Seizures and Epilepsy

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Seizures

- Sudden, transient alteration of brain function caused by an abrupt *explosive, disorderly* discharge of cerebral neurons
- Motor, sensory, autonomic, or psychic signs
- Some seizures can hardly be noticed, while others are totally disabling.
- **Convulsion**
  - Tonic-clonic (jerky, contract-relax) movements associated with some seizures

Epilepsy

- A condition that affects the central nervous system with the following criteria
  - Has had at least 2 seizures
  - Not caused by some known medical condition like alcohol withdrawal or very low blood sugar.
  - Not indicate anything about the cause of the seizures, what type thy are, or how severe they are

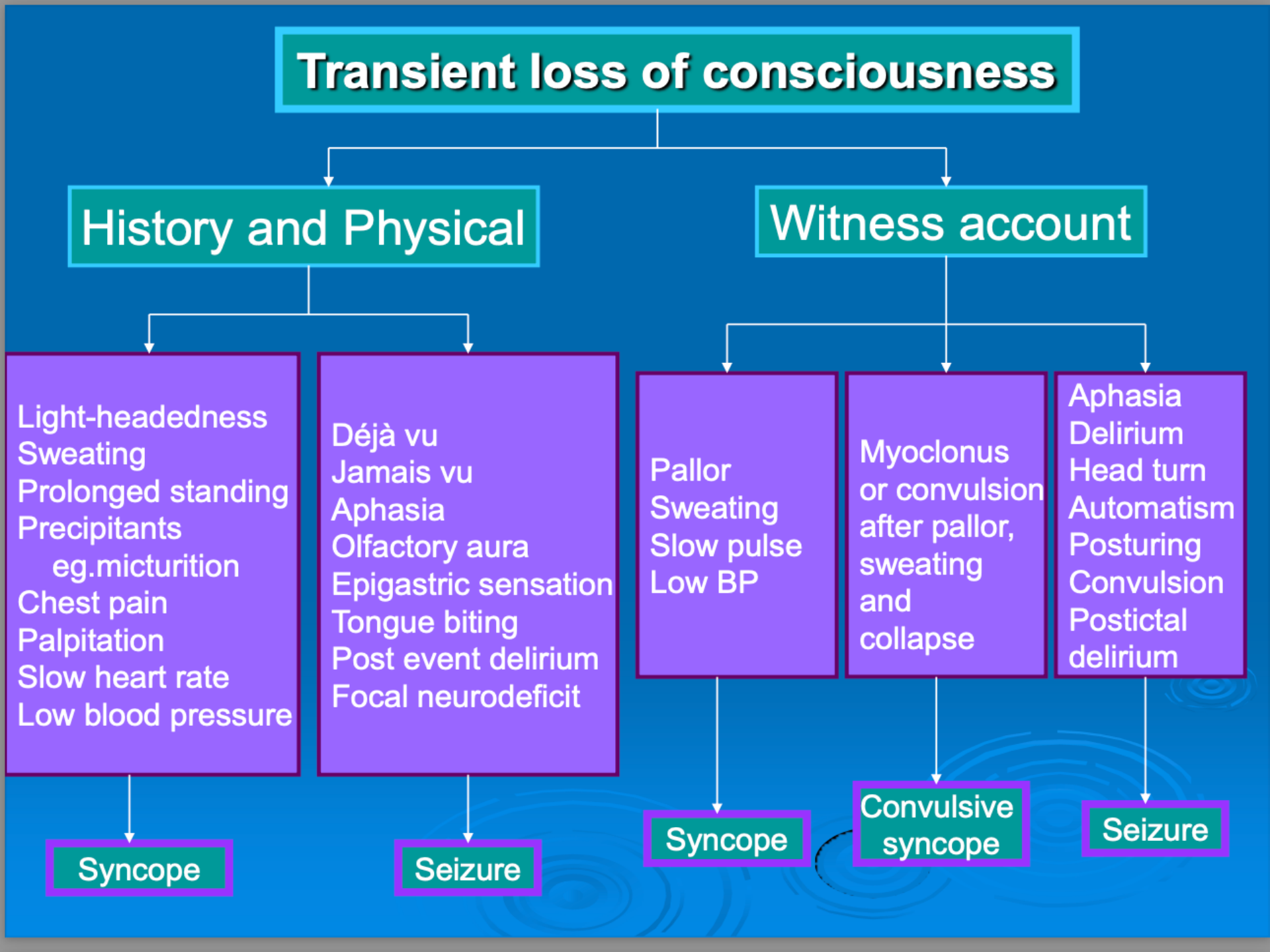
Epileptic Seizures

- Requires history of at least two seizures 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

Epileptic Seizures

- Most seizures begin at an **epileptogenic focus-** group of abnormal neurons that spontaneously depolarize, firing thousands 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


Transient loss of consciousness
History and Physical
Witness account
Light-headedness
Sweating
Prolonged standing
Precipitants
eg.micturition
Chest pain
Palpitation
Slow heart rate
Low blood pressure
Déjà vu
Jamais vu
Aphasia
Olfactory aura
Epigastric sensation
Tongue biting
Post event delirium
Focal neurodeficit
Pallor
Sweating
Slow pulse
Low BP
Myoclonus
or convulsion
after pallor,
sweating
and
collapse
Aphasia
Delirium
Head turn
Automatism
Posturing
Convulsion
Postictal
delirium
Syncope
Seizure
Syncope
Convulsive
syncope
Seizure

Character	Syncope	Epileptic Seizure
Position	Usually upright	any
Time	daytime	day or nighttime
Color	pallor	normal or cyanotic
Aura	dizziness, visual blurring	possible specific aura
Autonomic	common	uncommon
Duration	brief	brief or prolonged
Incontinence	rare	more common
Motor Activity	occasionally brief tonic seizure or clonic jerks	variable
Automatism	none	absence, CPS
Disorientations, posictal	rare	Can occur with GTC, CPS

Non-Epileptic Seizures

- Physiological
  - Tremor
  - Vasovagal syncope
  - Cardiac arrhythmias
  - Migraine
  - Medication side effects
  - Transient ischemic attacks
  - Autonomic dysfunction

Non-Epileptic Seizures

- Psychological
  - Anxiety
  - Panic attacks
  - Mood disorder
  - Personality disorder
  - Psychosis
  - Somatoform illness
  - Psychogenic seizures

Non-Epileptic Seizures

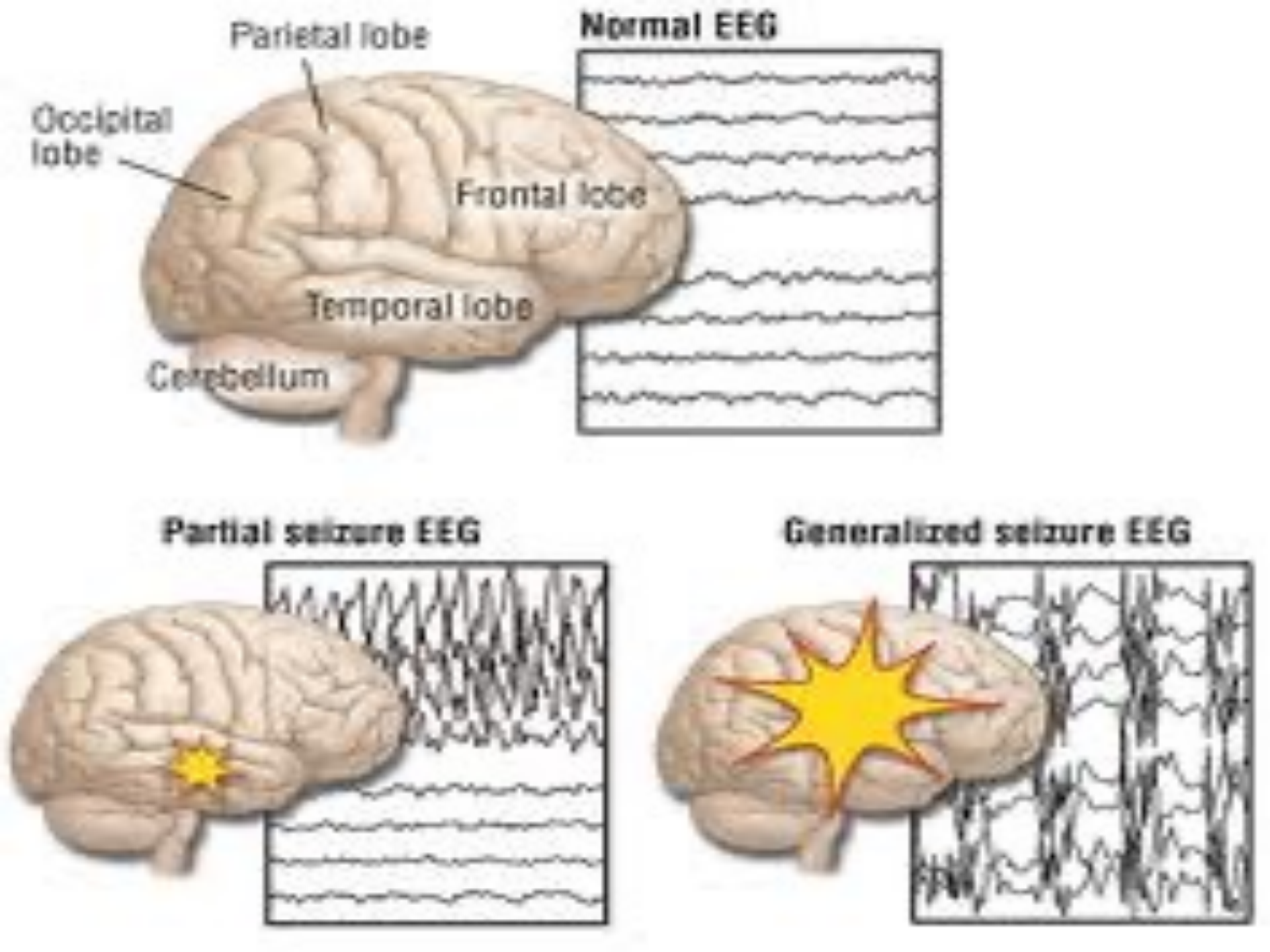
- May result from metabolic disruption associated with:
  - Withdrawal from sedative / hypnotic drugs (common with Xanax)
  - Prone to status elepticus (persistent seizure)
  - Bacterial meningitis
  - Renal and hepatic failure
    - Uremia/electrolyte changes cause convulsions

