LESSON 4.6 WORKBOOK

What causes epilepsy?

So far in this unit we’ve seen how the activity of circuits regulate behaviors, as well as how the activity of circuits can be regulated by feedback inhibition and feed-forward inhibition. In this lesson, we’ll turn our attention to a disorder in which the control of circuit activity is abnormal – epilepsy.

When neuronal activity is unregulated

All complex behaviors rely on precisely ordered communication between neurons in circuits. What happens to the circuit when the ordered communication between neurons breaks down? The result is called a seizure – one of the most dramatic examples of disordered electrical behavior in the mammalian brain.

Epilepsy is the chronic neurological condition that results from unprovoked seizures. It affects approximately 50 in every 1000 people in developed countries. In the US, about 3% of all people living to the age of 80 will be diagnosed with epilepsy. Three to four times that number will have epilepsy in developing countries – why the discrepancy? No one knows.

How seizures are classified

Not all seizures are the same, and they must be sorted out according to their clinical features before any treatment program can begin. Seizures can include both ‘positive’ and ‘negative’ motor or sensory symptoms. A positive symptom involves acquiring an abnormal behavior – like jerking an arm for instance. A negative symptom involves losing a normal behavior – like briefly losing sight for instance. What symptoms appear depends on the effected region of the brain and the extent to which the normal brain tissue is involved.

Seizures can be classified clinically into two categories: partial seizures and generalized seizures. This simple classification is very useful because the effectiveness of the treatment depends on the category of seizure being treated.
**LESSON MATERIALS**

**Partial Seizures**

Partial seizures originate in a small group of neurons that are called the *seizure focus*. The seizure focus can be any small group of excitatory neurons that are damaged in some way – for example because of a blood clot, a tumor, or a scar. The symptoms of a partial seizure depend on where the seizure focus is located (Figure 30).

If the activity in the focus is intense, the inhibitory neurons surrounding the area can't keep up with the excitation. The excitatory electrical activity then begins to spread to other brain regions (Figure 31). This spread follows the normal connections in the affected circuit. The cortex is heavily interconnected. Therefore seizure foci in the cortex are more likely to spread within that hemisphere of the cortex, then to the other hemisphere, and finally to the thalamus, which can redirect the seizure throughout the entire brain.

Partial seizures are further classified into two categories: simple and complex. **Simple partial seizures** often cause changes in consciousness, but do not cause loss of consciousness. Simple partial seizures involve localized symptoms, such as jerking of the arm. The simple partial seizure becomes a **complex partial seizure** if it progresses so that the patient loses consciousness.

People who experience partial seizures often describe symptoms that precede the actual seizure called auras. Common auras include a sense of fear, a rising feeling in the abdomen, or a specific odor.

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**DEFINITIONS OF TERMS**

- **Partial seizures** – seizures that do not involve the entire brain
- **Generalized seizures** – seizures that involve the entire brain
- **Seizure focus** – specific area of the brain where partial seizures begin
- **Simple partial seizures** – partial seizure without the loss of consciousness
- **Complex partial seizures** – partial seizure in which patient loses consciousness

For a complete list of defined terms, see the Glossary.

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**Workbook**

Lesson 4.6
Generalized seizures

In contrast to partial seizures that originate in the cortex, generalized seizures involve connections to the cortex from subcortical structures like the thalamus, and connections from the cortex to subcortical structures like the thalamus (Figure 32). Generalized seizures begin without an aura or a seizure focus and involve both hemispheres of the brain from the onset. They can be divided into non-convulsive or convulsive.

The best understood non-convulsive generalized seizure is the absence seizure (formerly called petit mal). These seizures begin abruptly, usually last less than 10 seconds and are characterized by repeated loss of attention or consciousness without any physical symptoms. Absence seizures can happen many times a day and are most common in children. In this case the issue is not a defective area in the brain but a sudden generalized cortical hyper-excitability. This hyper-excitability then synchronizes with the excitatory input from the thalamus to the cortex, which causes a massive depolarization. In response, the inhibitory neurons in the thalamus try to control the output. The resulting prolonged hyperpolarization causes the neurons to take a long time to repolarize, but once they do, the synchronized depolarization can happen again. Interestingly, the EEG in absence seizures is very similar to the EEG in the deep stages of sleep known as ‘sleep spindles’.

The most common convulsive generalized seizure is the tonic-clonic or grand mal seizure. These seizures also begin abruptly, often with a grunt or a cry as the thorax and diaphragm contract suddenly. The patient may fall to the ground with a clenched jaw, lose bladder or bowel control, and become blue in the face (cyanotic). This tonic phase typically lasts 30 seconds before evolving into jerking of the extremities lasting 1-2 min. This active phase is followed by an ictal phase during which the patient is sleepy and may complain of headache and muscle soreness.

DEFINITIONS OF TERMS

Non-convulsive seizure – seizure without jerking

Convulsive seizure – seizure involving uncontrollable jerking of the body

Absence seizure – seizure in which patients have a transient loss or impairment of consciousness

Grand mal seizure – (also known as tonic-clonic seizure) type of generalize seizure that affects the entire brain

For a complete list of defined terms, see the Glossary.
LESSON MATERIALS

You can imagine that it is often difficult to distinguish a generalized seizure from a complex partial seizure with a brief aura. The distinction isn’t academic – it’s vital to choosing the proper treatment as well as pinpointing the underlying cause.

Electrical activity and seizures

As you can imagine, the most accurate way to pinpoint the region that initiates a seizure would be to impale the brain with electrodes and then measure where activity is defective. This is obviously not feasible in human patients. So, the EEG is called into service. The EEG provides a non-invasive way of examining brain activity.

EEG recordings made during partial seizures show abnormal neuronal firing beginning first in a single region. This abnormal activity then may spread to other regions, but initially only one region is effected (Figure 33).

Conversely, EEG recordings made during generalized seizures show abnormal neuronal firing beginning simultaneously throughout many, if not all, brain regions (Figure 33).

DEFINITIONS OF TERMS

Homeostasis – tendency to relatively stable equilibrium

For a complete list of defined terms, see the Glossary.

How do doctors diagnose the origin of a seizure?

What would an EEG trace look like during a partial seizure?

What would an EEG trace look like during a generalized seizure?
Seizure disorders are treated with anticonvulsant drugs, many of which work by increasing the effectiveness of inhibitory synapses. Most patients respond well enough to drugs that they can lead a normal life. In a few instances, drugs provide little or no help. Sometimes, seizure foci remain so irritable that despite drug treatment, brain surgery is required (Figure 34). In these cases, the surgeon removes the seizure foci and some of the region of the brain surrounding the focus. Most patients recover well from surgery, with their seizures eliminated or greatly reduced in frequency.

For those patients who do not respond to anticonvulsant medications, and who are not considered good candidates for surgery (because their seizures are produced throughout the brain), vagus nerve stimulation (VNS) is another treatment option (Figure 35). VNS involves the implantation of a pace-maker device that generates pulses of electricity to stimulate the vagus nerve. While it is not exactly known how VNS works, it is thought that by stimulating the vagus nerve, electrical energy is discharged upward into a wide area of the brain, disrupting the abnormal activity that causes seizures. Another theory suggests that stimulating the vagus nerve causes the release of inhibitory neurotransmitters that decrease seizure activity.

**DEFINITIONS OF TERMS**

Homeostasis – tendency to relatively stable equilibrium

For a complete list of defined terms, see the Glossary.
If a friend of yours was diagnosed with epilepsy, what questions would you ask to find out whether it caused partial or general seizures?

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How would you tell the difference between a partial seizure that has spread or a generalized seizure?