INTRODUCTION TO NEUROLOGICAL DISEASE

Learning in Retirement: Epilepsy
Lesson Overview

- Seizures VS Epilepsy
- What Causes Seizures?
- Types of Seizures
- Epilepsy
- Pathology
  - General
  - Cellular
  - Molecular
- Diagnosis
- Treatment
- Relevance
- Epilepsy Myths
- Sample Questions
Seizures VS Epilepsy

• Epilepsy ≠ Seizure

• **Epilepsy** describes a condition of the brain that causes seizures

• **Seizures** are bursts of abnormal, highly synchronous, electrical activity in the brain

• This abnormal activity leads to **alterations in consciousness**, and often **convulsions** as well (involuntary muscle spasms)

• Seizures:
  • Come on suddenly
  • Vary in duration and severity
  • May occur only once, or be a recurring event
What Causes Seizures?

- The brain is most susceptible to seizures when it is **inactive** and in **times of transition** (i.e. sleep → wake)
- About **50% of seizures are symptomatic**, or have a known, specific cause
  - Tumour (accounts for 10% of **all** seizures)
  - Infection
  - Trauma
  - Toxic Chemicals
  - Drugs
- About **50% of seizures are idiopathic**, or have **no known cause**
  - Appear spontaneously in the absence of identifiable CNS disease
Types of Seizures

• Several factors may precipitate a seizure
  • E.g. drugs, emotional stress, fever, hormonal changes, hyperventilation, sleep deprivation

• Two major groups of seizures, which differ in how/where they start

• Focal onset seizures start at a precise spot (at a focus) on one side of the brain, then may (or may not) spread to surrounding regions

• Generalized onset seizures affect both sides of the brain (or groups of cells on both sides) at the same time

Focal onset seizures may or may not affect awareness, while generalized onset seizures always involve impaired awareness
Focal Onset Seizures

- **Focal onset seizures** can be further classified based on individual’s awareness
  - **Aware**: person is awake and aware during seizure; usually remembers/has some idea what happened
    - Usually involves small area of the brain
    - Patient may experience strange sensations (i.e. strange odours), but may also involve jerking movements (if neurons affecting muscle groups are affected)
    - Usually unilateral (wouldn’t typically cause fall)
  - **Impaired awareness**: person is confused/awareness is otherwise impaired during seizure
**Generalized Onset Seizures**

- **Bilateral:** involve both hemispheres
- Focal onset seizures can also quickly become generalized seizures (if this occurs, called **focal onset bilateral** seizure)
- Types of generalized seizures:

<table>
<thead>
<tr>
<th><strong>TONIC</strong></th>
<th><strong>CLONIC</strong></th>
<th><strong>MYOCLONIC</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>muscles become stiff/flexed</td>
<td>violent muscle contractions (convulsions)</td>
<td>small muscle twitches</td>
</tr>
<tr>
<td>person may fall (backward)</td>
<td></td>
<td>short, but can be many in a short period of time</td>
</tr>
<tr>
<td><strong>ATONIC</strong></td>
<td><strong>TONIC-CLONIC</strong></td>
<td><strong>ABSENCE</strong></td>
</tr>
<tr>
<td>muscles become limp</td>
<td><em>most common type of generalized seizure</em></td>
<td>period of impaired awareness or consciousness (only observable sign is that person appears ‘spaced out’)</td>
</tr>
<tr>
<td>person may fall (forward)</td>
<td>-tonic phase followed by clonic phase</td>
<td></td>
</tr>
</tbody>
</table>
Epilepsy

- **Epilepsy** is a seizure disorder
- Patients with epilepsy have unpredictable and recurring seizures
- Someone is said to have **epilepsy** if they have two or more unprovoked seizures separated by at least 24 hours
  - **OR**
- After experiencing one seizure with high risk for experiencing more
Pathology: General

• Highly synchronous electrical activity (of neurons) in the brain

• In epilepsy, too much excitation or too little inhibition is allowing neurons to fire excessively

• Can begin at a focus or be widespread

• Symptoms vary (as discussed, many types of epilepsy), and depend on seizure severity and location, and which neurons are affected

• Clusters of neurons temporarily become impaired, and begin sending out massive amounts of excitatory signals over and over
Pathology: Cellular

- Ion channels opening and closing (and thus allowing ions to pass through) determines whether or not a neuron will depolarize.

