NAME THAT SPELL: Seizure Classification and Treatment

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BARROW NEUROSCIENCE NURSING SYMPOSIUM
DISCLOSURES

• NONE
OBJECTIVES

- Describe the classification of seizures and epilepsy
- Describe the goals of treatment and the variables that affect anti-epileptic drug (AED) selection
- Seizure examples
HISTORICAL PERSPECTIVES
Hippocrates had the revolutionary view that epilepsy was a disorder of the brain.

“People think that epilepsy is divine simply because they don’t have any idea what causes epilepsy”
Although the characteristics of a seizure may differ from person to person, seizures are all caused by:

- A. A sudden change in how brain cells send electrical signals to one another
- B. A sudden change in how the spinal cord and brain talk to each other
- C. A sudden change in blood flow to the brain
- D. A sudden change in oxygen flow in the body
DEFINITIONS

- **Seizure** : [Latin] *sacire* = *to take possession of*

- Seizure is a paroxysmal event due to an abnormal, excessive, hyper synchronous discharge from an aggregate of CNS neurons
• *Epilepsy :*[Greek] *epilepsia : epi= upon + lepsis = to take hold of / seize*

• Epilepsy is a condition in which there are recurrent seizures due to a chronic, underlying process
  ○ Brain disorder characterized by an *enduring predisposition* to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of the condition. Definition requires occurrence of at least one epileptic seizure

*Recurrent (2 or more) *unprovoked* seizures

○ Not due to (acute provoking factors):  
  • Fever  
  • Head trauma  
  • Alcohol intoxication  
  • Metabolic disorder (hypoglycemia, hyponatremia)
The incidence follows a U-shaped curve, with highest incidence in childhood/adolescence (genetic causes) and again $\sim 60$ years of age (acquired causes such as tumor, stroke)
Approximately 5% of total yearly visits to the ER are related to the injuries resulting from seizures.

Relative risk of death is 2-3 times higher than in general population.

SUDEP (sudden unexpected death in epileptic people)
- may be the cause of death in 7-17% of epilepsy-related deaths
- Still not well known
<table>
<thead>
<tr>
<th>Pythagoras</th>
<th>William Pitt</th>
<th>Lewis Carroll</th>
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<tr>
<td>Buddha</td>
<td>Napoleon Bonaparte</td>
<td>Alfred Nobel</td>
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<td>Socrates</td>
<td>Ludwig van Beethoven</td>
<td>Fyodor Dostoyevsky</td>
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<td>Alexander the Great</td>
<td>Sir Walter Scott</td>
<td>Peter Tchaikovsky</td>
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<td>Julius Caesar</td>
<td>Nicolo Paganini</td>
<td>Guy de Maupassant</td>
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<td>St. Paul</td>
<td>Lord Byron</td>
<td>Vincent Van Gogh</td>
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<td>Alfred the Great</td>
<td>Percy Bysshe Shelley</td>
<td>Dame Agatha Christie</td>
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<tr>
<td>Mohammed</td>
<td>Hector Berlioz</td>
<td>Michael Wilding</td>
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<td>Dante</td>
<td>Edgar Allen Poe</td>
<td>Truman Capote</td>
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<td>Joan of Arc</td>
<td>Alfred Lord Tennyson</td>
<td>Richard Burton</td>
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<tr>
<td>Jean Moliere</td>
<td>Charles Dickens</td>
<td>Margaux Hemingway</td>
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<td>Blaise Pascal</td>
<td>Edward Lear</td>
<td>Danny Glover</td>
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<td>Peter the Great</td>
<td>Soren Kierkegaard</td>
<td>Hugo Weaving</td>
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<td>George Frederick Handel</td>
<td>Gustave Flaubert</td>
<td>Lil Wayne</td>
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CLASSIFICATION OF SEIZURES

Partial (Focal) Onset (75%)  Generalized from Onset (25%)
ILAE* Classification

GENERALIZED SEIZURES
- Tonic Clonic
- Absence
  - Typical
  - Atypical
  - Absence with special features
    - Myoclonic absence
    - Eyelid myoclonia
- Myoclonic
  - Myoclonic atonic
  - Myoclonic tonic
- Clonic
- Tonic
- Atonic

FOCAL (Partial) SEIZURES
- Without impairment of consciousness (Simple Partial Seizures / Auras OR †Focal onset seizure with {motor, autonomic, etc} features)
  - Motor
  - Autonomic symptoms
  - Subjective sensory
  - Subjective psychic phenomena only (déjà vu, jamais vu)
- With impairment of consciousness (Complex Partial Seizures, or †Focal dyscognitive seizure)
  †Newer terminology, but likely to be revised again....

