

## Seizures and encephalitis

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### What is a seizure?

The brain has millions of nerve cells (or neurons) that manage how we feel, think and move. Electrical signals are sent by the brain to send messages between nerve cells. However if the messages are interrupted, or the electrical signals do not switch off after they do their job, this can cause a sudden change in the way the brain works. The interruption or build up of electrical signals can lead to a seizure.

Encephalitis may be one of these factors by disturbing these control mechanisms and produce electrical irritability in the brain, causing seizures. Seizures are common during the initial stages of encephalitis, when people are typically quite unwell in hospital. Because they are occurring as a symptom of an acute illness (serious illness, these are referred to as 'acute symptomatic seizures.' In some instances, they can be quite difficult to bring under control and may need a period in the intensive care unit. It is estimated that between 2-67% of patients with encephalitis have seizures in the acute stage, but it may be even more common than this as subtle seizures may not be recognised. Seizures are also more common in children than in adults. In one study it was found that 71.9% of patients with autoimmune encephalitis had epileptic seizures, and of those patients with seizures 89% became seizure-free through immunology treatment.

After the acute phase, one paper found that autoimmune encephalitis associated epilepsy was the long-term result in 43.73% of patients. It also showed that severe seizures early on can increase the chance of chronic epilepsy in autoimmune encephalitis. Other risk factors include difficulty treating seizures with multiple anti-seizure medication in acute stage, continuous interictal epileptiform discharges, and poor response to immunology in acute stage.

Another study found that epilepsy after resolved encephalitis was rare, and seizure freedom is achieved faster and more often with immunotherapy. They also estimate the prevalence of autoimmune encephalitis as a cause of disorders such as epilepsy.

### **What is epilepsy?**

Seizures may also occur at a later stage, well after the acute illness is over. This is because the after-effects of encephalitis may leave the brain cells more likely to produce the bursts of abnormal synchronized activity which cause seizures. When seizures occur in the absence of a triggering event (such as the acute infection), they are known as 'unprovoked seizures.' Epilepsy is defined as a tendency to experience recurrent unprovoked seizures.

Many patients who go on to develop epilepsy after encephalitis will have had seizures during their acute illness, and then continue to have unprovoked seizures after they have recovered. They have evolved from acute symptomatic seizures to epilepsy without any period of freedom from seizures in between. However, others may not have had seizures at all during the acute illness or may have had some seizures which settled, but then go on to have unprovoked seizures (epilepsy) at a later stage after encephalitis. Although this most commonly occurs within the first year or two after encephalitis, seizures may begin much later in some people.

People who have had encephalitis are about 16 times more likely to develop epilepsy than the general population. The risk of later unprovoked seizures for people who had seizures during the initial acute encephalitis is about 10% at five years and 22% by 20 years. If there were no early seizures, the 20-year-risk of unprovoked seizures is around 10%. The risk of developing epilepsy will depend on the type of encephalitis. Some varieties such as herpes simplex encephalitis (HSE) are more likely to be followed by epilepsy than others.

### **Types of seizures**

Seizures may be classified into different types, according to the pattern of the abnormal electrical activity in the brain:

- Primary generalized seizures, when the whole of the brain is rapidly involved right from the beginning.
- Focal (partial) seizures, when the abnormal electrical activity begins in one localized area of the brain. As the seizure evolves, it may either remain in that area or spread to involve other nearby areas on the same side of the brain (regional spread), or it may spread more widely to involve both sides of the brain (secondary generalized seizure).

Most people who develop epilepsy after encephalitis have focal or secondary generalized seizures. Because encephalitis is commonly a diffuse process involving both sides of the brain, seizures may sometimes arise from several different locations and this is referred to as multifocal epilepsy.

Focal epilepsy is often classified according to the region or lobe of the brain where the abnormal electrical activity starts at the beginning of the seizure. So it is common to refer to frontal lobe epilepsy, temporal lobe epilepsy, parietal lobe epilepsy and occipital lobe epilepsy, when the seizures have their origin in those particular lobes of the brain.

