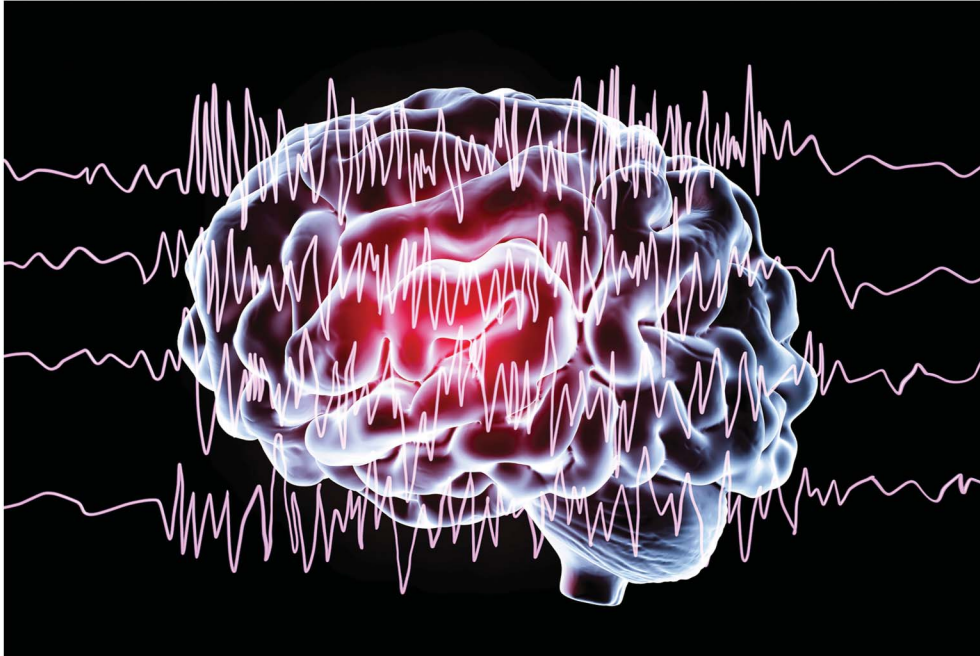


# Epilepsy and Depression

## How Are They Related?

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### Related Article

#### Directionality of the Association Between Epilepsy and Depression: A Nationwide Register-Based Cohort Study

<http://dx.doi.org/10.1212/WNL.0000000000201542>

In their study “Directionality of the Association Between Epilepsy and Depression: A Nationwide Register-Based Cohort Study,” the authors assessed the link between depression and epilepsy in a group of people in Denmark.<sup>1</sup> This idea is not new: for many years, studies have shown a connection between epilepsy and depression. Of note, 13%–37% of people with epilepsy experience depression also.<sup>2</sup> This is 2–5 times higher than the rate of depression in people *without* epilepsy. To better understand this connection, the authors looked at registry data on a very large group of people (more than 8 million), collected over 35 years (from January 1, 1980, to December 31, 2016).

When 2 medical conditions occur together more often than predicted by chance, they are called comorbid conditions. The observation that depression is connected to epilepsy (i.e., that they are comorbidities) raises many questions. How are the illnesses connected? Are both caused by a common underlying brain abnormality? Is there an abnormality of neurotransmitters responsible for both? Finally, does the same connection occur with other chronic medical illnesses? The authors of this study used asthma, another chronic medical illness, as a comparison. They looked at the rate of depression in people with asthma and compared this with that in people with epilepsy. Using the registry data, they were also able to look at the *opposite* possibility: that is, do people with depression have epilepsy more often?

### How Was the Study Conducted?

The authors used several national registers of data in Denmark. They identified a total of 8,741,955 individuals whose data were recorded between January 1, 1980, and December 31, 2016. They did not include data from anyone who had been diagnosed with these illnesses *before* January 1, 1980. This left 8,688,948 people for analysis. In this group, they found 219,990 who were initially diagnosed with depression, 358,821 who had asthma, and 139,014 who had epilepsy.

The authors further divided each group in the following ways: for those with depression, they separated the group into mild, moderate, or severe depression. For people with epilepsy, they analyzed different kinds of epilepsy: focal (or partial), generalized, or unspecified. The authors also evaluated the overall group for other illnesses or factors that could confuse the study results. For instance, they looked for substance use/abuse, whether people were taking their medication, and each person's socioeconomic status.

## What Did the Study Show?

First, the authors demonstrated that the link between epilepsy and depression was a "2-way street." The study found that if people were first diagnosed with epilepsy, they were 2 times more likely to develop depression. Furthermore, if people were diagnosed with depression first, they were 2.5 times more likely to develop epilepsy later. This effect was still observed even after accounting for things such as substance abuse and socioeconomic status. In comparison, if people were first diagnosed with asthma, their risk of developing epilepsy later was much lower (only 1.48). In comparison, for people first diagnosed with asthma, the likelihood of developing depression later was 1.63.

For people who were first diagnosed with epilepsy, the time they were most likely to be diagnosed with depression was within the first months and years after their epilepsy diagnosis. This was much more likely if a person was older (aged 40–59 years), and the risk was the lowest if they were young (aged 0–19 years). The authors could not find a difference in the rates of depression related to epilepsy subtype (that is, partial, generalized, or unspecified). One very interesting association was this: if people had epilepsy *and* depression, they were less likely to respond to seizure treatment.

