead to seizures.

NINDS conducts and supports research on epilepsy to better understand, diagnose, treat, and ultimately, prevent the disorder. Researchers hope to learn how the epilepsies develop, and how, where, and why brain cells display the abnormal firing patterns that cause seizures.

Improving treatments

The NINDS Epilepsy Therapy Screening Program (ETSP) (https://www.ninds.nih.gov/Current-Research/Focus-Research/Focus-Epilepsy/ETSP) provides a free compound screening service to identify candidate drugs to treat the epilepsies. The ETSP annually has screened hundreds of new chemical agents from academic, industrial, and government participants using a battery of models of potential efficacy and side-effect liability. Results are compared to those obtained with standard marketed antiepileptic drugs. The ETSP has played a role in the identification and development of numerous marketed antiseizure drugs, including felbamate, topiramate, lacosamide, and retigabine. Current efforts emphasize unmet medical needs in epilepsy, such as treatments for refractory epilepsies, the development of epilepsy in previously unaffected individuals, and disease progression.

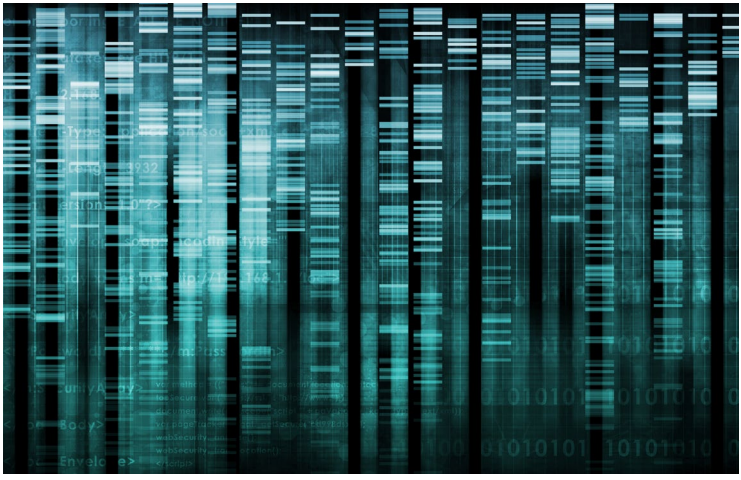
Other research initiatives include:

- identifying drug combinations that may boost the effectiveness of medication therapy
- engineering technologic advances to diagnose epilepsy and to identify the focus of seizures
- developing minimally-invasive approaches to treat an epilepsy focus using heat (thermoablation), transcranial ultrasound, or high-powered x-rays (stereotactic radiosurgery).
- developing better animal models that more closely reflect the mechanisms that cause epilepsy in humans so that they can be used to more effectively screen potential treatments for the epilepsies.

Genetics

NINDS has long supported efforts to identify genes responsible for epileptic conditions. The discovery of genetic mutations that are linked to specific epilepsy syndromes suggests the possibility of using gene-directed therapies to counter the effects of these mutations. A common approach in gene therapy research uses viruses modified to be harmless to introduce new genes into brain cells, which then act as "factories" to produce potentially therapeutic proteins.

NINDS established its Epilepsy Centers without Walls Program in 2010 to address challenges and gaps in epilepsy research. The innovative program encourages collaborations, including sharing of data and resources, between researchers from a variety of disciplines and institutions regardless of geographic location, that may lead to advances in prevention, diagnosis, or treatment of the epilepsies and related comorbidities.



Learning more about the human genome has increased efforts to identify genes responsible for epilepsy. Continued progress to identify genetic causes of the epilepsies could help affected families understand their risks.

- Epi4K is an NINDS-funded Epilepsy Center without Walls aimed at determining the genetic basis of various epilepsies. Epi4K investigators are analyzing the genomes of at least 4,000 people with well-characterized epilepsies. Through this work, researchers have successfully identified mutations associated with Dravet syndrome, infantile spasms, and Lennox-Gastaut syndrome.
- Future Centers without Walls projects will focus on the functional effects of gene changes that cause epilepsy in order to develop targeted treatments.

Other research is aimed at identifying the genes and their function(s) relevant to epilepsy syndromes to develop targeted treatments, and advancing gene sequencing tools and technologies to identify genetic mutations that cause various forms of epilepsy.

SUDEP (sudden unexpected death in epilepsy)

NINDS, non-profit lay and professional organizations, and the Centers for Disease Control and Prevention are providing significant funding toward studies aimed at better understanding SUDEP risk factors and mechanisms, which may point the way toward developing strategies for screening and prevention.

Early studies have described certain EEG patterns that may help identify people at elevated risk for SUDEP. Several devices in the early stages of development aim to provide a warning when a seizure has the potential to put someone at risk for SUDEP.

The NINDS-funded Center for SUDEP Research – an Epilepsy Center without Walls project – is investigating potential causes of SUDEP and any signs or symptoms that might make one more susceptible to SUDEP.

The project also hopes to identify biological processes that may be targets for preventing SUDEP.