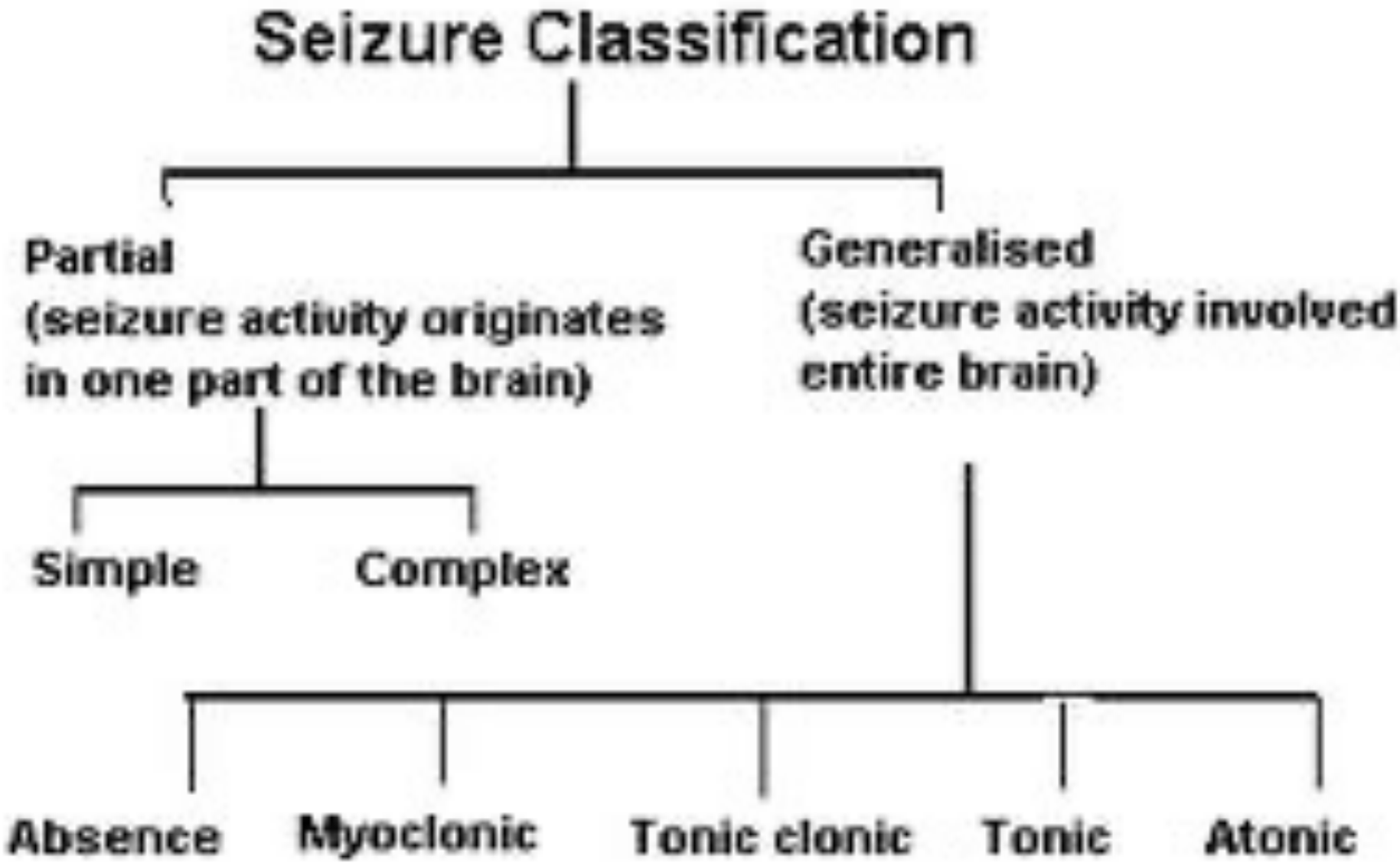
Non-Epileptic Seizures

- Hypoxic encephalopathy
  - Resulting from cardiac arrest, CO poisoning, near-drowning, suffocation, respiratory failure, etc.
- Febrile convulsions
- Brain tumor
- Cerebrovascular accident
  - Embolic, thrombotic or hemorrhagic

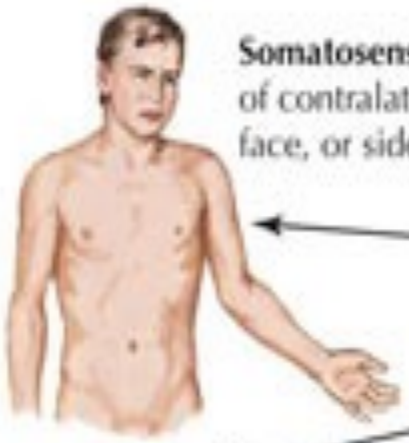
Seizures

- **Partial (focal) seizures**
  - Simple, complex, secondary generalized
- **Generalized seizures**
  - These are the most noticeable and most common
- **Unclassified epileptic seizure**
  - Idiopathic (arises spontaneously with no known cause)
  - Symptomatic
  - Cryptogenic (obscure or unknown cause)

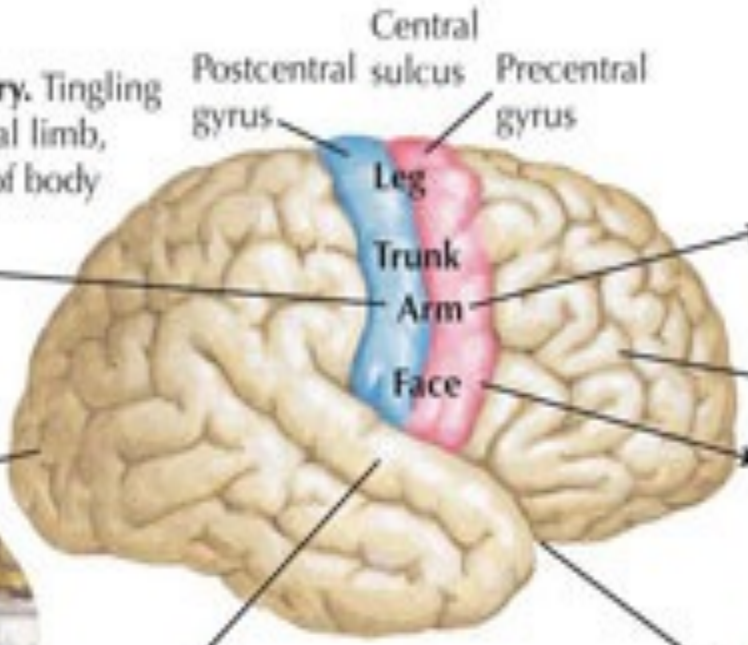

Parietal lobe
Occipital lobe
Frontal lobe
Temporal lobe
Cerebellum
Normal EEG
Partial seizure EEG
Generalized seizure EEG

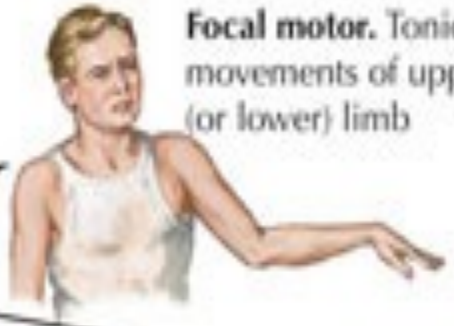

Seizure Classification
Partial
(seizure activity originates in one part of the brain)
Generalised
(seizure activity involved entire brain)
Simple
Complex
Absence
Myoclonic
Tonic clonic
Tonic
Atonic