Simple partial seizure is the term used for focal seizures which do not involve any disturbance of consciousness and complex partial seizure if awareness is disturbed.

### **What happens during a seizure?**

What happens during a seizure will depend on where the abnormal activity begins in the brain and where it spreads. Some seizures are very subtle and may just involve, for example, odd sensations in one limb or some slight jerking of the limb. In mild seizures of this kind, there may not be any disturbance of consciousness and people may remain fully aware of what is happening around them, still perfectly able to speak and interact. However, seizures will more often involve partial or complete disruption of awareness of the surroundings. In its milder forms, this may just lead to a brief interruption in activity with a rather blank look, a period of confusion and a failure to respond.

If the seizure activity spreads in the brain, there may be a sequence of events as different areas become involved. Temporal lobe seizures, for example, may begin with a warning or aura (such as a sudden, unexplained feeling of fear or anxiety, butterflies in the stomach or nausea), alerting the person to an imminent seizure. There may then be a loss of awareness with blank staring and an interruption of whatever they were doing. There may be some chewing movements and fumbling with the clothes or other objects (automatisms). The seizure may then fade away after a couple of minutes, often to be followed by a period of residual confusion and tiredness. However, if the seizure activity continues to spread more widely in the brain (secondary generalization) the initial stage may progress to a convulsion with loss of consciousness, falling to the ground and jerking of the limbs (generalized tonic-clonic seizure, grand mal seizure).

### **Making a diagnosis**

Although a convulsion will be quickly recognized as a seizure, it may be less straightforward to diagnose some of the more subtle types of seizure. The diagnosis of epilepsy depends mainly on getting a very clear account of what happens during the attack from both the person themselves and an eyewitness who has seen a typical attack. Occasionally other types of attack or convulsion can look similar to seizures, but do not have abnormal electrical activity in the brain. Functional, or dissociative seizures (non-epileptic), are one type of attack which can often be confused with epileptic seizures, but happen through a process called dissociation. Neurologists can often distinguish seizures from other types of attacks based on a witness description, or video, but further tests are also performed for diagnosis.

A magnetic resonance imaging (MRI) scan will often be done to look for local areas of abnormality in the brain, which could be a potential source of seizures, but this can be normal in epilepsy. An electroencephalogram (EEG) may be carried out, recording the electrical activity of the brain through small electrodes in adhesive stickers placed on the scalp. This is painless and normally takes 20-30 minutes to carry out. In between seizures, in people with epilepsy, there may be characteristic abnormalities in the EEG (spikes and sharp waves), representing the resting activity of groups of brain cells which are electrically irritable and which from time to time may produce the kind of abnormal synchronized activity which leads to a seizure.

Where there is more difficulty in confirming that events are seizures or uncertainty about the type of seizure, EEG videotelemetry may be useful. This involves simultaneous recording of the EEG and video, usually over a period of several days as an inpatient in hospital. The aim is to try and record one or more of the typical attacks. This enables the doctors to look very closely at what happens during the attack and at what is happening to the electrical activity in the brain at the same time. In most seizures, there will be clear changes in the EEG with characteristic brain wave patterns, confirming that they are indeed epileptic seizures. The EEG recording during focal seizures may also give information about where they originate in the brain. Although videotelemetry is still mainly based in specialist neurological centres, it is gradually becoming more widely available.

### **Treatment: anti-epileptic drugs**

Epilepsy is treated with medication (referred to as 'anti-epileptic drugs' or 'anticonvulsants.'). A range of different tablets and capsules is available for the treatment of epilepsy, so that there is scope for selecting the one which best suits an individual and which gives the best possible control of the seizures. As with medicines for other conditions, different tablets may suit different people and work best for them, so there may be an initial stage of trial and error, while the most suitable medicine for any particular person is identified. The goal of treatment is to achieve the best possible control of the seizures, while at the same time avoiding unacceptable side effects from the medication.

