# NINDS Contributions to Approved Therapies

*NINDS invests in and conducts research across the spectrum of neuroscience and neurology research, from basic studies on fundamental biological mechanisms, to clinical trials to test new treatments in patients. Here, we describe the path leading to the development and approval of one therapy for a neurological disorder, and we highlight contributions enabled by NINDS and NIH support.*

# Brain Stimulation Therapies for Epilepsy

## Overview

Epilepsy is a chronic neurological condition characterized by recurring seizures, or abnormal bursts of electrical activity in the brain that can trigger jerky movements, strange sensations or emotions, unusual behavior, and/or loss of consciousness. Although anti-seizure medications help many people with epilepsy, a third or more receive little or no relief from medical treatment. Some people with medically refractory epilepsy experience excellent outcomes with surgery to remove or disconnect brain tissue that initiates or propagates seizures, but for others, the seizure source is difficult to identify or target safely without causing new neurological deficits. In these cases, neurostimulation devices can offer another alternative.

Two FDA-approved devices deliver electrical stimulation to the brain in different ways to reduce seizure frequency in people who do not achieve seizure control with medication alone. Deep brain stimulation (DBS) for epilepsy delivers chronic stimulation to the anterior nucleus of the thalamus (ANT), a small brain structure involved in the spread of initially localized seizures. In contrast, responsive neuro-stimulation (RNS) delivers stimulation directly to the source of an individual's seizures, but only when continuously monitored brain activity suggests a seizure may be beginning. Research supported and conducted by NINDS figured prominently in the development of these devices, including studies to test early approaches, find stimulation targets, and develop seizure detection algorithms.

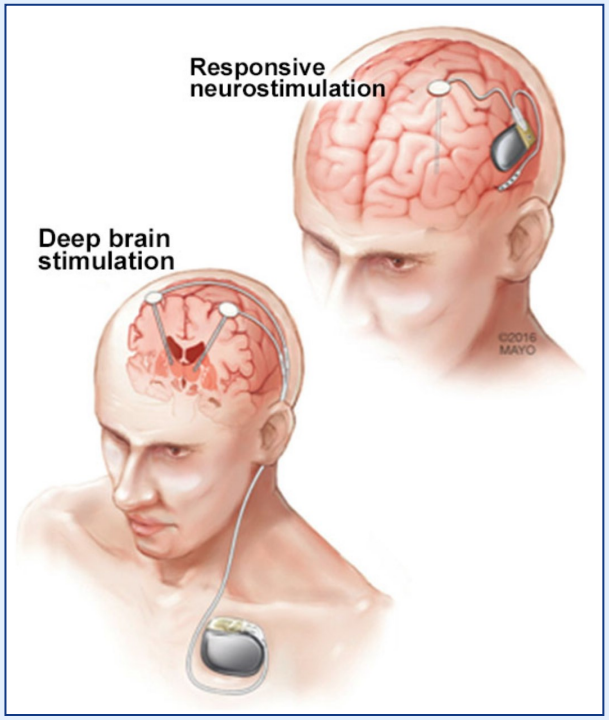
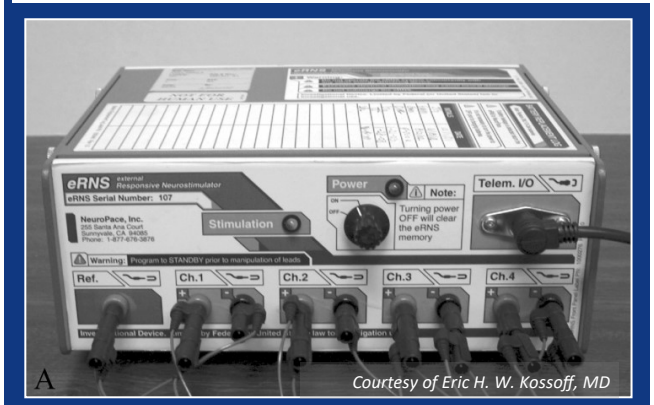



*Image modified from Edwards CA, Kouzani A, Lee KH, Ross EK. Neurostimulation Devices for the Treatment of Neurologic Disorders. Mayo Clin Proc 2017;92:1427-1444*

Learn more at: https://www.ninds.nih.gov/About-NINDS/Impact/NINDS-Contributions-Approved-Therapies

# Brain Stimulation Therapies for Epilepsy
# Development Timeline




Initial tests of responsive stimulation for safety and feasibility used prototypes with external neurostimulators in people undergoing evaluation for epilepsy surgery. NIH NINDS

**1954** During recordings of brain activity in people with epilepsy undergoing surgery, Wilder Penfield and Herbert Jasper observe that seizure-like activity could be halted with brief counter stimulation.

**1967-1972** Surgical lesions of the anterior nucleus of the thalamus (ANT) decreased the occurrence and duration of seizures in a small clinical study and in an animal model of epilepsy. NIH NINDS

**1980-1987** Small, unblinded studies show chronic ANT stimulation improves seizure control in people with medically refractory epilepsy. While promising, these early studies used external stimulators that were inconvenient to patients.

**1983-1999** Brief bursts of stimulation are shown to terminate seizures or seizure-like activity in people with epilepsy and animal models when delivered soon after onset. NIH NINDS

**1984-1986** Studies to understand seizure mechanisms place the ANT within a brain circuit involved in the spread of initially localized seizures. NIH NINDS

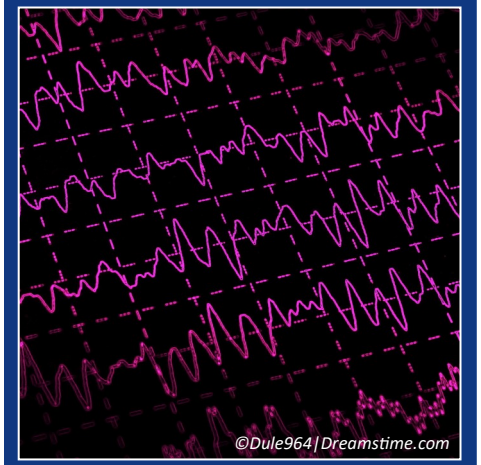
**1991** High frequency stimulation in the ANT is shown to protect against generalized seizures in an animal model.

**1997** The FDA approves two new implantable neurostimulation devices: Medtronic's deep brain stimulation (DBS) system as a treatment for tremor and Cyberonics' vagal nerve stimulator for medically refractory epilepsy.

**2001-2005** Pilot studies report improved seizure control with chronic bilateral ANT stimulation using Medtronic's implantable DBS system. NIH NINDS

**2002-2004** The SANTE (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy) trial and a seven-year follow up period show lasting reductions in seizure frequency in those who were treated and meaningful improvements in quality of life.

**2010-2015** Academic and industry investigators develop more refined seizure detection algorithms that will be adapted for use in the first responsive stimulation devices. NIH NINDS




**2011** The pivotal clinical trial of the NeuroPace responsive neurostimulation system (RNS®) shows that seizure frequency decreased in individuals receiving stimulation.

**2013** The NeuroPace RNS® receives approval from the FDA for use in adults with medically refractory focal epilepsy.

**2018** Medtronic's DBS system for epilepsy receives approval from the FDA for use in adults with medically refractory focal epilepsy.