For people who were first diagnosed with depression, the time to epilepsy diagnosis was similarly highest in the first

few months or years after their depression diagnosis. Epilepsy after depression was much more likely to occur in the young (aged 0–19 years) and lowest in older people (older than 80 years). Of interest, the diagnosis of epilepsy was also much more likely if the person had been initially diagnosed as having mild depression and lowest if they were initially diagnosed as having moderate depression.

## Why Is This Important?

First, the link between epilepsy and depression goes both ways. This study supports the same observations that were made in national studies conducted in Canada and Sweden.<sup>2</sup> One big difference with this study was the sample size: this study looked at this association in a much larger group of people with chronic medical illnesses than previous studies did. In addition, this study was conducted over almost 4 decades, much longer than many other studies. Not only did the authors of this study see a connection between epilepsy and depression, but they also showed that the risk of depression after epilepsy persisted over the *entire* course of the study.

This being said, there are several limitations to this study. One limitation to studies of this kind is that they rely on the accuracy of the diagnoses that are being entered into the registry (or registries) from which they are gathering data. Second, this study used data that were taken from *admissions* to a hospital. If a diagnosis of depression or epilepsy was made *outside* of a hospital setting, it would *not* be reflected in this data. Third, the date that a diagnosis is made may *not* reflect the true date of the onset of the illness. For example, what if a person had depression for months or years *before* being admitted to a hospital for depression treatment? This would affect the data regarding the *timing*: that is, how soon after 1 illness starts does the second one begin? Finally, studies such as this can establish a link between illnesses, but they do not tell us *how* or *why* these illnesses are connected. To answer those questions, further studies are needed.

## About Epilepsy

### What Is a Seizure?

Nerve cells are always talking to each other using a combination of electrical and chemical signals. These signals are called neurotransmitters. When a brain injury occurs, it can change the way nerve cells (also called neurons) communicate. This can cause neurons to send signals in abnormal ways. The nerve cells that receive the abnormal signals try to respond, but sometimes, they end up sending abnormal signals as well. If enough of these abnormal signals occur, it results in a seizure.

### What Is Epilepsy?

Epilepsy is not 1 illness. There are actually many kinds of epilepsy. And just as there are many kinds of epilepsy, there are many kinds of seizures. There are 2 commonly accepted definitions of epilepsy. One is that a person has had 2 or more unprovoked seizures in their lifetime. The second says that a person has epilepsy if they have had 1 seizure and are at a very high risk for having more. In this case, medical testing is helpful in assessing the risk of seizure recurrence.

One way to think about how that brain functions is this: the brain works similar to an orchestra. In an orchestra, there are many different sections. Each section is made up of many musicians, each with their own instrument. Although each instrument plays its own part, it is only when all are playing together that complex music is made. While playing, each musician must do 2 things. First, to play well with the other musicians, each player must listen to everyone else. Second, they must pay attention to the conductor. When they work together, the best music is made.

However, what if 1 person began playing a different tune? At first, only the musicians who were nearest would notice that someone was playing the “wrong” tune. The “neighbors” might become confused: which tune were they supposed to play? They might respond to the new tune by playing that instead. As more members of the orchestra begin playing the “wrong” tune, it would eventually become noticeable. At some point, the new tune might become louder than the original music.

This is similar to how a seizure gets started and how it keeps going. The nearby brain cells start playing the wrong tune, and they encourage other brain cells to do the same thing. Eventually, people cannot stay aware of what is going on around them because too many of their brain cells are busy doing something else—having a seizure.

### How Is Epilepsy Diagnosed?

When diagnosing epilepsy, the doctor will need to know as much as possible about what happened immediately before, during, and after the person’s seizure. How often do the seizures occur? Is there a warning sign? Does the person remember anything about the seizure? All these questions help the doctor to better understand the kind of seizures (and the kind of epilepsy) the person has. In addition, talking with a witness to the seizures can provide valuable information. If the patient does not remember

their seizures, the observer may provide information that the patient may not know.

Medical testing can also help to better understand a person’s seizures. EEG is a simple procedure that records the brain’s electrical activity. Doctors look for specific brain wave patterns that occur more often in people with epilepsy. These patterns occur in between seizures when a person is awake or asleep. These patterns are not seizures, but they provide critical information about the person’s epilepsy and often help with the diagnosis.

Imaging studies are critical in understanding the cause of a person’s seizures. The 2 most common studies are MRI and CT. The scans take pictures of the structure of the brain and are helpful in locating tumors, scars, or other abnormalities that may cause seizures.

### How Are Seizures Treated?

There are many treatments for seizures. Medicines are tried first. If these do not work, your doctor may consider special diets, brain surgery, or devices for the treatment of seizures. Usually, the physician tries to stop *all* seizures while causing *no* side effects. Clear discussions between the patient and their doctor are critical to achieving the best quality of life. By telling your doctor about the kinds of problems you might experience while on a medication (or any treatment), you will make the best choice of treatments. Portions of this section were adapted from “Seizure Detection and Wearables: Integrating Technology in Patient Care.”<sup>3</sup>

#### For More Information

**Brain & Life**  
brainandlife.org

**Epilepsy Foundation**  
epilepsy.com

**Cure Epilepsy**  
cureepilepsy.org

**American Epilepsy Society**  
aesnet.org

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