Objectives

- Review basic seizure definitions and subtypes
- Review work up for seizures
- Discuss treatments for seizures and epilepsy, medications and beyond
- Discuss when to refer to either a neurologist or epileptologist
Seizures 101

• What is a seizure?
  • A sudden change in behavior that is associated with brain dysfunction
  • Epileptic seizures are characterized as electrical hypersynchronization of neuronal networks of the cerebral cortex

• What is epilepsy?
  • A propensity for recurrent unprovoked seizures
  • 2 or more unprovoked seizures

• Two important classifications (of epileptic seizures)
  • Primary generalized seizures (idiopathic/genetic)
  • Focal onset seizures
Primary generalized seizures

- On EEG, seizures appear to have a “generalized onset”

- Examples:
  - Absence seizures
    - Very short events, usually are manifested by pt staring
  - Generalized tonic clonic seizure
    - No warning, sudden onset
  - Tonic
  - Myoclonic
  - Atypical absence
Absence seizure
Myoclonic seizure
Focal onset seizures

- Have a point of origin on EEG
- Commonly, you will hear us talking about temporal onset seizures, but can be from anywhere
- Have many causes which may not be apparent on imaging
- These seizures will usually have an aura (seizure warning), which are technically very small seizures
- Can secondarily generalize
Focal onset epilepsy: temporal lobe

- Classically, think of staring, automatisms (chewing, picking)
- Insular (autonomic symptoms)
- Lateral temporal (vertigo, auditory hallucinations)
- Mesial temporal (gastric rising, fear, automatisms)
- Left temporal lobe seizures more likely to have some kind of language involvement
Focal onset epilepsy: frontal lobe

- Can have bizarre semiologies
  - Retained consciousness
  - Complex movements, bicycling of legs
  - Very little post-ictal confusion
  - Bizarre inter-ictal and post-ictal behavior
Frontal lobe seizure
Temporal lobe seizure
Non-epileptic spells

- Pt can look like they are having a seizure, but there is in fact no abnormal electrical activity occurring in their brain while this is happening.

- Clues:
  - Patient characteristics
    - Hx of trauma (physical or sexual abuse)
    - Hx of mental illness
    - Developmental delay
    - La belle indifference
    - Usually have a seizure model (relative with seizure or healthcare professional)
Epileptic seizure vs non-epileptic spell

- Spell features
  - Long prodrome
  - Non-physiologic spread
  - Pelvic thrusting
  - Side to side head shaking
  - Opisthotonus
  - Forced eye closure
  - Waxing and waning/lack of synchronization of sx's
  - Distractibility
  - Abrupt cessation
  - Long duration of spells
  - Lack of stereotypy between events
  - Suggestibility
  - Post convulsive breathing that is fast or normal
  - Disproportionate post-ictal mental status
Psychogenic non-epileptic spell
What is this?
First time seizure work up

- Provoked vs unprovoked
- Many neurologists would start with an MRI and EEG, looking for risk factors for further seizure.
- First time seizures do not necessarily need antiepileptic drug (AED) treatment
Update on AAN guidelines on treatment of 1\textsuperscript{st} time unprovoked seizure in adults (April 2015)

- Clinical variables of increased risk of recurrent seizures
  - A prior brain insult
  - An EEG with epileptiform abnormalities
  - A significant brain imaging abnormality
  - **A nocturnal seizure**
Treatments for epilepsy

- Medications

- Surgical options for pharmacologically intractible epilepsy
  - Surgical resection
  - Laser ablation (Visualase)
  - Vagal nerve stimulator (VNS)
  - Responsive neurostimulation (RNS)
Medications

- No seizures, no side effects
- How to choose an agent
  - Rational polypharmacy
  - Broad vs narrow spectrum agents
  - Unique aspects of some medications
  - Safe and easy to use agents
<table>
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<tr>
<th>Antiepileptic drug (AED) options</th>
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<tbody>
<tr>
<td>Phenytoin (Dilantin)</td>
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<td>Valproic acid (Depakote)</td>
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<td>Topiramate (Topamax)</td>
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<td>Lamotrigine (Lamictal)</td>
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<td>Levetiracetam (Keppra)</td>
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<td>Phenobarbital</td>
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<td>Pregabalin (Lyrica)</td>
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<td>Gabapentin (Neurontin)</td>
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<td>Primidone (Mysoline)</td>
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<td>Zonisamide (Zonegran)</td>
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<td>Carbamazepine (Tegretol)</td>
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<td>Oxcarbazepine (Trileptal)</td>
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<td>Ezogabine/Retigabine (Potiga)</td>
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<td>Eslicarbazepine (Aptiom)</td>
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<td>Felbamate (Felbatol)</td>
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<td>Acetazolamide (Diamox)</td>
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<td>Stiripentol (Diacomit)</td>
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“Rational Polypharmacy”

- Best to control a patient with monotherapy if possible
- If have to use two or more agents, best to utilize medications with different mechanisms of action
  - enhancing inhibition (i.e. GABAergic drugs)
  - inhibiting excitation (i.e. Na channel blockers (lamotrigine, lacosamide))
  - inhibitors of release (levetiracetam)
  - anti-glutamatergic drugs (perampanel)
  - multiple mechanisms (topiramate, valproate)
Broad spectrum AEDs