Simple Partial Seizures

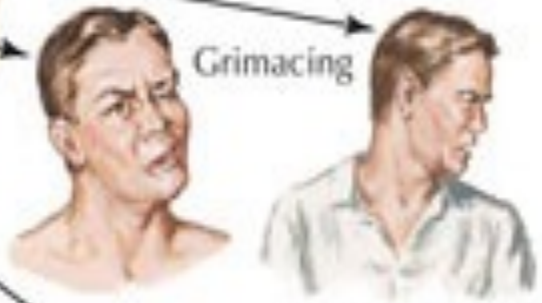


Somatosensory. Tingling of contralateral limb, face, or side of body





Focal motor. Tonic-clonic movements of upper (or lower) limb

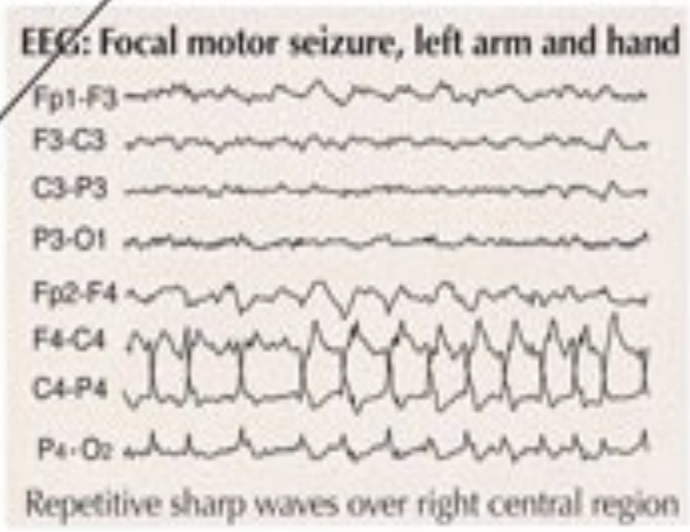


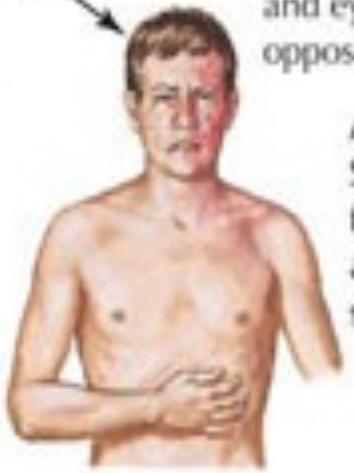
Grimacing

Contraversive: head and eyes turned to opposite side

Visual. Sees flashes of light, scotomas, unilateral or bilateral blurring

Auditory. Hears ringing or hissing noises





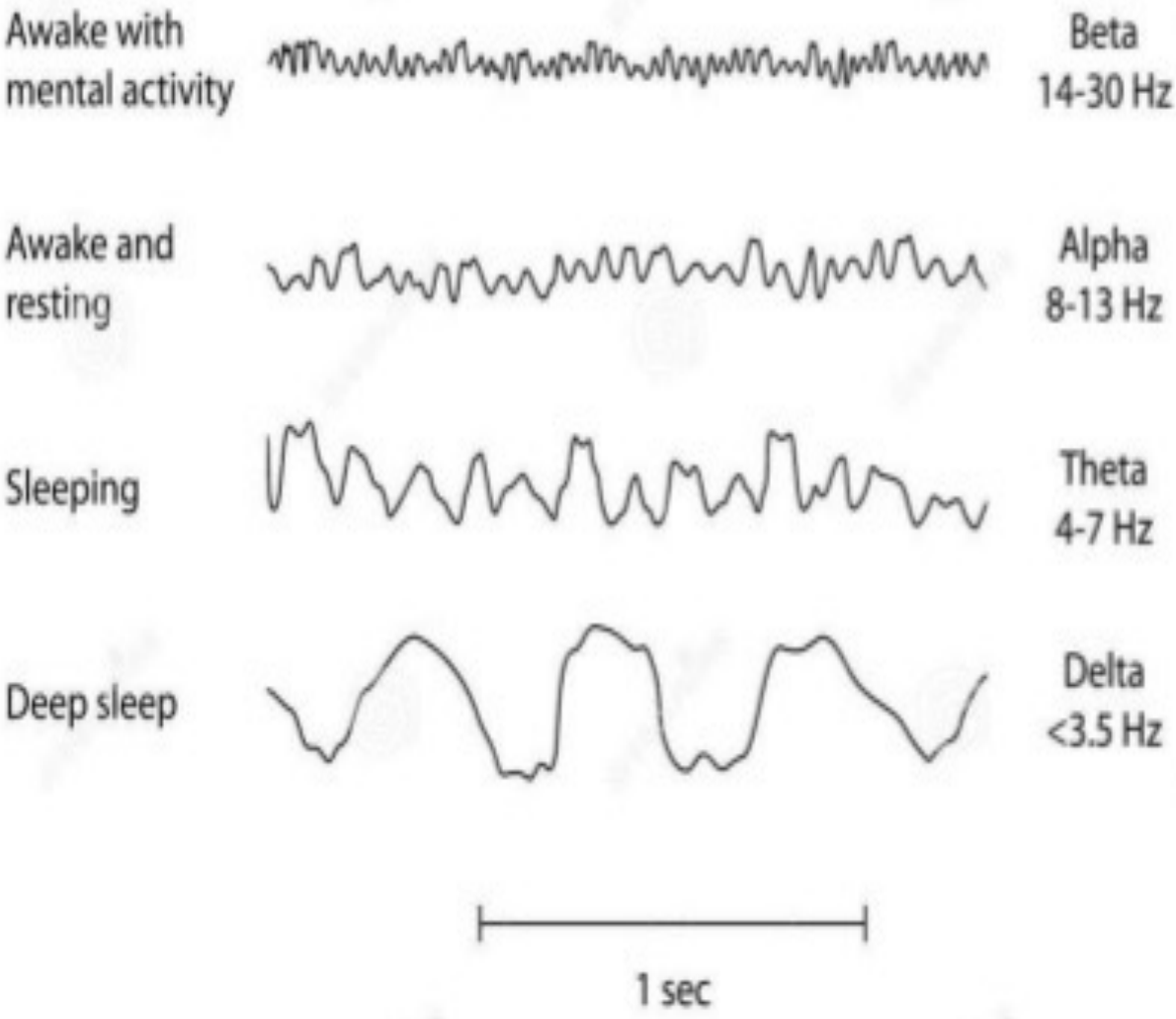
Autonomic. Sweating, flushing or pallor, and/or epigastric sensations

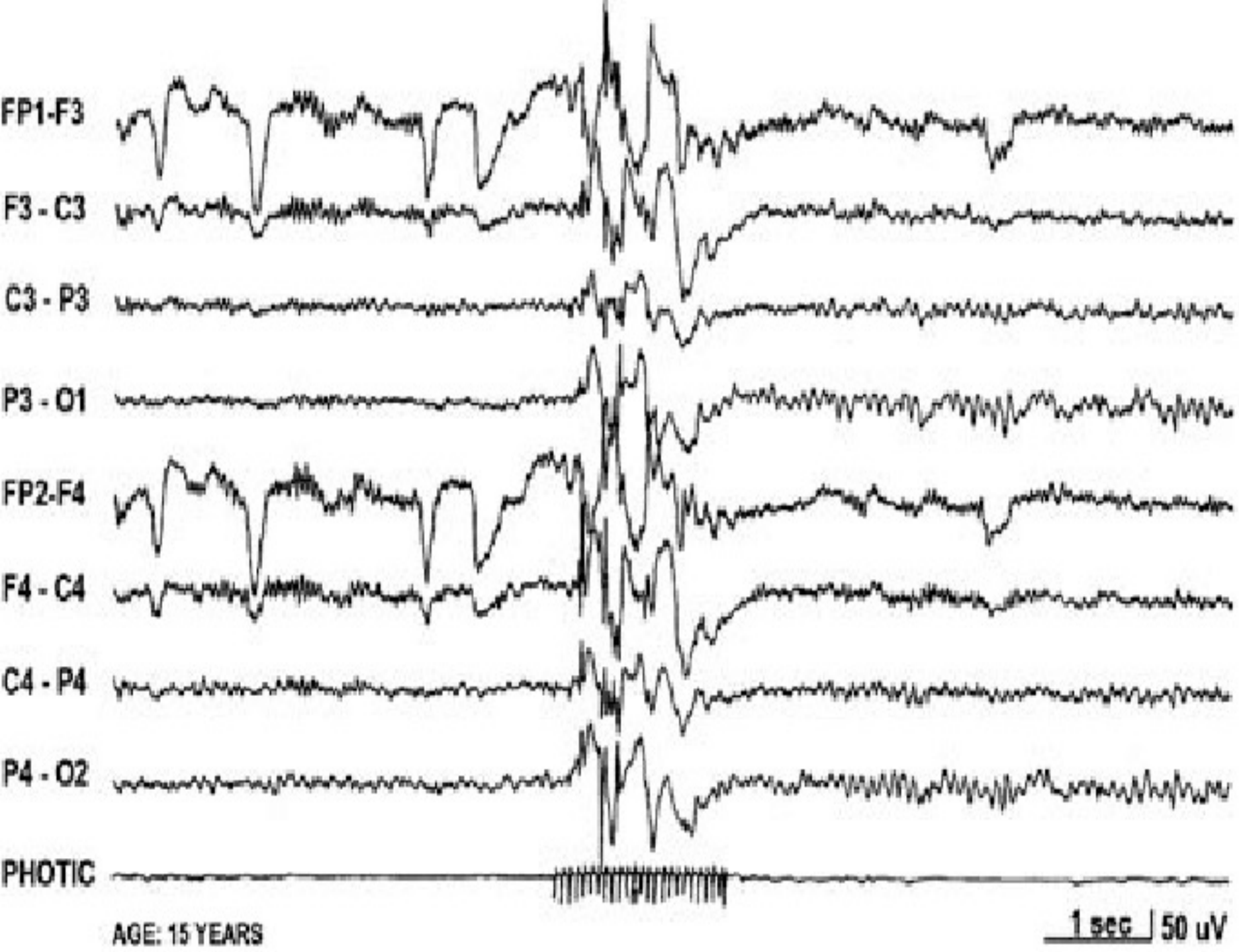
General Concepts

- **Convulsion-** 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

Normal Adult Brain Waves




FP1-F3
F3 - C3
C3 - P3
P3 - O1
FP2-F4
F4 - C4
C4 - P4
P4 - O2
PHOTIC
AGE: 15 YEARS
1 sec
50 uV

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

Seizure Terminology

- **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.

Phases of Seizure

- Preictal phase
  - Aura or warning time
- Ictal phase
  - Simple or complex partial or generalized tonic-clonic seizure
- Postictal phase
  - Recovery period
  - Can last from seconds to minutes to hours

Precipitants of Seizures

- Sleep or lack of sleep
- Drugs and alcohol
- Intercurrent illness such as infection
- Electrolyte imbalance
- Menstruation
- Stress and worry

Classifications of Seizures

- Partial seizures
  - Focal, localized
- Generalized seizures
  - Convulsive or non-convulsive
- Unclassified epileptic seizures

Partial Seizures
Focal, Localized

- Simple partial seizures
  - Preserved consciousness
- Complex partial seizures
  - Impaired consciousness
- Partial seizures evolving to secondarily generalized seizures

Simple Partial Seizures

- Preserved consciousness
- With motor signs
  - Somatosensory or special sensory systems
  - Autonomic signs and symptoms
  - Psychic symptoms

Complex Partial Seizures

- Impaired consciousness
- Simple partial onset followed by impairment of conscious
- With impairment of consciousness at onset

Partial seizures evolving to secondarily generalized seizures

- Simple partial seizure evolving to generalized seizures
- Complex partial seizures evolving to generalized seizures
- Simple partial seizures evolving to complex partial seizures evolving to generalized seizures

Generalized Seizures Convulsive or Non-convulsive

- Absence seizures
  - Typical absences
  - Atypical absences
- Myoclonic seizures
- Clonic seizures
- Tonic seizures
- Tonic-clonic seizures
- Atonic seizures aka astatic seizures

