Neuropsychology of Epilepsy

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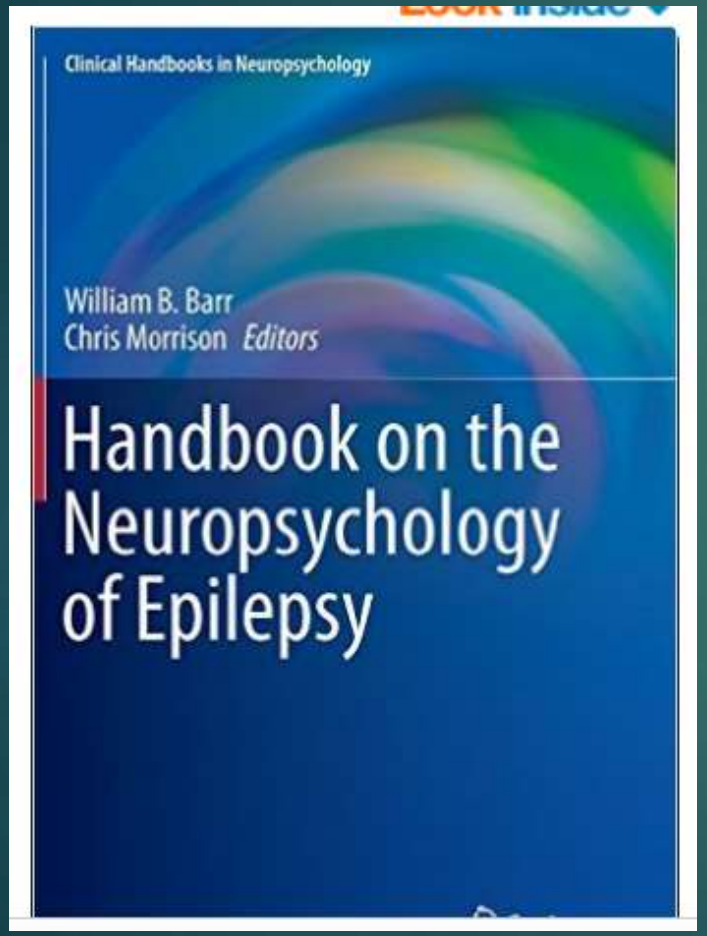
THANKS:
AMER. EPILEPSY SOCIETY, DAVID LORING PHD

Handbook on the Neuropsychology of Epilepsy – December 3, 2014

by William B. Barr (Editor), Chris Morrison (Editor)



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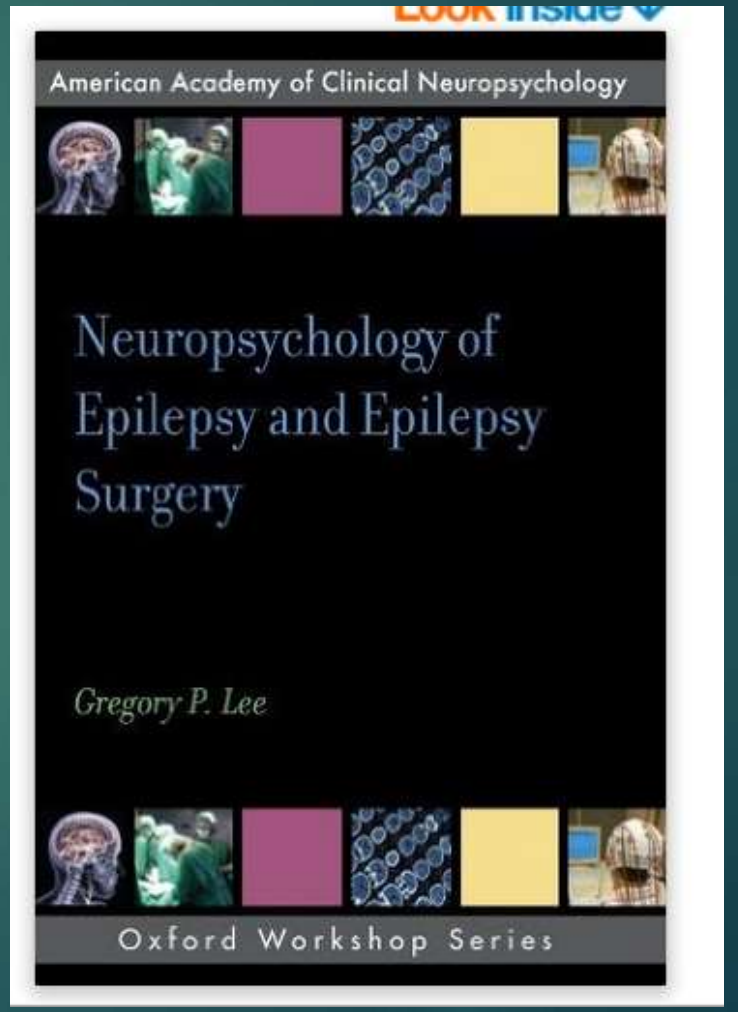