Beginning or adjusting anti-epileptic medication is usually done in a hospital neurology clinic or specialist epilepsy clinic. Once anti-epileptic medicines have been started, the dose is usually built up gradually over a period of weeks or months, until the optimum dose for a particular individual is identified. It is important to take the medication regularly, to minimize the likelihood of seizures occurring. Also, abruptly stopping the medication may provoke seizures (withdrawal seizures). If the medicines need to be stopped or changed, the dose is usually reduced slowly, in gradual steps.

Epilepsy is a common condition worldwide and many people take anti-epileptic medication with good results over many years. Some people will go into remission and the seizures will stop. If someone has been free of seizures for a number of years, the question of coming off the medication may arise. Some people are able to stop the medication and remain seizure free.

Unfortunately, in others the seizures return when the medication is withdrawn and they will need to go back on it. The decision about whether to try coming off medication if there have been no seizures for several years is very

much an individual one, which will depend on personal circumstances and what the consequences would be if seizures returned (for example, for someone who has got their driving licence back or who is working). A number of factors can help predict the risk for a particular individual of seizures recurring if medication is withdrawn after a period of seizure freedom, so that the doctors in the neurology or epilepsy clinic will be able to give some guidance to people in making this decision. The decision should always be made after taking medical advice.

If the decision is made to come off the drugs, as emphasized, they need to be tapered off slowly over a period of weeks or months, to avoid withdrawal seizures. It is important for medication to be tapered under medical supervision with guidance about how to proceed and appropriate support during the process of gradually reducing the medicine, as well as a clear contingency plan for what to do if seizures recur as the medication is reduced.

### **Other treatments: epilepsy surgery and vagus nerve stimulation (VNS)**

In some people, medication does not give satisfactory control of seizures. In selected cases, epilepsy surgery may be an alternative. If seizures consistently originate in one localized part of the brain, it may be possible for a neurosurgeon to remove this area, if this can be done safely. This may lead to better control of seizures than medication is able to achieve. Epilepsy surgery is only likely to be suitable for a small number of people, but it is now well-established as a treatment option for drug-resistant epilepsy, which is mostly carried out in specialist epilepsy surgery centres. There is some experience with using this approach in people with seizures following encephalitis where these cannot be controlled with medications. Unfortunately, the nature of encephalitis is such that inflammation will typically have affected several regions of the brain, so that seizures may not necessarily all be coming from a single area. This means that epilepsy surgery of this kind is likely to have a limited role in people who have had encephalitis.

However, there is another type of surgical treatment available, which does not involve removing brain tissue and doesn't depend on a single origin for all the seizures. This is vagus nerve stimulation (VNS). In this method, a small electrode is implanted around the vagus nerve in the neck and the nerve is stimulated on a repeating cycle with small electrical pulses, originating from a battery implanted in the chest (very much like a heart pacemaker). Indeed, the VNS is sometimes referred to as a "pacemaker for the brain". The stimulation settings can be adjusted easily from outside the body, to establish the most effective pattern for each individual. It would be unusual to become completely free of seizures with VNS, but some people with seizures which have not been controlled by drugs may have a significant benefit. VNS is available in the same centres which carry out the other types of epilepsy surgery, where very specialized assessment is available to make sure that the best treatment option is recommended for each person's circumstances.

Finally, there is some very preliminary experience with using external electrodes, placed on the surface of the skin at various sites on the head to stimulate other nerves originating in the brain, using the same principle as VNS but without the need for an implanted electrode. These devices are designed to be used intermittently, usually overnight during sleep. This is really an experimental method at the moment, which is not routinely available, but it does indicate how research into epilepsy is evolving in several directions. Certainly, as epilepsy is such a common

condition worldwide, there is a great deal of active interest in finding new methods to improve treatment for people who have not responded well to the commonly used medications.

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