- If a neuron depolarizes, it releases NTs – when these bind to their post-synaptic Rs, they will either promote or inhibit the opening of the ion channels:
  - Glutamate promotes (by allowing Ca\textsuperscript{2+} ions to enter pre-synaptic neuron)
  - GABA inhibits (by allowing Cl\textsuperscript{-} ions to enter pre-synaptic neuron)
Pathology: Molecular

- **NMDA receptors** are the primary receptor type that glutamate (excitatory) binds to; when Glu binds to NMDA receptor, Ca$^{2+}$ open, which tells neuron to fire
  - Some patients with epilepsy have fast or long-lasting activation of NMDA receptors

- **GABA receptors**, when activated, allow Cl⁻ ions to enter the cell, which leads to hyperpolarization
  - Some patients with epilepsy have **genetic mutations** that render their GABA receptors dysfunctional (cannot inhibit signals)

Important: Both NMDA and GABA receptors may be influenced by things like infection, brain tumour, or trauma. Neurological exams and brain imaging used to help clarify cause of seizure
Diagnosis

- **Electroencephalogram (EEG)** is the most common test used to diagnose epilepsy

- Electrodes placed on the patient’s scalp record electrical activity of neurons

- Even when not having a seizure, individuals with epilepsy generally show abnormal patterns of neural activity

- **High-density EEG** is a variant of EEG that spaces electrodes much closer together – used to help localize seizure activity more precisely

- **Neurological exam** and medical history helps determine type of epilepsy

- **Blood Tests** help identify infections, genetic conditions/other conditions that may be causing seizures
Treatment

- **Anti-epileptic medications**: most people with epilepsy are able to live seizure-free by taking one anti-epileptic medication

- Others may be able to reduce the frequency and severity of their seizures by taking a combination of medications

- If medication isn’t doing it, doctor may recommend surgery to remove affected area (if it is a small, focal region)

- Nerve stimulation – *vagus nerve* (thought to influence NT release), helps in 20-40% of cases

- In extreme cases of widespread and severe seizures that do not respond to anti-epileptic medications, *callosotomy* may be considered
Treatment

- Anti-epileptic medications come in 3 main categories (all are anti-convulsants)

1) Na\(^+\) and Ca\(^{2+}\) channel inhibitors
   - Reduces inward positive current
   - Prevents NT release

2) Drugs that increase GABA activity
   - Increases inhibition (promotes hyperpolarization of neuron)
   - Receptor agonists
   - Breakdown inhibitors

3) Drugs that decrease glutamate activity
   - Decreases excitation (inhibiting depolarization)
   - Receptor antagonists
Relevance

• Although genetic factors have been identified in some cases of epilepsy, the majority of cases are idiopathic.
Epilepsy Myths

• You can swallow your tongue during a seizure
  • *It is physically impossible to swallow your tongue*

• You should force something into the mouth of someone having a seizure
  • *No!! Roll individual on side, place something soft under head to prevent injury*

• You should restrain someone who is having a seizure
  • *Never. Seizure will run its course and cannot be stopped*
Sample Question 1:

• NAME THAT TYPE OF EPILEPSY!

• Joey has epilepsy. His seizures involve his muscles going completely limp, and he falls forward to the ground.

• Based on Joey’s symptoms, what would you name this type of epilepsy?

Name of Epilepsy = Onset Type + Symptoms Observed

• Generalized onset
• Symptoms: Atonia

Generalized Onset
Atonic Seizure
Sample Question 2:

• NAME THAT TYPE OF EPILEPSY!

• Roman has epilepsy. When he experiences a seizure, he stays awake and usually remembers what has happened.

• Based on Joey’s seizures, what would you name this type of epilepsy?

  Name of Epilepsy = Onset Type + Symptoms Observed

• Focal onset (generalized always involves impaired awareness)
• Symptoms: Recall of events (awareness)

Focal Onset Aware Seizure
Sample Question 3:

- NAME THAT TYPE OF EPILEPSY!

- Sally has epilepsy. When she experiences a ‘fit’, it always occurs the same way. First, she smells a strange odour and sometimes other odd sensations. Then, her muscles first stiffen, causing her to fall backward. Finally, she experiences 30-60 seconds of convulsions.

- Based on Sally’s symptoms, what would you name this type of epilepsy?

- Focal onset (strange sensations)
- ...becomes generalized (so we don’t worry about classifying awareness): ‘Bilateral’
- Symptoms: Tonic, then clonic (tonic-clonic)

Name of Epilepsy = Onset Type + Symptoms Observed

Focal Onset Bilateral Tonic-Clonic Seizure