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A seizure may appear as:

A sudden cry and fall, followed by

- Convulsive movements of all limbs
- Shallow/interrupted breathing – cyanosis (blue lips)
- Loss of bowel/bladder control
- Slow return to consciousness, post-seizure confusion and/or fatigue

This is a generalized tonic-clonic or
“grand mal” seizure.

or a seizure may be…

- Blank staring, chewing, other repetitive purposeless movements
- Wandering, confusion, incoherent speech
- Crying, screaming, running, flailing
- A sudden loss of muscle tone and fall
- Picking at clothes, disrobing

This is one type of focal seizure known as a complex partial seizure.

Epilepsy: Once sacred disease

- Hieroglyphics: nesejet - “Danger coming from God”
- Origin of term, Epilepsy: from Greek, “to be seized by forces from without.”
- Historically, more terms than any other disease
- Oliver Wendell Holmes: If you want to see how difficult it is to arrive at the true medical explanation of something, look at the history of epilepsy.

History 2: Disorder of great men

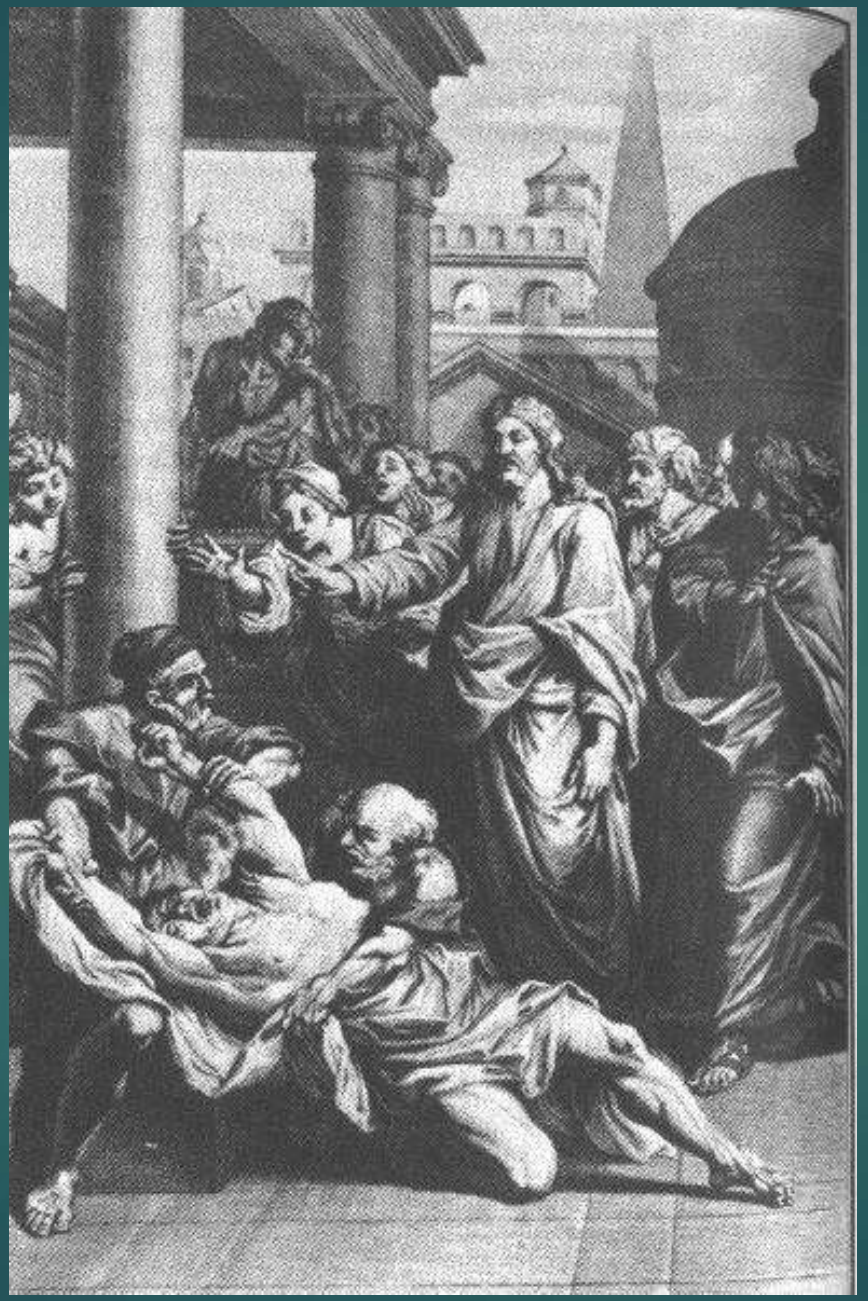
Famous epileptics (Lenox (1960): Aristotle noted it was disorder of great men:

Plato, Pythagorus, Socrates, Alexander the Great, Caligula, Caesar, Beethoven, Dante, Van Gogh, Handel, St. Ignatius, Mohammed, Pascal, Rousseau, Moliere, Napoleon, Tolstoy, Dostoyevsky, Phineas Gage, Alfred Nobel, Lenin, Neil Young, Danny Glover, Justice John Roberts

Neurologist John Hughes concluded that the majority of famous people alleged to have epilepsy did not in fact have this condition. Evidence for those underlined. Lenin & Gage died of status epilepticus.

Fyodor Mikhaylovich Dostoyevsky

Exorcism



History 2

- Famous beliefs:
  - Demons (Catholic)
  - Dybbuk (Jewish)

- Legal history: Until 1956,
  - 18 states required sterilization
  - 17 denied marriage (1980 last)
  - in 1960, impediment to becoming a priest in Catholic Church
  - 1990 - ADA

- First Pharmacology: 1859, bromide of potassium

Hughlings Jackson: Great 19th century British Neurologist: named 3 types of epilepsy

Wife had epilepsy

History 3

- Hughlings Jackson (1861):
  - definition of Petit Mal, Grand Mal, Focal seizures
- Pre-1900 belief: Seizures lead to deterioration, insanity, moral depravity
- 1900-1930: Constitutional disorder; Kraepelin's "emotionally unstable" personality

History 4

1930-2006:

- Freud: Seizure as psychic phenomena; 1928 analysis of Dostoevsky's "The Idiot", seizure as expression of latent homosexuality
- Reich, 1931: seizure as extra-genital orgasm satisfying narcissistic needs
- Concept of "Temporal lobe personality"; never proven
- Current: a neurological disorder
- Not a popular disease; No Jerry Lewis marathon donation collections

Epilepsy

- A chronic neurologic disorder
  - manifesting by repeated epileptic seizures (attacks or fits)
  - which result from paroxysmal uncontrolled discharges of neurons within the central nervous system (grey matter disease).

- The clinical manifestations range from a major motor convulsion to a brief period of lack of awareness.

- The stereotyped and uncontrollable nature of the attacks is characteristic of epilepsy.

Definition

- Hughlings Jackson, 1870:
- Epilepsy is a group of disorders with paroxysmal and excessive neuronal discharge that cause sudden disturbance in neurological function
- Sudden development, cease spontaneously, tend to recur
- Under 1 hour sudden change in intellectual, sensory, motor, autonomic or emotional activity, associated with neuronal overactivity.

Pathogenesis

- The 19th century neurologist Hughlings Jackson suggested “a sudden **excessive** disorderly **discharge of cerebral neurons**“ as the causation of epileptic seizures.

