

Epilepsy

Making a Difference Today

Julius Caesar had it. So did Peter the Great, Pope Pius IX, Fyodor Dostoevsky, and Lord Byron. In epilepsy, clusters of nerve cells suddenly signal abnormally, causing seizures and sometimes convulsions, muscle spasms, and loss of consciousness. This brain disorder has many possible causes including genetic predisposition, illness, brain damage, or abnormal brain development. It most often appears either in early childhood or old age. Although many people with epilepsy lead normal lives, the risk of seizures limits their independence, especially for people with epilepsy who cannot get a driver's license. And children who experience the teasing, bullying, and ostracism associated with epilepsy often have behavioral and emotional problems.

Fortunately, research funded by NIH and others is helping pave the way to new methods of diagnosing epilepsy and to more effective treatments.

A Matter of Control

Treating epilepsy involves controlling seizures. Currently, about 80 percent of people with the disorder benefit from seizure medications and surgery. Other treatment options include dietary changes, primarily for children, and electrical stimulation of the vagus nerve, a large nerve that leads into the brain. When it comes to medications, however, the challenge is to choose a drug that can stop seizures without too many adverse side effects, and to help those who are resistant to some of the available medications. Some patients who are resistant to medications may benefit from brain surgery to remove epileptic tissue, especially if performed early in the course of their disease.

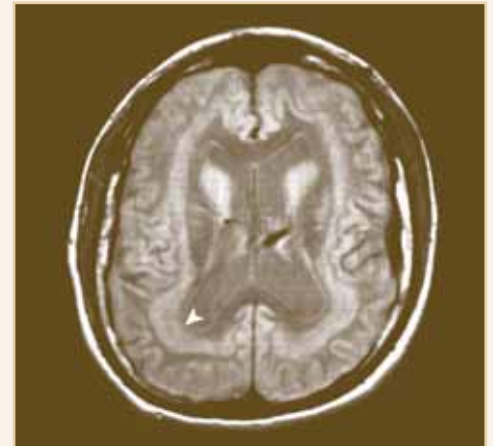
Research Leads to Better Diagnosis and Treatments

Use of techniques for imaging brain function such as PET scans, magnetic resonance imaging, and electroencephalography allows physicians to see the abnormal activity of brain lesions that cause epilepsy and thus to diagnose it more accurately.

Advanced molecular genetic tools have helped NIH-funded scientists isolate the genes responsible for more than 30 forms of epilepsy. Some of these genes guide neurons to their correct positions in the developing brain. Mutations in these genes alter migration, leaving the brain malformed in certain areas. These areas have overly excitable circuits. Many of these defects, which have now been replicated in mouse models, will help scientists learn why different forms of epilepsy begin at different ages and eventually develop molecular targets for therapy.

Scientists have also discovered key mutations in other genes that play a critical role in how seizures begin. Many genes for epilepsy encode ion channels, the membrane pores that determine neuronal firing patterns. These discoveries may lead to the development of entirely new generations of antiepileptic drugs that offer greater options for treatment with fewer side effects. Advances in bioimaging research that pinpoint epileptic brain lesions are helping doctors identify patients who will benefit from surgical removal of the epilepsy-causing lesion. Researchers are also experimenting with cell transplant therapies that could help control seizures and with devices that may be able to predict them up to three minutes before onset.

For more information please email brss@sfn.org.



Mutations in genes that normally guide neurons during development to their correct position in the brain can result in epilepsy. In this MRI scan of an epileptic patient's brain, mutation of an X-linked gene has resulted in faulty migration of a band of neurons (arrow) causing epilepsy.

Continued funding for research could lead to:

- Genetic testing for clinical diagnosis and therapy.
- Neuroprotective drug therapies to prevent seizures.
- Devices to predict seizures in advance.
- Drug therapies that can be applied at the seizure site in the brain.

Epilepsy

Making a Difference Tomorrow

Diagnosis and treatment of epilepsy have improved greatly, thanks to new technologies and drugs developed with the help of research funding. But epilepsy continues to stigmatize and traumatize those who suffer from it. Did you know that:

- About 2.3 million Americans have experienced epilepsy and seizures.
- The annual cost to the nation in terms of medical expenses and lost or reduced productivity is estimated to be \$12.5 billion.
- Worldwide, there are 50 million people affected by the disorder, and about 35 million people lack access to appropriate treatment—either because services do not exist or because epilepsy is not perceived as a medical problem that can be treated.
- Up to 17 percent of people with epilepsy die suddenly. The rate of unexpected death among epileptics is 24 times that of the general population.

Researchers are pursuing several lines of work that promise to yield better treatments and diagnostic tools. With continued NIH funding, physicians will soon have in hand far more options for treating patients according to their specific type of epilepsy. And patients will have medications with far fewer side effects.

Research into a Better Future

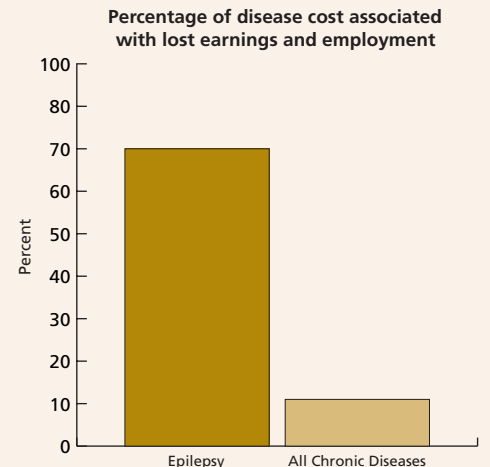
Today's anti-seizure drugs act on particular targets. The drug phenytoin, for example, acts on sodium channels to slow the firing frequency of neurons during seizures. But because of their action on specific targets, phenytoin and other available medications have limitations in treating forms of epilepsy that involve more than one drug target. Up to one-third of patients with seizures are resistant to drug therapy.

More research is needed to develop anti-seizure drugs that are effective in cases where drugs such as phenytoin do not work. One promising approach may be to use gene therapy that could one day stop seizures in people with common forms of epilepsy by modifying the excitability of hyperactive brain cell circuits.

Research is also needed to develop a set of mathematical rules that could be used to understand the complex brain activity that seems to develop in the minutes and hours before a seizure occurs. Such rules could be used to develop devices for implantation in the brain to help forewarn doctors and patients of an impending seizure. These tiny devices could then deliver drugs directly to the epileptic brain region in doses that could be regulated by the patient or the doctor. However, much more study is needed before such a system could be used widely in people with epilepsy.

Only with continued funding will scientists be able to bring about the medical advances needed to prevent epilepsy from hindering the lives of millions of Americans.

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Compared with other major chronic diseases, such as heart disease and cancer, epilepsy has a much higher percentage of costs resulting from lost earnings and employment. The unpredictable nature of seizures translates into less earnings potential and fewer employment opportunities. Recent treatment advances hold promise for reducing the frequency and severity of seizures, and could lessen the disorder's economic burden.

Already research has led to:

- Isolation of genes responsible for 30 forms of epilepsy.
- Discovery of genetic mutations that play a role in how seizures begin.
- Development of a new generation of antiepileptic drugs.
- Higher spatial resolution images of the epileptic brain, assisting diagnosis.