Seizures and Epilepsy

Dr. Gary Mumaugh – Campbellsville University

Seizures

- Sudden, transient alteration of brain function caused by an abrupt *explosive, disorderly* discharge of cerebral neurons
- Motor, sensory, autonomic, or psychic signs
- Convulsion
    - Tonic-clonic (jerky, contract-relax) movements associated with some seizures
- Partial (focal) seizures
- Simple, complex, secondary generalized
- Generalized seizures
- Unclassified epileptic seizure
    - Idiopathic
    - Symptomatic
    - Cryptogenic

General Concepts

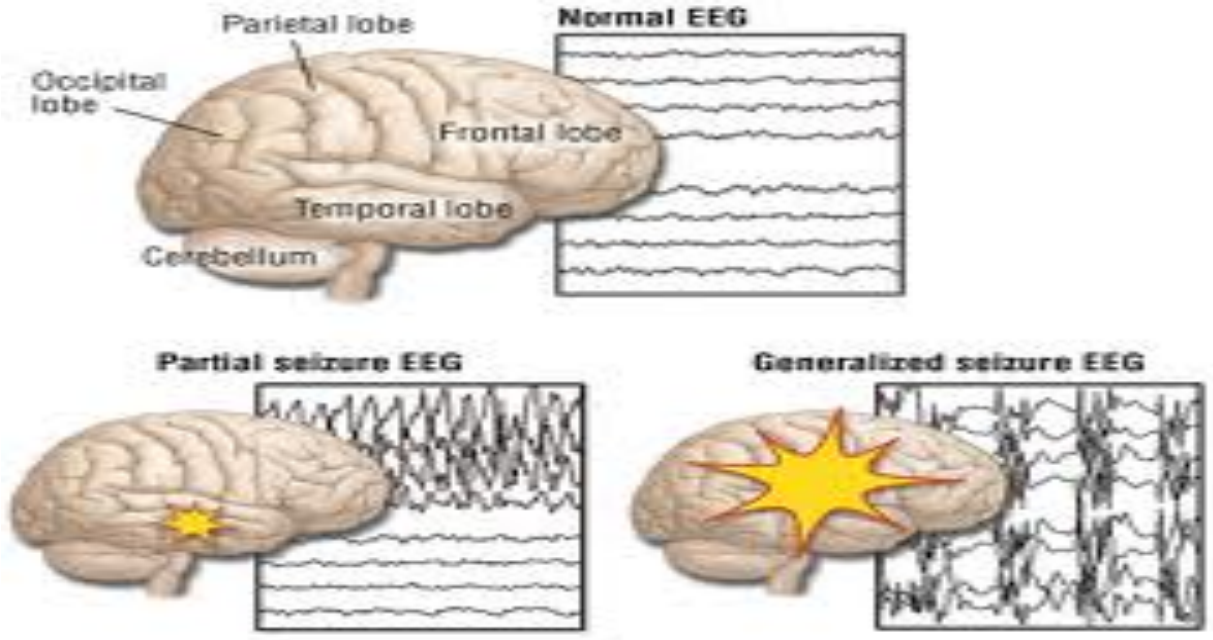
- **Convulsio**n- an episode of widespread and intense motor activity
    - May be isolated or in a series
- **Seizure**- an episode of rapidly evolving disturbances of brain function that may produce impaired consciousness, abnormalities of sensation or mental functions, or convulsive movements
    - Level of consciousness can be of central importance
- **Epilepsy-** long-term disturbance of brain structure and/or function, leading to an increased susceptibility to seizures
    - Underlying abnormality lies within the brain itself

Seizure Terminology

- **Interictal:** period of time between seizure activity
- **Photic Stimulation:** use of an intense flashing light to elicit an abnormal EEG or an actual seizure
- **Partial Seizure:** seizure activity that is caused from a relative restricted set of brain structures
- **Generalized Seizure:** occurs over large areas of the cerebral cortex of both hemispheres at once
- **Tonic-Clonic Seizure (Grand mal):** generalized convulsive seizure involving loss of consciousness
- **Myoclanic Seizure:** refers to muscle twitching and/or limb jerking movements due to abnormal cortical activity
- **Clonus:** hyperactivity of the stretch reflexes

Tonic vs. Clonic Seizures

- **Tonic** seizures involve sudden stiffening and contraction of the muscles.
- **Clonic** seizures involve rhythmic twitching or jerking of one or several muscles.
- **Tonic-clonic** seizures are a combination of these two types in a specific pattern.