- Recent studies in animal models of focal epilepsy suggest a central role for
  - excitatory neurotransmiter **glutamate** (increased in epilepsy)
  - inhibitory gamma amino butyric acid (**GABA**) (decreased)
  - hypothesized that the neuronal hyperexcitability in epilepsy is due to imbalance between glutamate-mediated excitation and GABA-mediated inhibition

Definitions 2

- **Seizure**: sudden abnormal behavior caused by excessive hypersynchronous neuronal firing
- **Epilepsy**: chronic brain condition predisposing to recurrent seizures
- **Epilepsy Syndrome**: frequently associated cluster of signs and symptoms allowing better prognostication and treatment of epilepsy

Definition 3

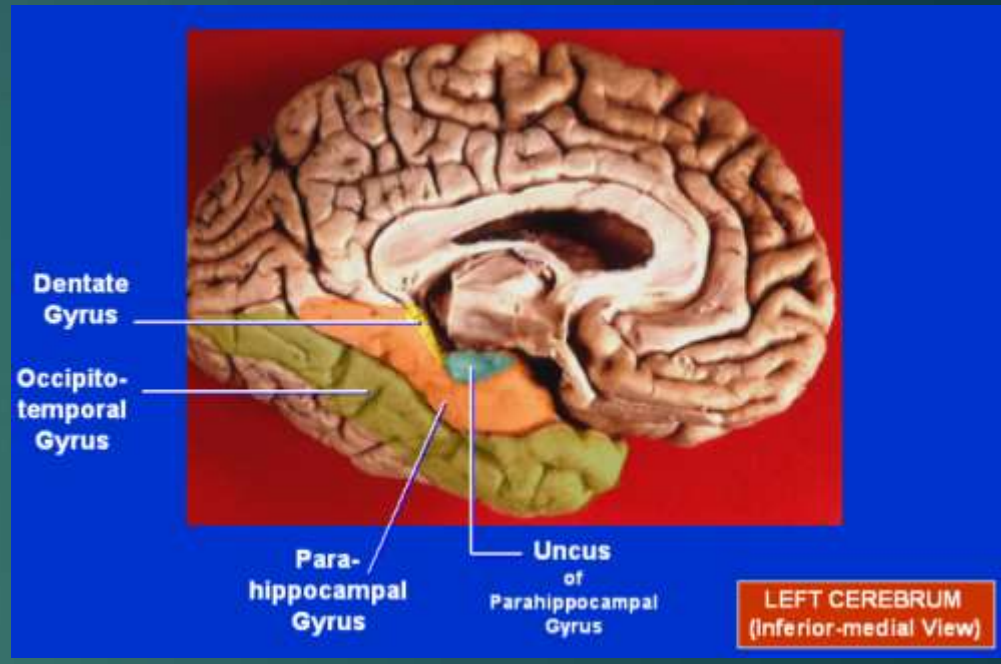
- Recurrent paroxysmal dysfunction of cerebral functioning manifested by somatic, psychic, or behavioral phenomena, with or without loss of consciousness.
- Symptoms: episodic and reversible
- Caution:
  - Do not use term “epileptic”: patient has epilepsy; these are symptoms of a brain disorder

Terminology 1

- Seizure: recurrent neurological paroxysmal event
- Convulsion: paroxysm of involuntary muscles
- Clonic: alternating muscle contraction and relaxation
- Tonic: increased muscle tone sustained, rigidity
- Epileptogenic focus: area of brain where electrical discharge give rise to seizure

Terminology 2

- Gliosis: proliferation of neuroglial tissue (reactive change of glial cells in response to damage) in CNS
- Ictus: time in which seizure occurs
- Paroxysm: sudden, periodic attack or recurrence of symptoms; a convulsion
- Uncus: hook shaped area in anterior hippocampal gyrus



Epilepsy

- Common neurological disorder – recurrent seizures (.5-1%)
- NP deficits greatest for pts with symptomatic epilepsies & catastrophic epilepsy syndromes
- Controlling seizures is strongly related to reducing cognitive comorbidity
- 30-40% of pts with epilepsy are refractory to current medication