BRAIN Initiative

Several projects relevant to epilepsy are funded through the Brain Research through Advancing Innovative Neurotechnologies® Initiative – a public/private collaboration aimed at better understanding the inner workings of the human mind and improving ways to treat, prevent, and cure brain disorders. Epilepsy-related research projects aim to better understand, measure, and monitor how the brain generates neural activity, as well as to develop new technologies and devices that measure brain activity, predict seizure onset, and deliver therapeutic stimulation to limit seizure activity.

How can I help research on the epilepsies?

There are many ways that people with epilepsies and their families can help advance research.

- Pregnant women who are taking antiseizure drugs can help researchers learn how these drugs affect unborn children by participating in the Antiepileptic Drug Pregnancy Registry, which is maintained by the Genetics and Teratology Unit of Massachusetts General Hospital. Women who enroll in the registry are given educational materials on pre-conception planning and perinatal care and are asked to provide information about the health of their children. (This information is kept confidential.) Information about the registry is available at

http://www.aedpregnancyregistry.org/ or by calling 1-888-233-2334. Information also is available from sites of the NIH-sponsored study, Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD): https://clinicaltrials.gov/ct2/show/NCT01730170?term=MONEAD&rank=1.

- Participating in a clinical study is an excellent opportunity to help researchers find better ways to safely detect, treat, or prevent epilepsy and therefore offer hope to people now and in the future. NINDS conducts clinical studies on the epilepsies at the NIH research campus in Bethesda, Maryland, and supports epilepsy studies at medical research centers throughout the United States. Interested healthy individuals and people with epilepsy should talk with their health care professional about clinical studies for epilepsy. For information about participating in a clinical study at the NIH and contact information for each study, see http://patientinfo.ninds.nih.gov and search for epilepsy. For information about additional NINDS-funded clinical studies on epilepsy and ways to participate, see http://www.clinicaltrials.gov and search for "epilepsy AND NINDS".

Clinical studies help researchers find better ways to detect, treat, or prevent disorders such as epilepsy. Participation in a clinical study is an excellent opportunity to offer hope to people with neurological disorders now and in the future.

- People with epilepsy can help further research by donating tissue either at the time of surgery for epilepsy, or at the time of death. Researchers use the tissue to study epilepsy and other disorders so they can better understand what causes seizures. The NIH NeuroBioBank (https://neurobiobank.nih.gov/) is an effort to coordinate the network of brain banks it supports in the United States. The brain tissue and data are collected, evaluated, stored, and made available to researchers via a network of brain and tissue repositories in standardized way for the study of neurological, psychiatric and developmental disorders, including epilepsy.

Where can I get more information?

For more information on neurological disorders or research programs funded by the NINDS, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
301-496-5751
800-352-9424
www.ninds.nih.gov

In addition to NINDS, several other NIH institutes and centers also support research relevant to understanding, treating, or preventing seizures and epilepsy. More information on epilepsy and seizures research supported by the NIH is available through the NIH RePORTER (http://projectreporter.

nih.gov), a searchable database of current and previously funded research, as well as research results and publications.

Information also is available from the following organizations:

Citizens United for Research in Epilepsy (CURE)
430 W. Erie, Suite 210
Chicago, IL 60654
312-255-1801
800-765-7118
www.CUREepilepsy.org

The Charlie Foundation for Ketogenic Therapies
515 Ocean Avenue, Suite 602N
Santa Monica, CA 90402
310-393-2347
www.charliefoundation.org

Epilepsy Foundation
8301 Professional Place East, Suite 200
Landover, MD 20785-2353
301-459-3700
800-EFA-1000 (332-1000)
www.epilepsy.com

Hope for HH (Hope for Hypothalamic Hamartoma)
P. O. Box 721
Waddell, AZ 85355
http://hopeforhh.org

Intractable Childhood Epilepsy Alliance
PO Box 365
6360 Shallowford Road
Lewisville, NC 27023
336-946-1570
www.ice-epilepsy.org

LGS Foundation (Lennox-Gastaut Syndrome)
192 Lexington Avenue, Suite 212
New York, NY 10016
718-374-3800
www.lgsfoundation.org

National Organization for Rare Disorders (NORD)
55 Kenosia Avenue
Danbury, CT 06810
203-744-0100
Voice Mail 800-999-NORD (6673)
www.rarediseases.org

RE Children's Project (Rasmussen's Encephalitis)
79 Christie Hill Road
Darien, CT 06820
917-971-2977
www.rechildrens.org

Sturge-Weber Syndrome Foundation
P.O. Box 418
Mt. Freedom, NJ 07970-0418
973-895-4445
800-627-5482
www.sturge-weber.org

Tuberous Sclerosis Alliance
801 Roeder Road, Suite 750
Silver Spring, MD 20910
301-562-9890
800-225-6872
www.tsalliance.org

U.S. National Library of Medicine
National Institutes of Health
8600 Rockville Pike
Bethesda, MD 20894
301-594-5983
888-346-3656
www.nlm.nih.gov