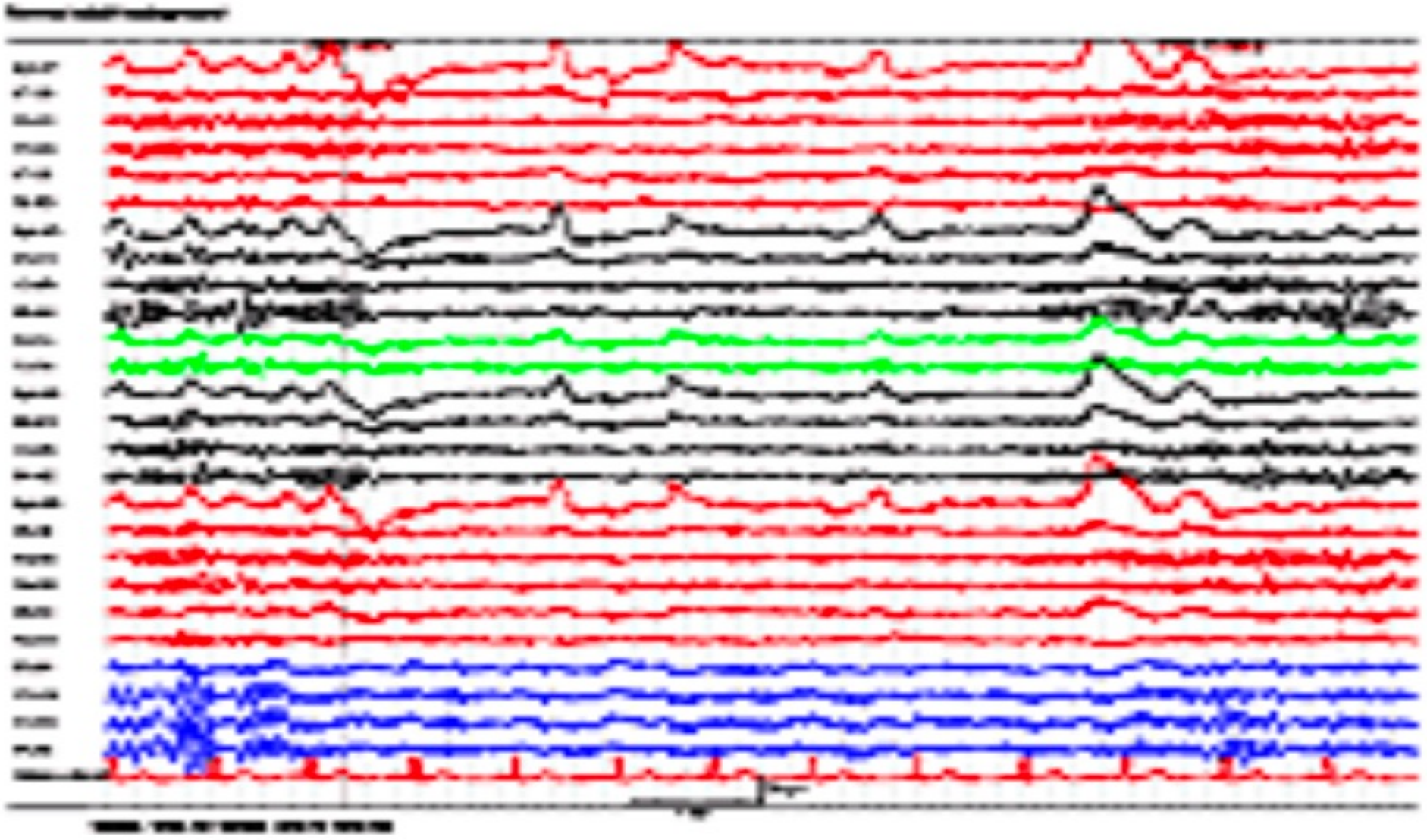
Unclassified Epileptic Seizures

- Neonatal seizures
- Recurrent status epilepticus
- Rare or “isolated” seizures

Electroencephalogram EEG

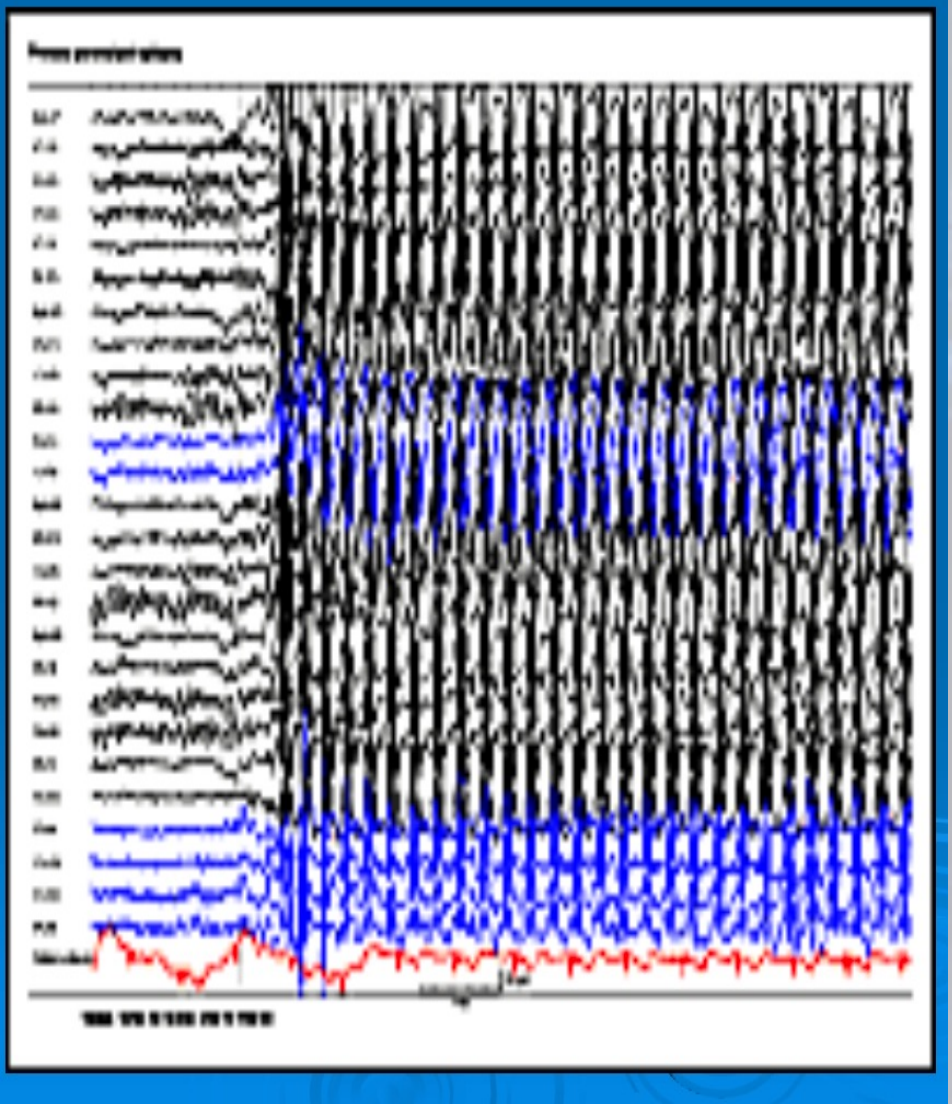
- Value of EEG
  - Verifies the diagnosis
  - Aids in classification of epilepsy
  - Detection of the structural brain lesion
- 30 minute interictal EEG
  - Useful when clinical suspicion of epilepsy
- Timing is essential
  - Within 24 hours of generalized convulsion - 50% will have abnormal EEG
  - Within 48 hours - 20-35% will have epileptiform activity
- Sleep EEG or sleep deprived EEG might increase diagnostic yeild