Prevalence

- Seizures
  - Incidence: approximately 80/100,000 per year
  - Lifetime prevalence: 9%
  - 10% of people will have a seizure; but only 10% of these have epilepsy; anyone can have a seizure
- Epilepsy
  - Incidence: approximately 45/100,000 per year
  - Point prevalence: 0.5-1% (90 Million people worldwide)

Prevalence

- 2nd most common neurological disorder (after CVA)
- 70 % successfully treated
- 30% non-responsive/intractable
- Men > women; Women get treated more often
- 50-65% unknown etiology
- Use of anterior temporal lobectomy for most severe, medically refractory patients

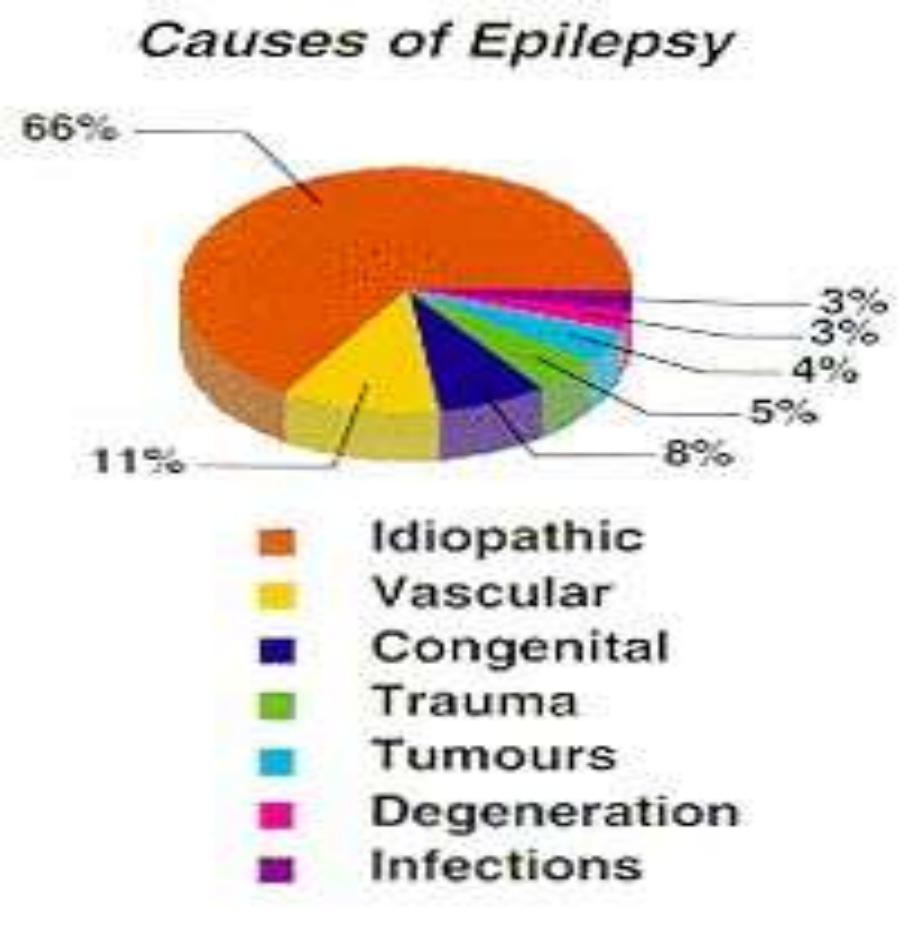
Epilepsy versus epileptic syndromes

Epilepsy is not a nosological entity – not one disease! Does not have a unique etiology.

Might be a symptom of numerous disorders – **symptomatic epilepsy** (TBI, tumours, inflammation, stroke, neurodegeneration, ...)

Sometimes the cause remains unclear despite careful history taking, examination and investigation!

Causes of Epilepsy



Slight increase in mortality for idiopathic epilepsy; more significant mortality risk for symptomatic.