- Will treat focal or primary generalized seizures
  - Levetiracetam (Keppra)
  - Lamotrigine (Lamictal)
  - Valproate (Depakote)
  - Topiramate (Topamax)
  - Zonisamide (Zonegran)
  - Clobazam (Onfi)
  - Rufinamide (Banzel)
  - Felbamate (Felbatol)
  - Primidone (Mysoline)
  - Ezogabine (Potiga)
Choice of AEDs

- **Kind of epilepsy?**
  - Idiopathic/genetic generalized epilepsy vs focal onset epilepsy

- **Allergies to medications?**
  - Sulfa? (avoid topiramate/zonisamide)

- **Current medications**
  - Warfarin
  - Birth control

- **Previous/concurrent medical conditions**
  - Kidney stones (no TPM, ZNS)
  - Pregnancy (LMT)
  - Mental health conditions (LMT, VPA, ? Avoid LEV)
  - Headaches (VPA, TPM/ZNS, ?GBP, LEV)
Handy meds to know as a PCP

- **Levetiracetam (Keppra)**
  - Common side effects: fatigue, mood change (Kepp-rage)
  - Benefits: easy to use, very little interaction with other meds
  - Dosing: 500mg BID starting, can uptitrate to 1000mg BID or to 1500mg BID if needed

- **Lamotrigine (Lamictal)**
  - Common side effects: fatigue, dizziness, balance issues
  - Can be mood stabilizing
  - Have to be careful of SJS so slow titration
Handy meds, cont

- **Topiramate (Topamax)**
  - Common side effects: fatigue, cognitive slowing, word finding difficulties
  - Can help with weight loss, migraines
  - Can cause kidney stones
  - Dosing: 50 mg BID x 1 wk, 100mg BID x 1 wk, etc, can dose up to 200mg BID

- **Zonisamide (Zonegran)**
  - Common side effects: fatigue, cognitive slowing, word finding difficulties
  - Can help with weight loss, migraines
  - Can cause kidney stones
  - Dosing: 100mg QHS x 2 wks, 200mg QHS, etc or can dose BID (ex: 50mg BID x 2 wk, 100mg BID, etc)
Surgical treatment options for epilepsy

- Pharmacologically intractible epilepsy: epilepsy which is not controlled with adequate trials of two or more AEDs
- Surgical resection
- Laser ablation
- Vagal Nerve Stimulator (VNS)
- Responsive neurostimulation (RNS)
Surgical resection

- Only effective for focal onset epilepsy
- Localize seizures with EEG and determine if patient would benefit from having that zone removed
- Risk assessment
  - Wada testing
  - Neuropsych testing
  - Functional MRI for language mapping
- Intracranial EEG monitoring with intracranial electrodes prior to resection
Laser ablation (Visualase)

- Only effective for focal onset epilepsy
- Would still localize seizures with EEG and determine if zone could be ablated with MRI guided thermal ablation.
- Temporal lobe epilepsy
- Less invasive, less risk of complications
Vagal Nerve Stimulation (VNS)

- Indicated for adjunct therapy for focal onset seizures
- Delivers a fixed current to the vagus nerve at a set interval
  - Can also use a magnet to trigger burst of stimulation to abort seizures
  - Newer aspire model has a tachycardia detection setting to recognize the rapid rate of rise of heart rate just prior to many people’s seizures
- Mechanism not clear
- Can allow for improved seizure control without additional medication side effects
- VNS side effects: hoarseness, SOB, headache, throat pain
Responsive neurostimulation (RNS)

- Only effective for focal onset epilepsy
  - Can be multifocal or in eloquent cortex

- Monitors for seizures and stimulates area of the brain where the seizures originate to stop them before they spread.

- Have to teach computer to recognize seizures and it will automatically stimulate

- Also has a magnet that if swiped can deliver an extra stimulation

- Usually has capability to stimulate at two different seizure foci simultaneously
When do I refer to neurologist?

- At any point you want!
- First unprovoked seizure: depends on your comfort level
  - Can refer right away without ordering tests, can order tests
  - In many situations will not have to start medication
- Second unprovoked seizure and beyond
- When you aren’t sure if events are seizures
  - Can also refer straight to the epilepsy monitoring unit (EMU)
When to refer, cont

- A neurologist might refer to an epileptologist (seizure specialist) when:
  - multiple medications have failed and assistance is required with medication management vs consideration for surgery
    - Let us think about the intricacies of multiple different and newer medications
    - Multiple different types of surgical procedures (resection, ablation, VNS, RNS)
    - Remember, pharmacologically intractable epilepsy is defined as seizures refractory to adequate trials of 2 or more AEDs.
  
- REFER SOONER RATHER THAN LATER!!!
Epilepsy Monitoring Units (EMUs)

- Seizure/spell characterization (is it an epileptic seizure, if so, what type)
- Seizure localization (figuring out where seizure is coming from for surgical work up)
EMUs, cont

- Locations:
  - Lutheran Medical Center (2 beds)
  - Swedish Medical Center (8 beds, level 4 epilepsy center)
    - Certified to provide more complex forms of epilepsy care including evaluation and performance of treatment alternatives outside of medications (resection surgery, VNS, RNS)
  - St. Joseph Hospital
  - University of Colorado (level 4 epilepsy center)
  - Children’s Hospital Colorado (level 4 epilepsy center)
  - Denver Health (level 4 epilepsy center)
  - St. Mary’s Hospital (Grand Junction)
  - Littleton Adventist Hospital
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