Normal EEG

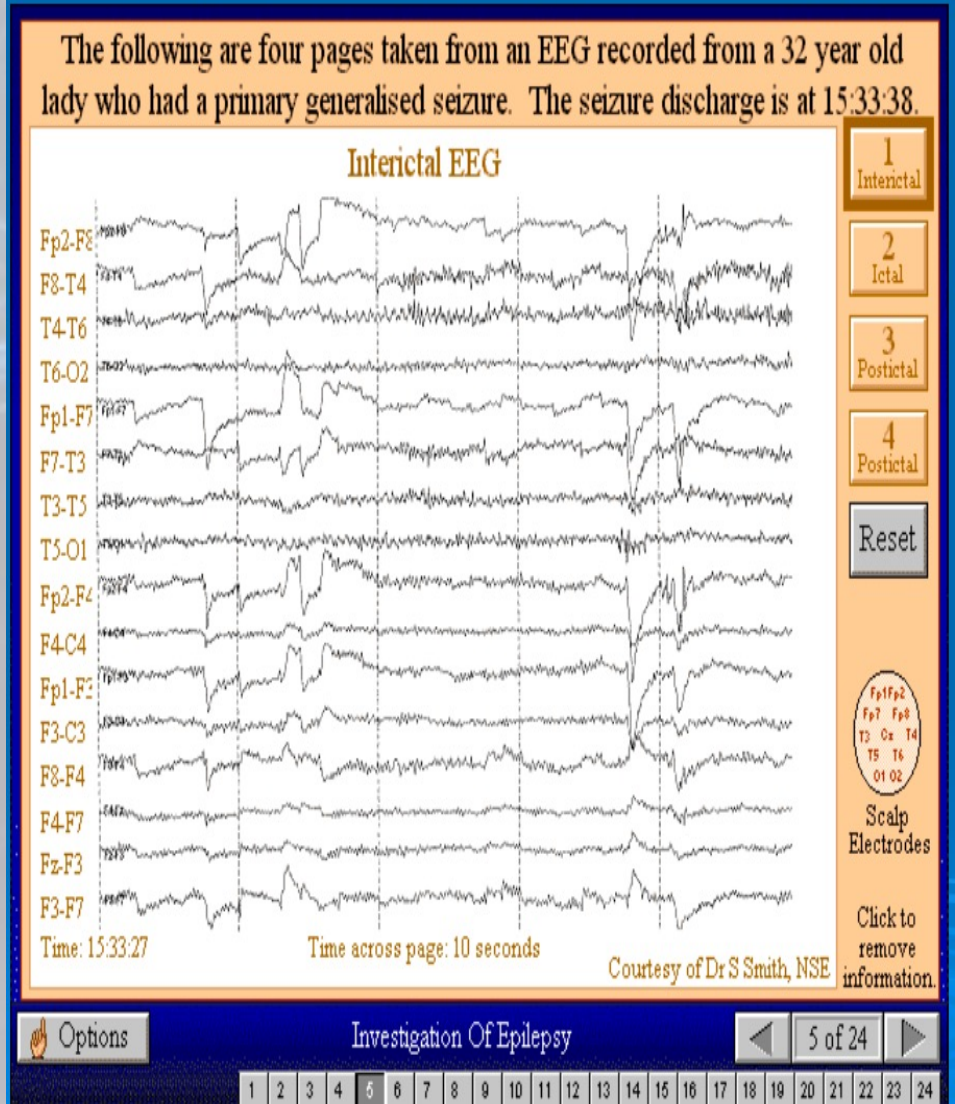


Primary generalized epilepsy

Ictal



Interictal



Burst of generalized spike and wave discharges - typical absence seizure

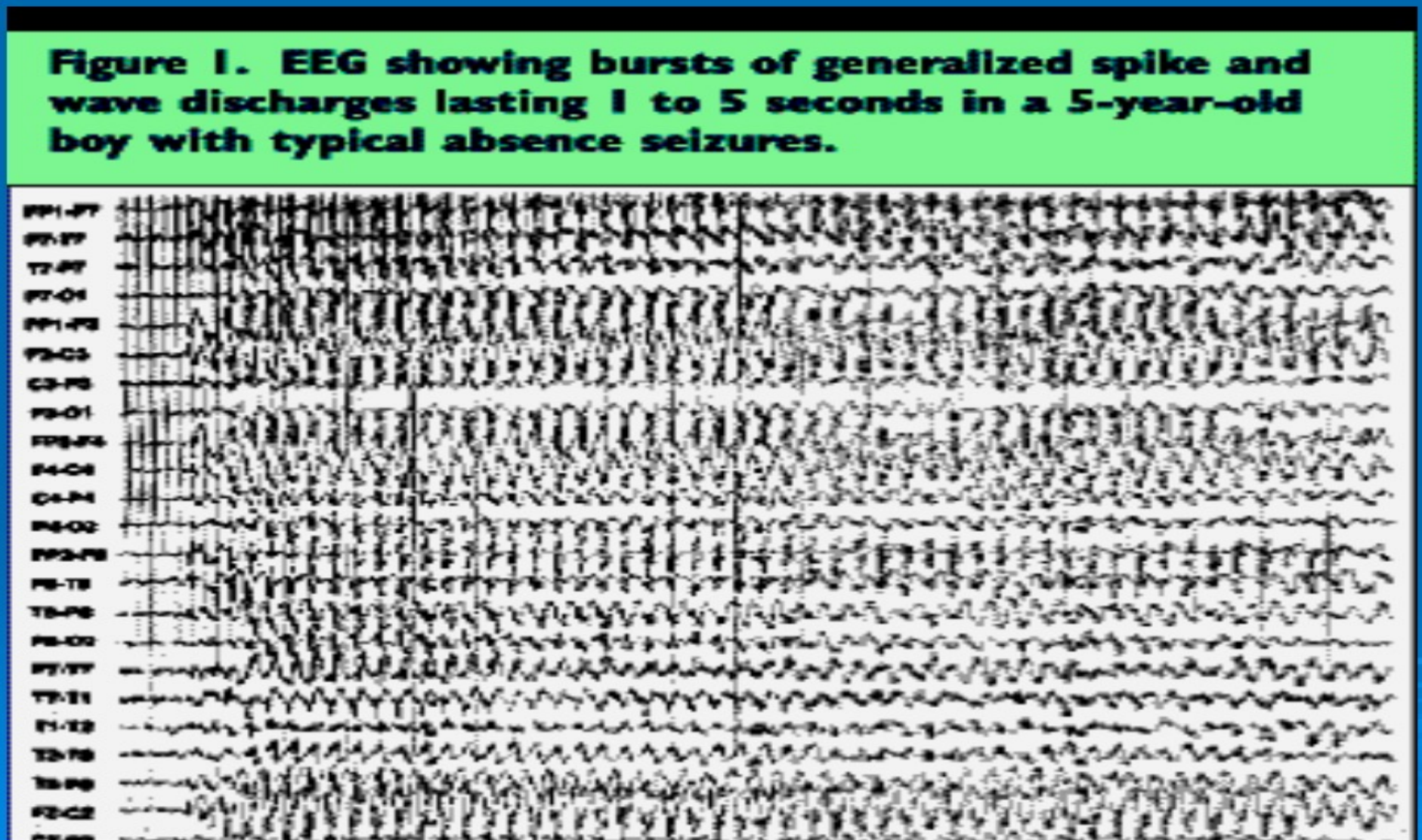


Figure 1. EEG showing bursts of generalized spike and wave discharges lasting 1 to 5 seconds in a 5-year-old boy with typical absence seizures.

EEG Monitoring

Video Monitoring

Helpful in determining nature of seizure disorder such as epilepsy, convulsive syncope, or psychogenic seizures

Indications for diagnostic imaging in patients with seizures

- Partial seizures
- Late onset unprovoked seizure over age 25
- Unexplained neurological signs
- Focal slow waves on EEG
- Poor control or new signs and symptoms

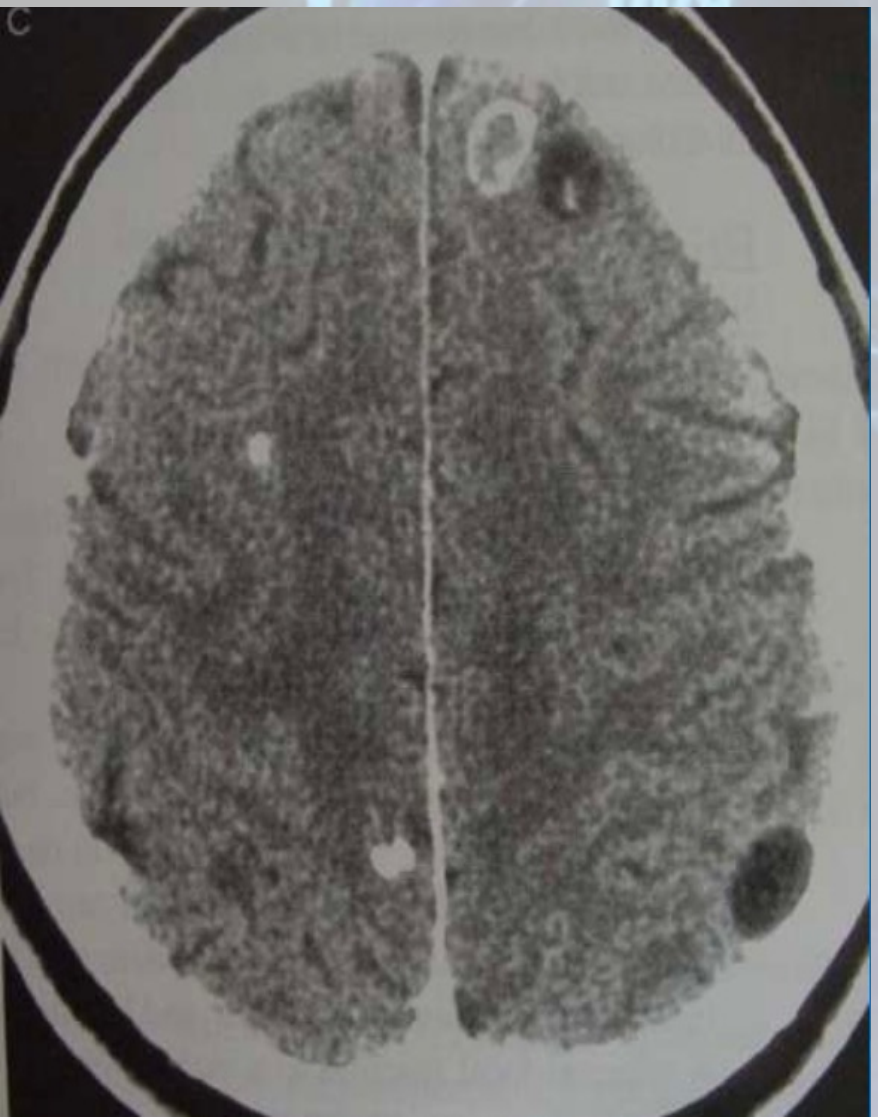
Neuroimaging Studies

- In the absences of trauma
  - CT and MRI brain for patients presenting with suspected first unprovoked seizure or with a focal neurological deficit
- MRI preferred looking for
  - Migrational disorders
  - Major malformations
  - Vascular anomalies
  - Tumors

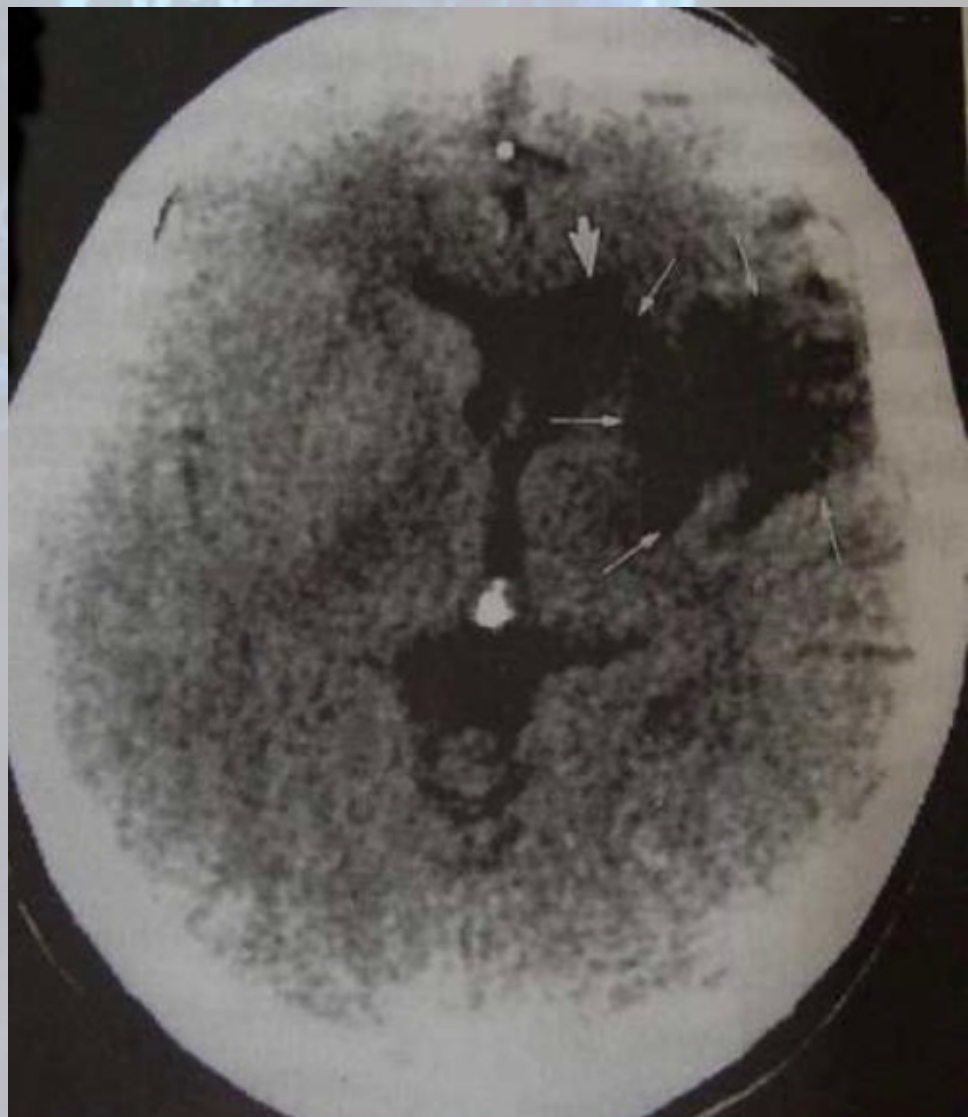
Causes of Epilepsy

- Genetic factors
- Congenital abnormalities
- Trauma and side effect of craniotomy
- CNS infection
- Cerebral vascular disease
- Cerebral tumors
- Alzheimer's disease or other degenerative disease
- Other unknown causes - idiopathic