Cause and Age of Onset

- Pre 6 month: birth trauma, congenital neurological, metabolic or infectious
- 2-20: genetic, trauma
- 20-35: trauma, infection, chemical dependency
- 35+: vascular, tumor, chemical dependency
- All ages: 78% idiopathic; 6% trauma; 6% birth trauma, congenital; 4% infection; 3% tumor
- 20% have multiple types of seizures

Age of Diagnosis

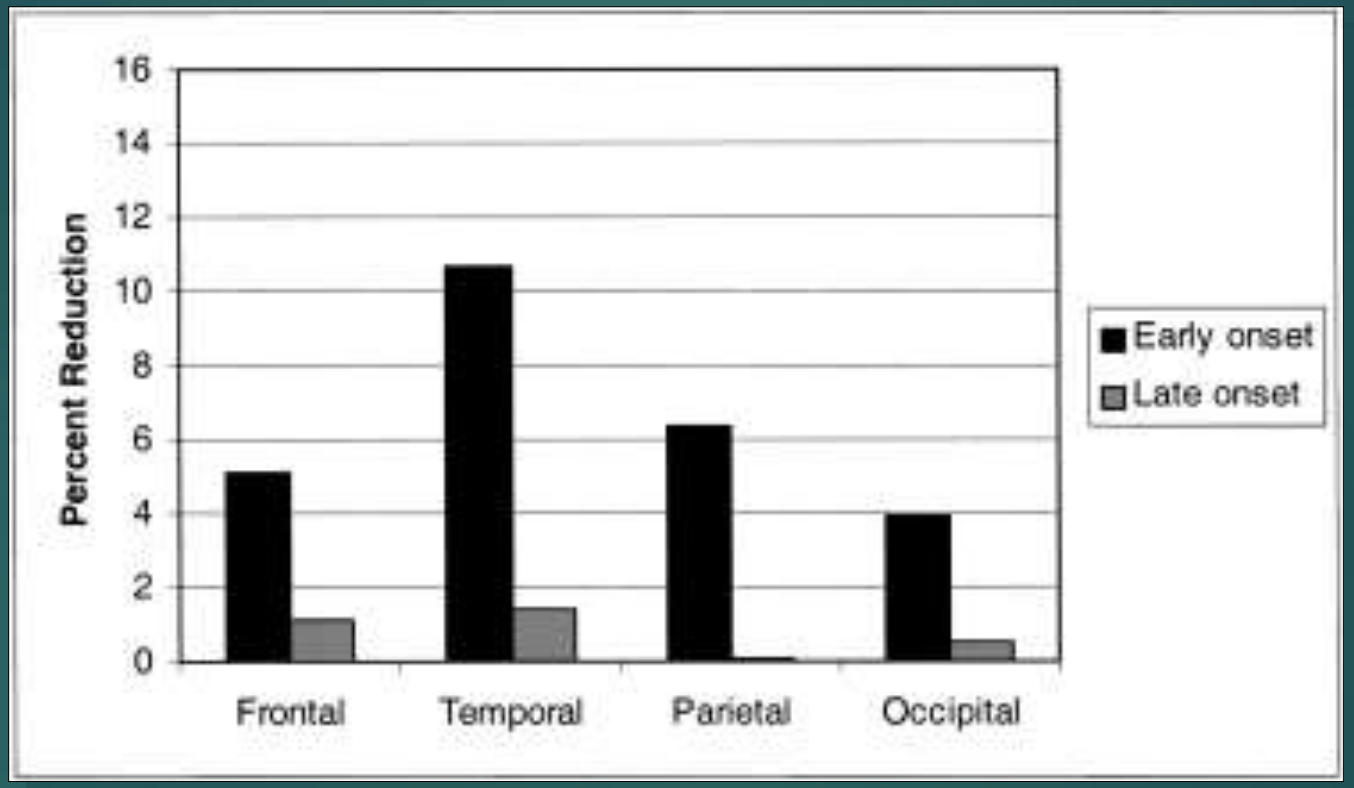
- Cumulative Diagnosis:
  - age 6 (30%),
  - age 13 (64%),
  - age 18 (77%),
  - age 20 (93%)
- Seizure onset in adulthood are more symptomatic (i.e. tumor), etiological

Adults with Childhood Seizure Onset

- Earlier the diagnosis, more severe the outcomes:
- Less Education
- Decreased rates of employment
- Lower rates of marriage
- Poorer physical health
- Increased incidence of psychiatric disorders
- But remember that most have normal lives

Jalava et al., 1997a,b,c, Sillanpää (1998)

Total Lobar White Matter reduction: Cause or Effect?