Nonepileptic Seizures

- May result from metabolic disruption associated with:
  - Withdrawal from **sedative / hypnotic drugs**
    - Prone to **status elepticus** (persistent seizure)
  - **Bacterial meningitis**
  - **Renal and hepatic failure**
    - Uremia/electrolyte changes cause convulsions
- **Hypoxic encephalopathy**
  - Resulting from cardiac arrest, CO poisoning, near-drowning, suffocation, respiratory failure, etc.
- **Febrile convulsions**
- **Brain tumor**
- **Cerebrovascular accident**
  - Embolic, thrombotic or hemorrhagic

Epileptic Seizures

- Requires history of <u>at least two seizures</u> that can't be attributed to some other disease
- Abnormality is centered within the brain itself
  - Gray matter/cortical tissue is origin of seizure activity, specifically the cortical tissue that forms gyri, sulci, and fissures
- Most seizures begin at an **epileptogenic focus-** group of abnormal neurons that spontaneously depolarize, firing <u>thousands</u> of action potentials without an identifiable cause
  - Can be examined by electrocorticography (ECoG) or EEG
    - Multiple electrodes placed on surgically exposed surface of a section of cortex

Patterns of Seizure Activity

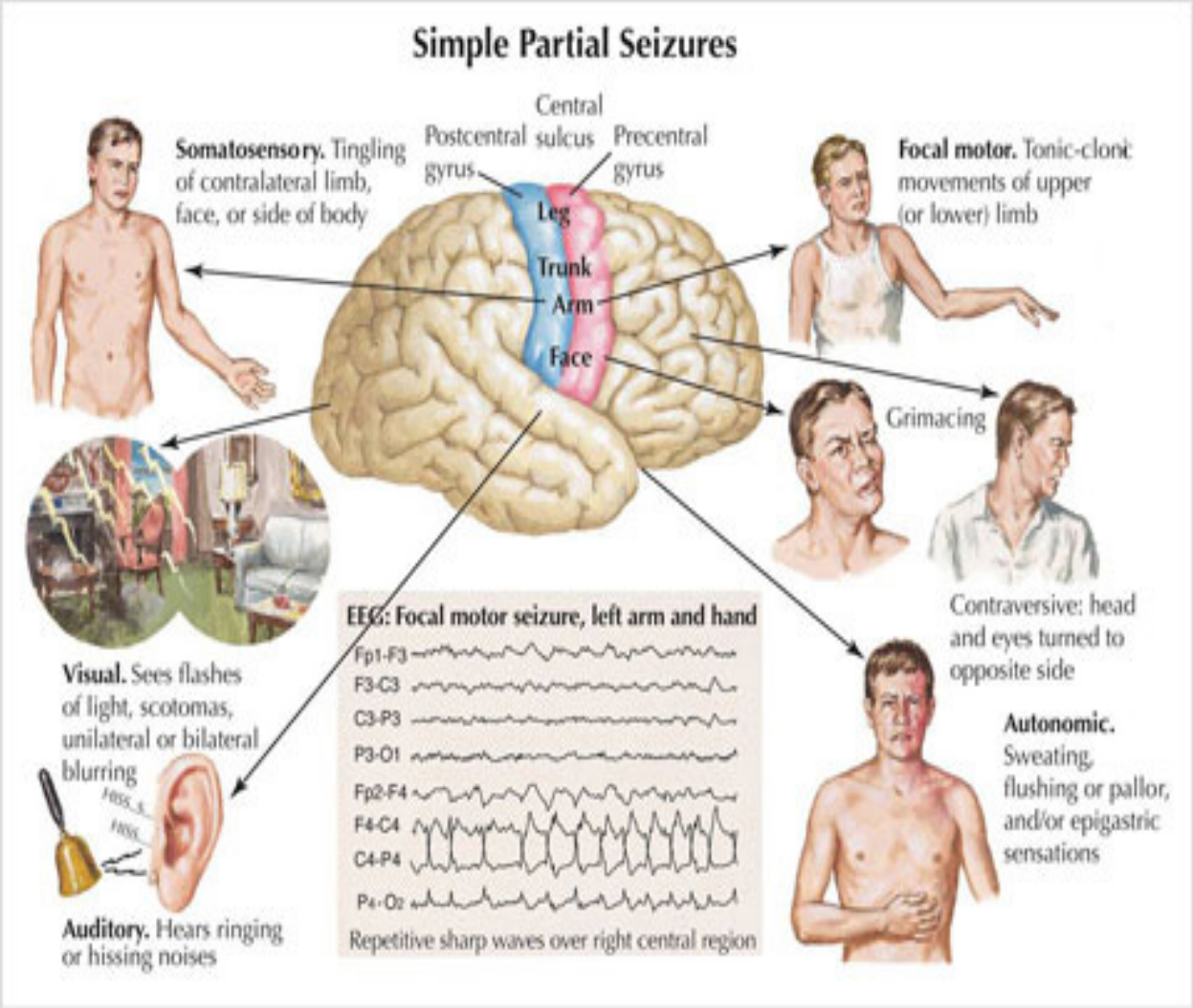
- Clinical observations of a given seizure's components are useful in diagnosing and response to therapy
- **Prodrome:** set of symptoms that warns of a seizures approach
    - Minutes, hours or even days before it occurs
- **Aura:** occurs as the seizure begins; includes mental, sensory or motor phenomena that is remembered as signaling the onset of the seizure
    - Useful in pinpointing the area(s) of brain in which the seizure activity is initiated