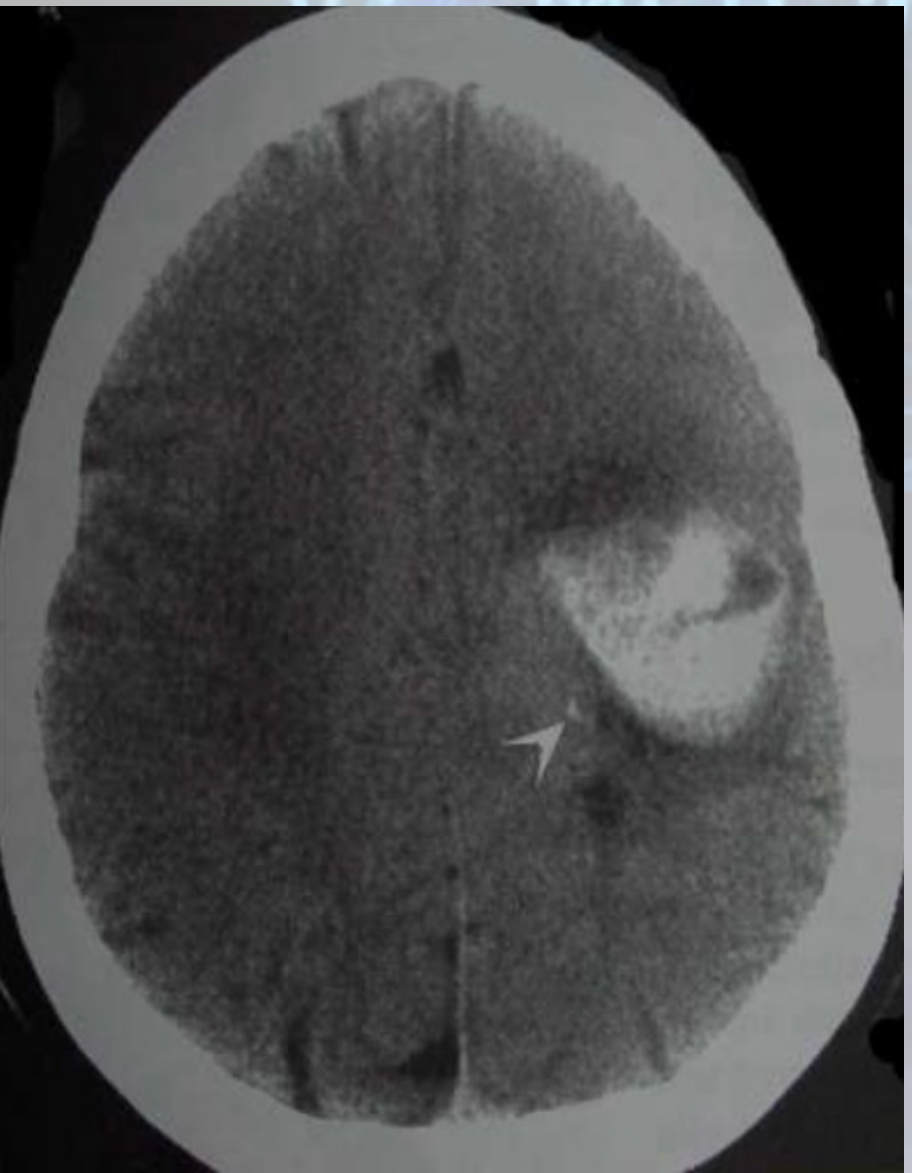
Neurocysticercosis



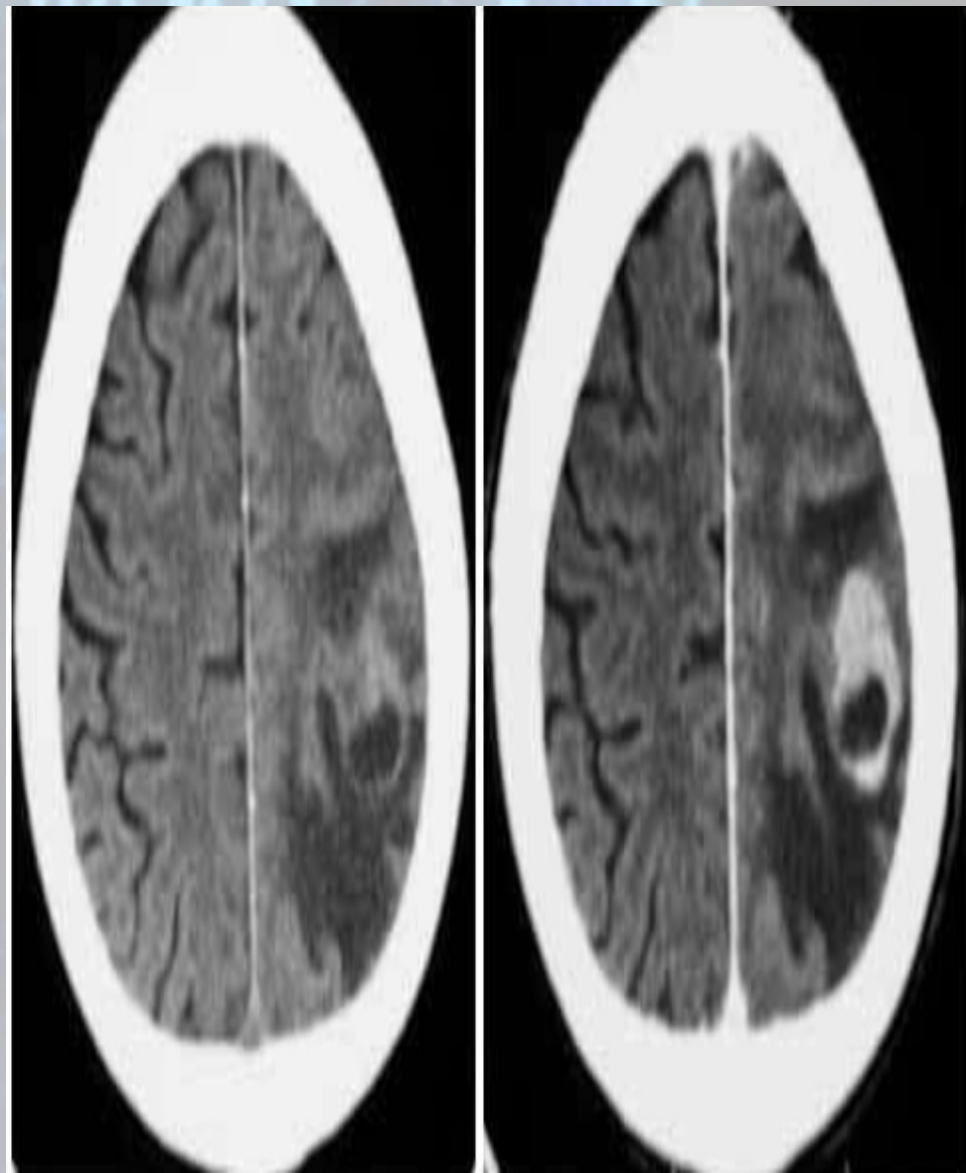
Cerebral infarction



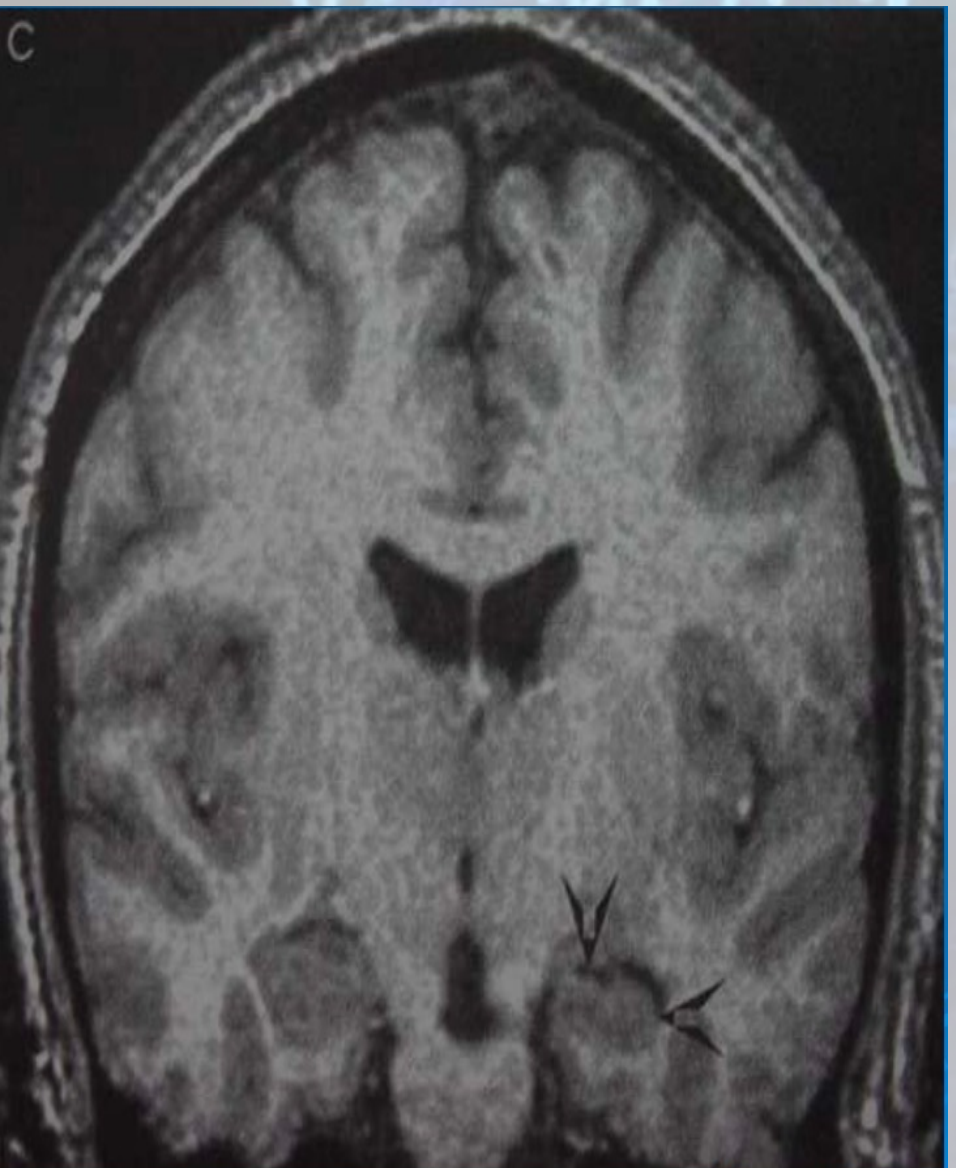
Intracerebral hemorrhage



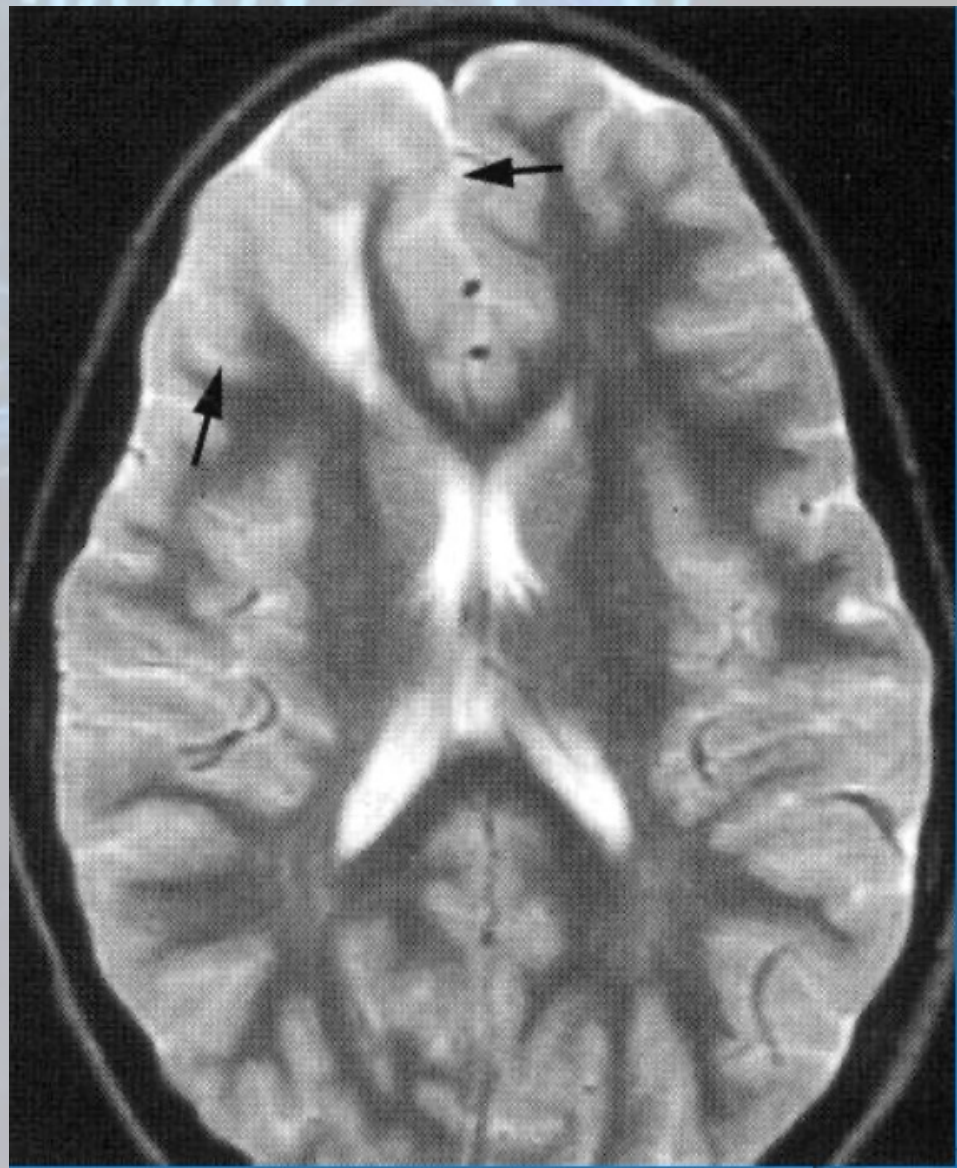
Brain tumor or metastasis

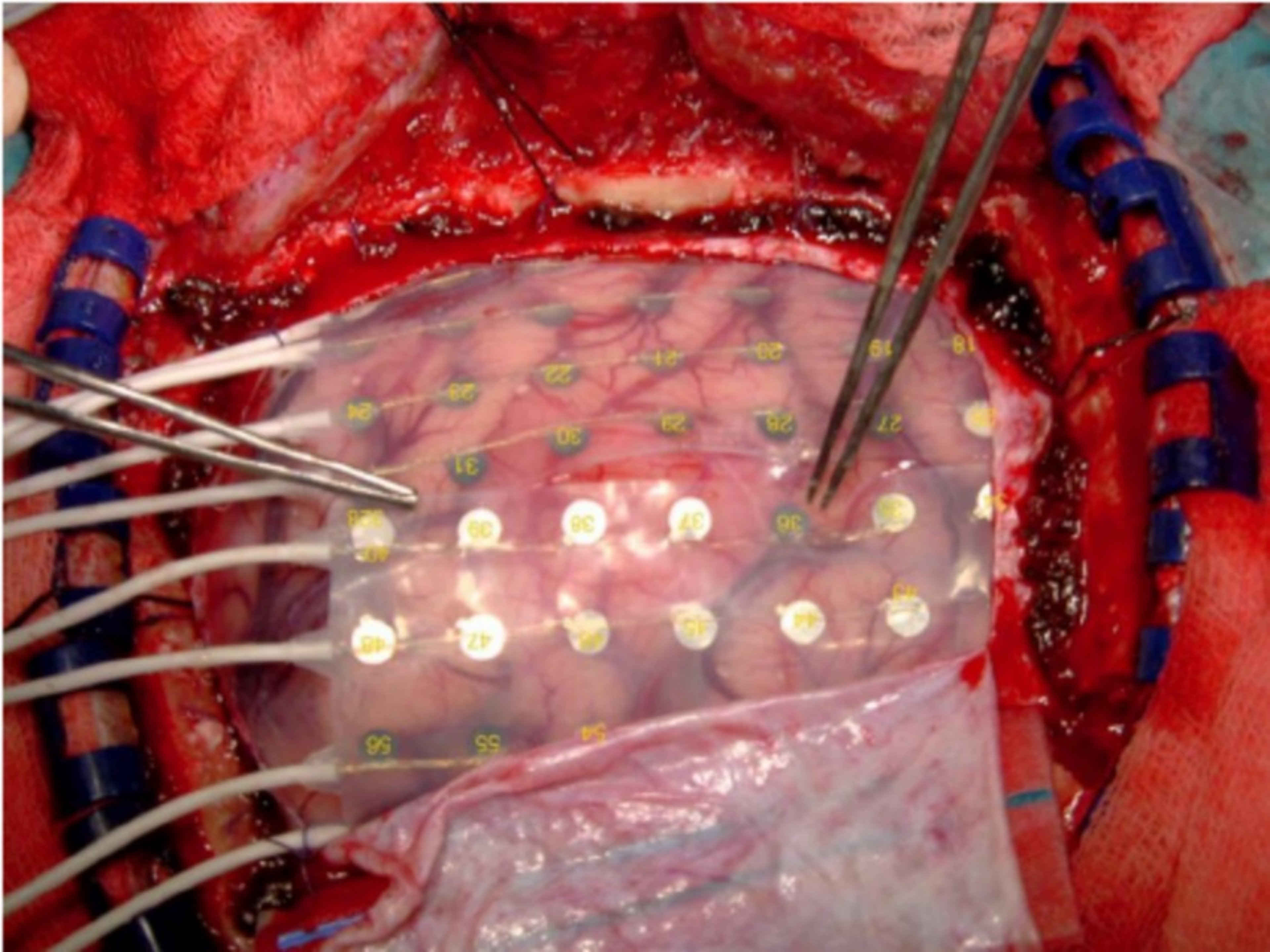


Lt mesial temporal sclerosis

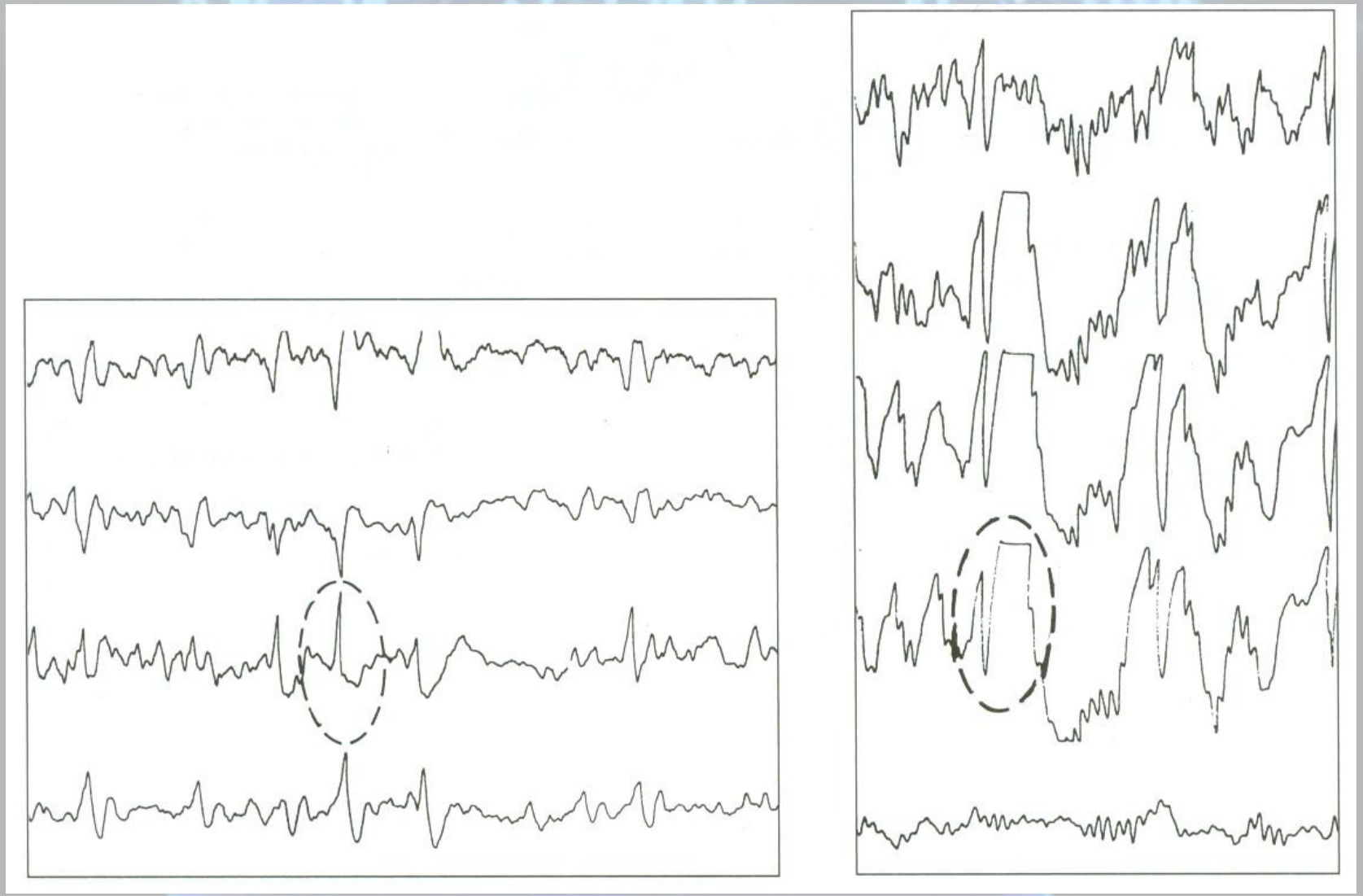


Cortical dysplasia





Typical EEG Traces



Spike-and-wave, circled, are electrical signs of an epileptogenic focus

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

Patterns of Seizure Activity

- **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

Seizure Classifications