Greater WM reduction with early onset.

Hermann et al, *Epilepsia* 2002;43:1062-71

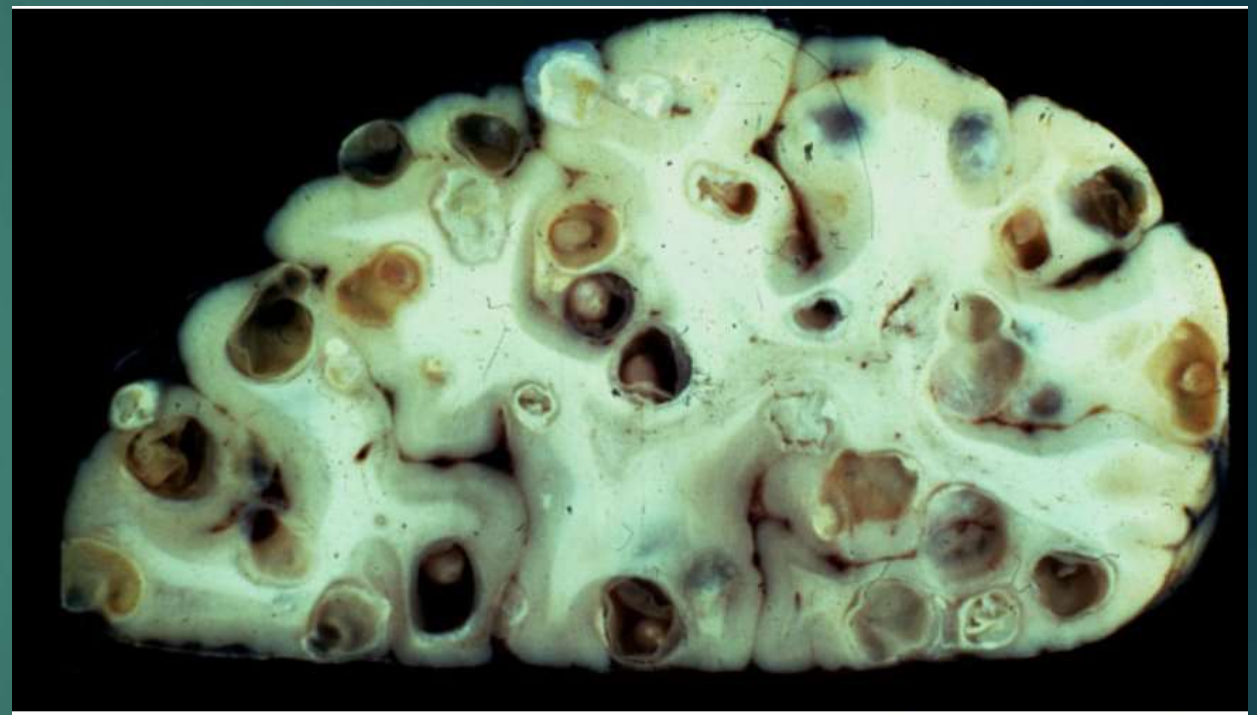
Childhood TLE Onset

- Generalized cognitive compromise
- Reduction in cerebral volume, particularly white matter (~6-12%)
- Cerebral volume reduction not limited to temporal lobe
- Less focal impairment (e.g., memory)
- Less surgical risk
- Greater likelihood of functional reorganization (e.g., bilateral language, pathologic left handedness)

Etiology

- Individuals with known causes for their epilepsy (e.g., head injuries, brain infections) typically have more detectable cognitive difficulties than those with no known etiology

According to WHO, what is the most reversible cause of epilepsy in the world?



A human brain overrun with cysts from *Taenia solium*, a tapeworm that normally inhabits the muscles of pigs.

Cysticercosis: infection with the *Taenia soleum*, or pork tapeworm.