Seizure Classifications

- Partial Seizures
    - Simple partial seizures
    - Complex partial seizures
    - Partial seizure progression
- Generalized Seizures
    - Absence seizures - petit mal
    - Simple absence seizure
    - Atypical absence seizure
    - Tonic - Clonic Seizure (Grand Mal)
    - Clonic seizure
    - Tonic seizure
    - Atonic seizure

Partial Seizures- Begins at a discrete and relatively limited focus, pattern depends on area of brain stimulated

- **Simple Partial Seizures**
    - Spread is very limited
    - Elementary symptoms- relatively uncomplicated
- **Partial Seizure Progression**
    - Limited number of ways a seizure may progress
    - Unpredictable
- **Complex Partial Seizures**
    - Alteration of consciousness following the initial simple seizures
    - May exhibit **automatisms-** purposeless, automatic behaviors
        - Ex. Lip smacking, sucking, chewing or swallowing, fumbling with clothing, or interrupted continuation of habitual acts



7 Kinds of Generalized Seizures

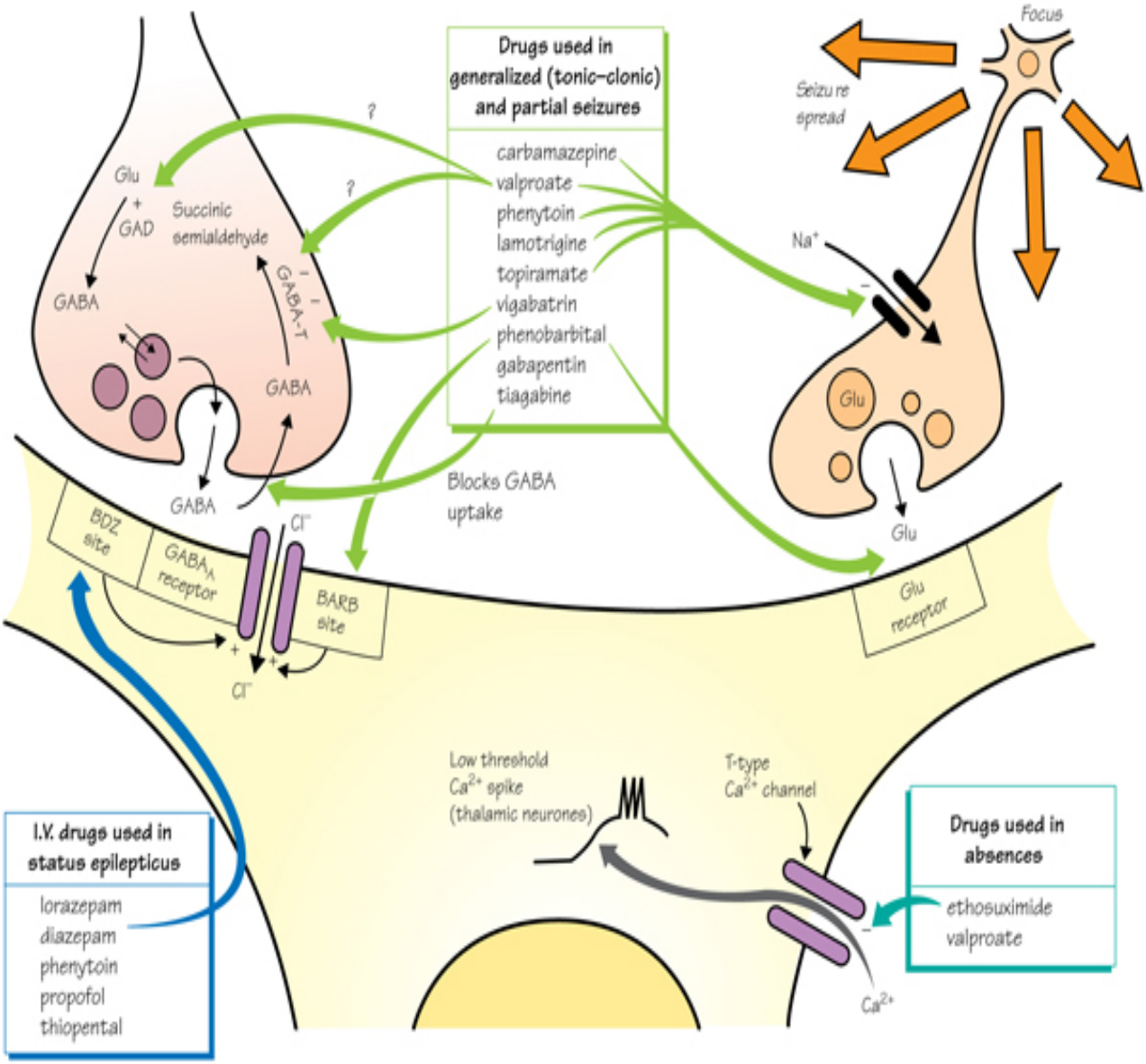
- **Absence Seizures (Petit Mal)**
  - Typical brain wave patterns, but involve minor impairments or neural function arising from changes in relatively small areas of the brain
    - Blank stare or other facial signs indicate impaired consciousness
- **Simple Absence**
  - **T**ypically an epilepsy of childhood or adolescence
  - Often spontaneously remits as nervous system matures
- **Atypical Absence**
  - Associated with Lennox-Gastaut that usually affects children 1 year and older
  - Wide range of seizures
  - Mildly retarded
  - Difficult to treat effectively

7 Kinds of Generalized Seizures

- **Tonic - Clonic Seizure (Grand Mal)**
  - Represent a maximal seizure response of the brain in which all brain systems can be recruited into the paroxysmal discharge