- 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

Incapable of being linked to a specific focus

- **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**
  - Typically 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

- **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
- **Clonic phase:** 1½ - 2 minutes long
- **Terminal Phase:** 5 minutes long – longest and final phase

Grand Mal Seizure

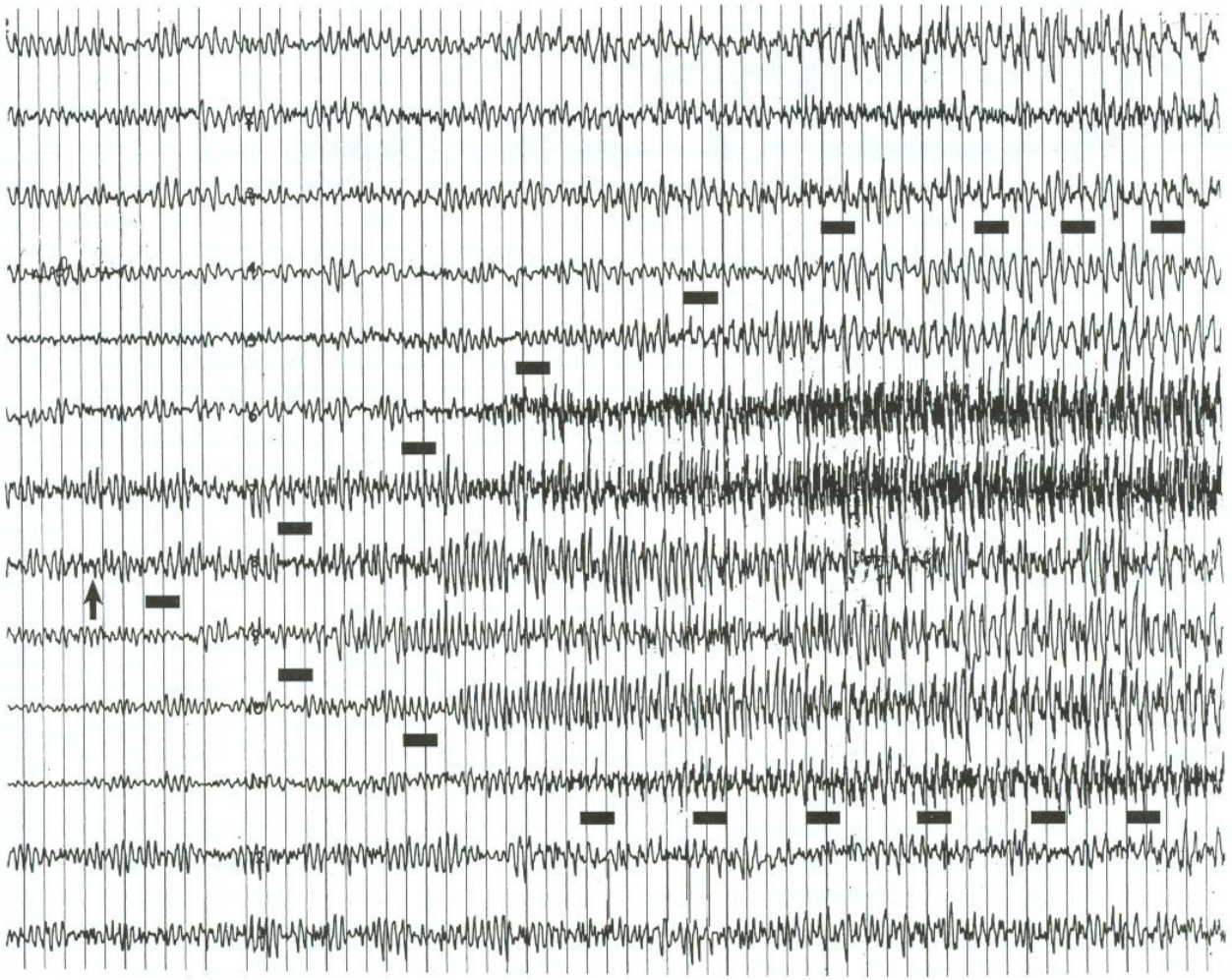


Figure 22.6 **Profile of a Grand Mal Seizure.** A generalized tonic-clonic (grand mal) seizure as it appears in a typical EEG. This trace shows generalization from a simple focus (→), as is typical of most tonic-clonic seizures. The generalization, however, is very rapid. Dark bars outline the abnormal EEG activity.