Glossary

Note: Due to the large number of epilepsy syndromes and treatments, only a few are discussed in this booklet. Additional information may be available from health care professionals, medical libraries, patient advocacy organizations, or by calling the NINDS Office of Communications and Public Liaison.

absence epilepsy — epilepsy in which the person has repeated absence seizures.

absence seizures — seizures seen in absence epilepsy, in which the person experiences a momentary loss in consciousness. The person may stare into space for several seconds and may have some twitching or mild jerking of muscles. An older term for absence seizures is petit mal seizures.

atonic seizures — seizures which cause a sudden loss of muscle tone, also called drop attacks.

auras — unusual sensations or movements that warn of an impending, more severe seizure. These auras are actually simple focal seizures in which the person maintains consciousness.

clonic seizures — seizures that cause repeated jerking movements of muscles on both sides of the body.

convulsions — sudden severe contractions of the muscles that may be caused by seizures.

corpus callosotomy — surgery that severs the corpus callosum, or network of neural connections between the right and left hemispheres

déjà vu — a sense that something has happened before.

de novo — new, for the first time.

Dravet syndrome — a type of intractable epilepsy that begins in infancy.

febrile seizures — seizures in infants and children that are associated with a high fever.

focal seizures — seizures that occur in just one part of the brain.

frontal lobe epilepsy — a type of epilepsy that originates in the frontal lobe of the brain. It usually involves a cluster of short seizures with a sudden onset and termination.

generalized seizures — seizures that result from abnormal neuronal activity in many parts of the brain. These seizures may cause loss of consciousness, falls, or abnormal movements such as convulsions.

hemispherectomy — surgery involving the removal or disabling of one hemisphere of the brain.

hemispherotomy — removing half of the brain's outer layer (cortex).

hypothalamic hamartoma — a rare form of childhood epilepsy that is associated with malformations of the hypothalamus at the base of the brain.

infantile spasms — clusters of seizures that usually begin before the age of 6 months. During these seizures the infant may bend and cry out.

intractable — hard to treat; about 30 to 40 percent of people with epilepsy will continue to experience seizures even with the best available treatment.

juvenile myoclonic epilepsy — a type of epilepsy characterized by sudden muscle (myoclonic) jerks that usually begins in childhood or adolescence.

ketogenic diet — a strict diet rich in fats and low in carbohydrates that causes the body to break down fats instead of carbohydrates to survive.

Lafora disease **—** a severe, progressive form of epilepsy that begins in childhood and has been linked to a gene that helps to break down carbohydrates.

Lennox-Gastaut syndrome **—** a type of epilepsy that begins in childhood and usually causes several different kinds of seizures, including absence seizures.

lesionectomy **—** surgical removal of a specific brain lesion.

lobectomy **—** surgical removal of a lobe of the brain.

monotherapy **—** treatment with only one antiepileptic drug.

multiple subpial transection **—** a type of operation in which surgeons make a series of cuts in the brain that are designed to prevent seizures from spreading into other parts of the brain while leaving the person's normal abilities intact.

myoclonic seizures **—** seizures that cause sudden jerks or twitches, especially in the upper body, arms, or legs.

neocortical epilepsy **—** epilepsy that originates in the brain's cortex, or outer layer. Seizures can be either focal or generalized, and may cause strange sensations, hallucinations, or emotional changes.

nonepileptic seizures **—** any phenomena that look like seizures but do not result from abnormal brain activity. Nonepileptic events may include psychogenic seizures or symptoms of medical conditions such as sleep disorders, Tourette syndrome, or cardiac arrhythmia. Pseudoseizure is an older term for nonepileptic seizure.

prodrome **—** a feeling that a seizure is imminent, which may last hours or days prior to the seizure.

Rasmussen's encephalitis **—** a progressive type of epilepsy in which half of the brain shows continual inflammation.

seizure focus **—** an area of the brain where seizures originate.

seizure triggers **—** Seizure triggers do not cause epilepsy but can lead to first seizures or cause breakthrough seizures in people who otherwise experience good seizure control with their medication.

status epilepticus **—** a potentially life-threatening condition in which a seizure is abnormally prolonged. Although there is no strict definition for the time at which a seizure turns into status epilepticus, most people agree that any seizure lasting longer than 5 minutes should, for practical purposes, be treated as though it was status epilepticus. Repeated seizures without regaining consciousness between the events is also considered a form of status epilepticus.

sudden unexpected death in epilepsy (SUDEP) **—** death that occurs suddenly for no discernible reason. Epilepsy increases the risk of sudden unexplained death about two-fold.

temporal lobe epilepsy **—** the most common epilepsy syndrome with focal seizures.

tonic seizures **—** seizures that cause stiffening of muscles of the body, generally those in the back, legs, and arms.

tonic-clonic seizures **—** seizures that cause a mixture of symptoms, including loss of consciousness, stiffening of the body, and repeated jerks of the arms and legs. In the past these seizures were sometimes referred to as grand mal seizures.

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