  - **Initial tonic phase**
    - 10-20 seconds long
    - Starts with a brief period of muscle flexing, raising of arms and opening of the eyes/mouth
    - Jaws close → **epileptic cry**
    - Pupils become unresponsive to light
  - **Clonic Phase**
    - 1½ - 2 minutes long
    - Initial muscle relaxation
    - Violent spasms of contraction/relaxation
      - Can result in torn muscles or bone fractures
    - Autonomic system active
      - Pronounced perspiration
      - Heavy salivary secretion
      - Constriction/dilation of pupils
  - **Terminal Phase**
    - 5 minutes long – longest and final phase
    - Victim becomes limp and quiet – coma-like state
    - Normal breathing restored
    - May be followed by up to an hour of deep sleep
    - Patient may become conscious with no recollection of event
- **Clonic Seizure**
  - Generalized seizure characterized by rhythmic contraction of all muscles
  - Loss of consciousness
  - Marked autonomic manifestations
- **Tonic Seizure**
  - Brief, generalized tonic extension of all four limbs and head extension
  - Marked autonomic manifestations
  - Both of these seizures are more common in children and rare in adults.
- **Atonic Seizure**
  - Characterized by a sudden loss of muscle tone
  - Head or body sagging with full consciousness→ Loss of consciousness→ Falling→ Complete loss of muscle tone
    - **Akinetic-** transient arrest of all motor activity
    - **Astatic-** drop attacks, sudden spells during which the person, usually a child, falls without warning
    - **Infantile Spasms-** varied expression of flexor, extensor, lightning spasms or neck flexion
      - Associated with **West's syndrome** (affect infants 8+ months old)
      - Severe neurological impairments/progressive encephalopathy