*International League Against Epilepsy
ETIOLOGY

• **Idiopathic (Primary)**
  - Occurring in the setting of normal neurologic status and imaging, without clear cause (genetic + other factors)

• **Symptomatic (Secondary)**
  - Involving abnormal neurologic or psychological findings & diffuse or multifocal brain lesions

• **Cryptogenic**
  - Presumed symptomatic, but cause unknown (e.g., person with clear cognitive abnormalities, but normal imaging)
  - Terminology falling out of favor
DIAGNOSIS OF EPILEPSY

- **History**
  - Aura and sequence of events, witnesses, triggers
  - H/o CNS infection, TBI, febrile szs, FH of epilepsy, meds (triggers), PMH (syndromes), PSH (lesions)

- **Physical Exam** *(Look for underlying syndromes)*
  - Focal neurological findings, injuries from seizures

- **Laboratory Tests** *(Triggers)*
  - CBC, CMP (Gluc, Na+, K+), TSH, Urine Tox

- **EEG** *(Only positive in 40% of epilepsies if interictal)*
  - May need 24-hour video monitoring

- **Neuroimaging** *(Only positive in ~50% of epilepsies)*
  - CT-scan, MRI (seizure & dysplasia protocols), PET scan, SPECT

- **Other:** Post-ictal increased temp, WBCs, lactase, prolactin
1) Symptoms during the seizure

- **Aura:**
  - subjective sensations (earliest portion of the seizure. But, not all patients have these, and even if they do, many do not remember after the seizure)

- **Behavior:**
  - mood or behavioral changes before the seizure

- **Pre-ictal symptoms:**
  - described by patient or witness

- **Vocal:**
  - cry or gasp, slurred or garbled speech
2) Symptoms during the seizure

- **Motor:**
  - head or eye turning, eye deviation, posturing, rhythmic jerking, stiffening, automatisms, generalized or focal movements

- **Respiration:**
  - change in pattern, cessation, cyanosis

- **Autonomic:**
  - pupillary dilatation, drooling, change in respiration or heart rate, pallor, vomiting, incontinence

- Loss of consciousness or inability to speak or understand
AUTOMATISMS

- A “Release Phenomenon”
  - When unilateral, usually ipsilateral to seizure-onset side (but behaviors can be bilateral and tougher to localize)
  - Movements that appear purposeless or repetitive
Complex partial seizure
(FOCAL ONSET DYSCOGNITIVE SEIZURE)

- The patient displays right sided automatisms and lip/oral movements, typical for temporal lobe epilepsy
What is the side of onset based on the automatisms?

A. Left
B. Right
Complex Partial Seizure
(FOCAL ONSET DYSCOGNITIVE SEIZURE)
3) Symptoms following a seizure

- Amnesia for events
- Confusion
- Lethargy
- Sleepiness
- Headache and muscle aches
- Transient focal weakness
  - (Todd’s paresis/paralysis) → contralateral to seizure onset side: this is the oldest and most well known localizing sign
- Nausea or vomiting
- Tongue biting
TREATMENT OF EPILEPSY

- Anti-Epileptic Drugs (AEDs)
- Vagus Nerve Stimulation (VNS)
- Epilepsy Surgery
  - Amygdalo-hippocampectomy
  - Lobectomy / Lesionectomy
  - Multiple sub-pial transections (MST)
- Ketogenic Diet
- Transcranial Magnetic Stimulation
- Deep Brain Stimulation
• Start AEDs after 2 unprovoked seizures

• Risk of seizure recurrence (>1 seizure):
  ○ 34% at 5 years in low risk patients
  ○ 80% at 5 years in high risk patients

• High risk patients:
  ○ History of serious brain injury, or intellectual disability
  ○ Lesion on CT or MRI, or abnormal EEG
  ○ Focal abnormalities on neurological exam
  ○ Partial (focal) seizure as first seizure
CHOOSING AN AED