Grand Mal Seizure
Initial Tonic Phase

- **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

Grand Mal Seizure
Clonic Phase

- **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

Grand Mal Seizure Terminal Phase

- **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

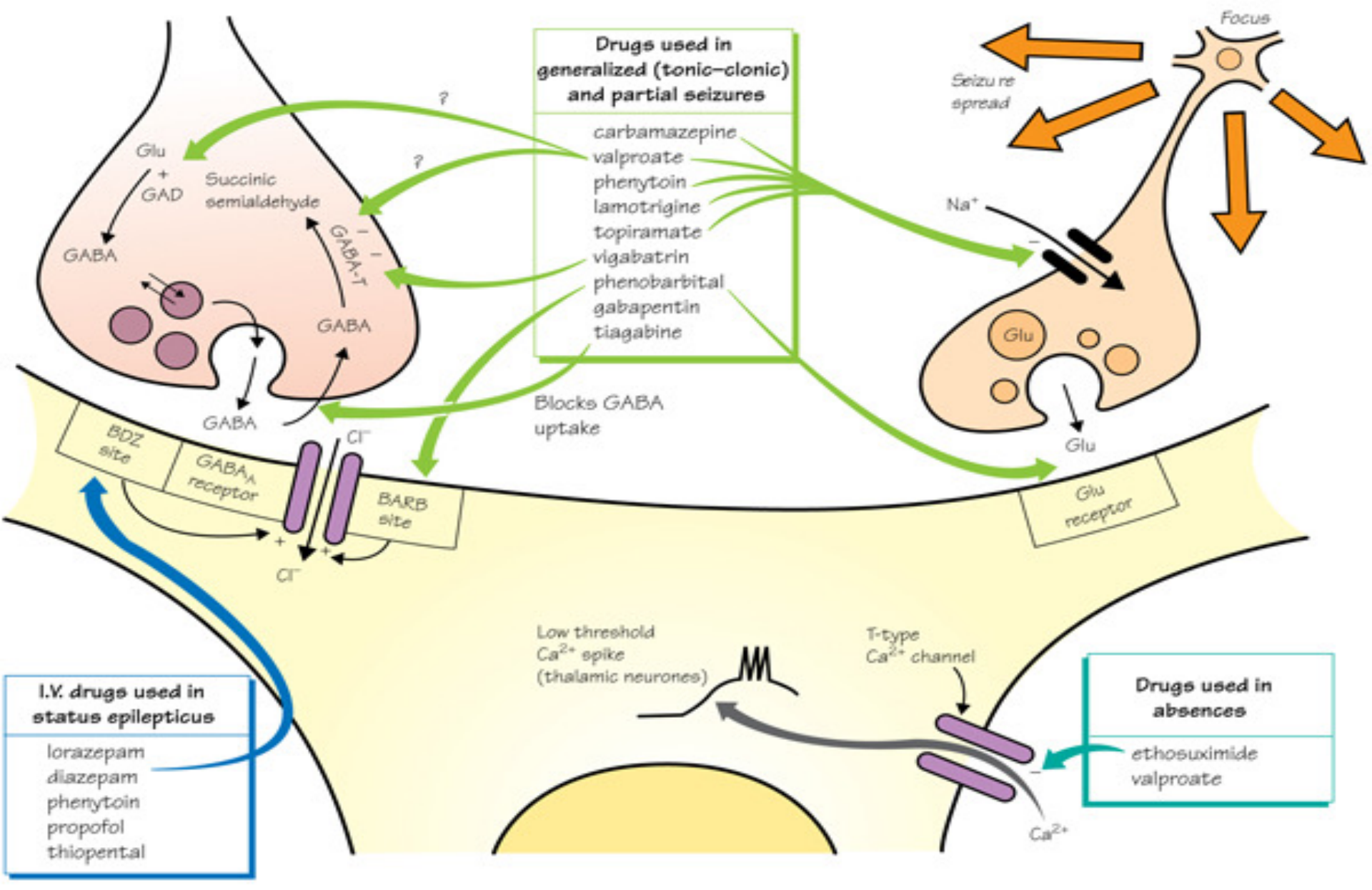
- Effectively managing stress
- Eating well

Medical Management of Epilepsy

- Sufficient rest

- Avoiding epileptic triggers
  - Inadequate sleep
  - Food allergies
  - Alcohol
  - Smoking
  - Flashing lights

• Antiepileptic Medication



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