Medical Management of Epilepsy

- Antiepileptic medication
- Surgery-epileptogenic focus is first identified and then surgically removed
- Effectively managing stress
- Eating well
- Sufficient rest
- Avoiding epileptic triggers
- Inadequate sleep
- Food allergies
- Alcohol
- Smoking
- Flashing lights



Drug*	Presumed main mechanism of action	Approved use (FDA, EMA)	Main uses	Main limitations
Vigabatrin (1989)	GABA potentiation	Infantile spasms, complex partial seizures (currently for adjunctive use only)	No clinical hepatotoxicity. Use for infantile spasms, focal and generalized seizures with focal onset	Not useful for absence or myoclonic seizures. Causes a visual field defect and weight gain. Not as efficacious as carbamazepine for focal seizures
Lamotrigine (1990)	Na^+ channel blocker	Partial and generalized convulsive seizures, Lennox-Gastaut syndrome, bipolar disorder	First line drug for focal and generalized seizures	Enzyme inducer, skin hypersensitivity. Not as effective as valproate for new onset absence seizures
Oxcarbazepine (1990)	Na^+ channel blocker	Partial seizures	First line drug for focal and generalized seizures with focal onset	Enzyme inducer, hyponatremia, skin hypersensitivity. Not useful for absence or myoclonic seizures
Gabapentin (1993)	Ca^{2+} blocker ($\alpha 2\delta$ subunit)	Partial and generalized convulsive seizures, postherpetic and diabetic neuralgia, restless leg syndrome	No clinical hepatotoxicity. Use for focal and generalized seizures with focal onset	Currently for adjunctive use only. Not useful for absence or myoclonic seizures and can cause weight gain. Not as effective as carbamazepine for new onset focal seizures
Topiramate (1995)	Multiple (GABA potentiation, glutamate (AMPA) inhibition, sodium and calcium channel blockade)	Partial and generalized convulsive seizures, Lennox-Gastaut syndrome, migraine prophylaxis	First line drug for focal and generalized seizures. No clinical hepatotoxicity	Cognitive side effects, kidney stones, speech problems, weight loss. Not as effective as carbamazepine for new onset focal seizures
Levetiracetam (2000)	SV2A modulation	Partial and generalized convulsive seizures, partial seizures, GTCS, juvenile myoclonic epilepsy	First line drug (intravenous) for focal and generalized seizures with focal onset and myoclonic seizures. No clinical hepatotoxicity. As efficacious as carbamazepine for new onset focal seizures	Not useful for absence or myoclonic seizures. Psychiatric side effects
Zonisamide (2000)	Na^+ channel blocker	Partial seizures	First line drug for focal and generalized seizures. No clinical hepatotoxicity. Non-inferior to carbamazepine for new onset focal seizures	Cognitive side effects, kidney stones, sedative, weight loss
Stiripentol (2002)	GABA potentiation, Na^+ channel blocker	Dravet syndrome	Use for seizures in Dravet syndrome. No clinical hepatotoxicity	Currently for adjunctive use only
Pregabalin (2004)	Ca^{2+} blocker ($\alpha 2\delta$ subunit)	Partial seizures, neuropathic pain, generalized anxiety disorder, fibromyalgia	Use for focal and generalized seizures with focal onset. No clinical hepatotoxicity	Currently for adjunctive use only, not useful for absence or myoclonic seizures, weight gain
Rufinamide (2004)	Na^+ channel blockade	Lennox-Gastaut syndrome	Use for seizures in Lennox-Gastaut syndrome. No clinical hepatotoxicity	Currently for adjunctive use only
Lacosamide (2008)	Enhanced slow inactivation of voltage gated Na^+ channels	Partial seizures	Use (intravenous) for focal and generalized seizures with focal onset. No clinical hepatotoxicity	Currently for adjunctive use only
Eslicarbazepine acetate (2009)	Na^+ channel blocker	Partial seizures	Use for focal and generalized seizures with focal onset	Currently for adjunctive use only, enzyme inducer, hyponatremia
Perampanel (2012)	Glutamate (AMPA) antagonist	Partial seizures	Use for focal and generalized seizures with focal onset	Currently for adjunctive use only. Not useful for absence or myoclonic seizures