- **First Generation AEDs:**
  - Less expensive, more drug-drug interactions
  - Require monitoring
  - Ex: phenytoin, phenobarbital

- **Second Generation AEDs:**
  - Fewer drug-interactions and side-effects
  - No monitoring
  - More expensive
  - Ex: levetiracetam

- **Generics now available for many AEDs**

- **No significant difference in the effectiveness of first and second generation AEDs**
AED PEARLS

**Broad Spectrum***
- Lamotrigine
- Levetiracetam
- Topiramate
- Zonisamide
- Valproate
- Clonazepam
- Perampanel

**May Worsen IGE**
- Phenytoin
- Carbamazepine
- Oxcarbazepine
- Gabapentin
- Tiagabin
- Vigabatrin
- Pregabalin

*Use for IGE, but generally good for any seizure type*
AED PEARLS

- Many AEDs are CYP450 inducers or inhibitors
- Older meds are hepatically metabolized, must be carefully monitored
- Newer meds are renally excreted
- Older meds can interfere with OCPs
- All fertile women should be on Folate
- Long-term AEDs can cause bone-loss
AEDs and Hormones

- Enzyme inducing (CYP 450) medications can alter female sex steroid hormone levels AND induce production of sex hormone binding globulin
  - Net effect: decrease endogenous hormones and exogenous OCPs
- Sexual dysfunction and lower arousal in woman on enzyme inducing AEDs
▶ **Strong Inducers**
- Phenobarbital
- Phenytoin
- Carbamazepine
- Primidone
- Oxcarbazepine
- Clobazam

▶ **Weak Inducers**
- Topiramate
- Lamotrigine
- Felbamate
- Rufinamide

▶ **Noninducers**
- Ethosuximide
- Valproate
- Gabapentin
- Clonazepam
- Tiagabine
- Levetiracetam
- Zonisamide
- Pregabalin
- Vigabatrin
- Lacosamide
- Ezogabine\(^b\)

\(^a\) Avoid concomitant use with the lowest-dose oral contraceptive pills.
\(^b\) United States Adopted Name; known in rest of world as retigabine.
CONTRACEPTION ISSUES

- Can we just use higher dose OCPs?
  - Available but infrequently used

- Preferred methods if on enzyme inducers:
  - Progestin implant
  - IUD
  - Depo-Provera
  - Barrier methods
500,000 WWE are of childbearing age in the US
In utero exposure to AEDs is likely considerably higher
North American AED Pregnancy Registry

http://www.aedpregnancyregistry.org/
# Timing of Developmental Pathology

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Malformations</th>
<th>Postconceptional Age</th>
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<tbody>
<tr>
<td>CNS</td>
<td>Neural tube defect</td>
<td>28 d</td>
</tr>
<tr>
<td>Heart</td>
<td>Ventricular septal defect</td>
<td>42 d</td>
</tr>
<tr>
<td>Face</td>
<td>Cleft lip</td>
<td>36 d</td>
</tr>
<tr>
<td></td>
<td>Cleft maxillary palate</td>
<td>47–70 d</td>
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Valproic acid (Depakote) exposure has higher risk of major malformations compared to carbamazepine, phenytoin, lamotrigine

1st trimester: 6-9%

Dose dependence in risk

- Risk if dose <700mg/day: ~4%
- Some reports as high as 20% if dose >1500mg/day
Major Congenital Malformations in 1st Trimester Exposure
Monotherapy

Figure from: Continuum: Lifelong Learning in Neurology 19(3 Epilepsy): 697-714, June 2013; data from Hernandez-Diaz et al.
• **Atonic seizure**
  - Characterized by loss of muscle tone; if upright, patients may fall to the ground and injure themselves.
  - Note the subtle, brief dropping of the patient’s head
- Eyelid Myoclonia
- Jeavon’s Syndrome
  - Reflex IGE
  - Characterized by:
    - Eyelid myoclonia w/wo absence
    - Eye closure induced seizures
    - Photosensitivity
Frontal Lobe Seizure
- Usually brief
- Characterized by hypermotor/hyperkinetic behaviors
35th Annual
Barrow Nursing Symposium
Looking Back: Nursing Forward