Pathophysiology: no single underlying pathology

- Pathophysiology:
  - Epileptic focus is a group of neurons that evidence a paroxysmal depolarization shift and sudden changes in neuron's membrane potential.

- Plasma membrane is more permeable.
  - May be due to abnormalities in K^+ or Ca^{++} conductance.
  - Defects in GABA inhibitory system.
  - Abnormality in N-methyl-D- aspartate receptor.

- Neuronal discharge spreads to adjacent neuronal tissue.

Acute Reactive Seizures

Causation:

- Fever, Infection (incl. meningitis)
- Drug withdrawal or intoxication
- Sleep deprivation
- Video games
- Metabolic disturbances:
  - Hypoglycemia, hyponatremia, hypocalcemia,
  - Hypomagnesemia, hypoxia

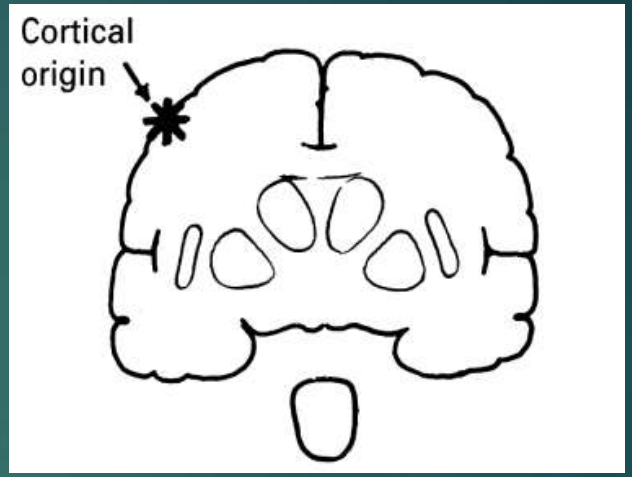
Epilepsy - Classification

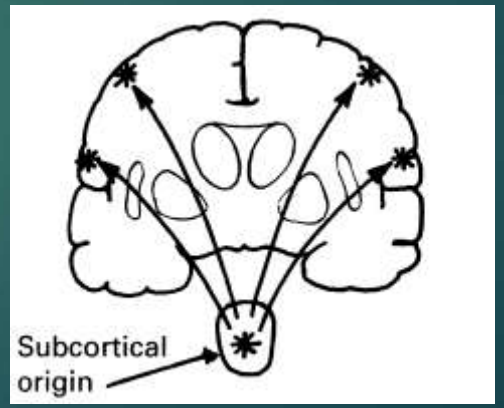
- The modern classification of the epilepsies is based upon:
  - the nature of the seizures
  - rather than the presence or absence of an underlying cause.

- Seizures which begin
  - **focally** from a single location within one hemisphere are thus distinguished
  - from those of a **generalised** nature which probably commence in a deeper structures (brainstem? thalami) and project to both hemispheres simultaneously.

Epilepsy - Classification

- Focal seizures – *account for 80% of adult epilepsies*
  - Simple partial seizures
  - Complex partial seizures
  - Partial seizures secondarilly generalised





- Generalised seizures

Seizure Classification

- Seizures are classified as being *focal or generalized* in onset.
- Focal: begin in focal area;
  - usually underlying structural abnormality (developmental malformations, vascular malformations, traumatic scarring, neoplasm));
  - not necessarily small
- Generalized: onset on ictal scalp EEG that occurs simultaneously in both hemispheres
- Diagnosis by clinical hx, sz semiology, EEG, neuroimaging.

Seizure semiology (seizure behaviors related to location)

Features of Seizure Semiology which may be Localizing

Brain region	Interictal features	Early ictal features (including "aura")
Frontal lobe	disinhibition	hyperkinetic activity
Temporal lobe		Abdominal pain, nausea, vomiting
Insula		hypersalivation, drooling, gutteral automatisms
Cingulate gyrus	behavioral (aggression, personality disorder, poor judgment)	Emotional (fear or laughter)
Primary motor area	Weakness or clumsiness (especially after seizures)	Clonic motor seizures with **no** impairment of consciousness ▪ face - inferior motor strip ▪ hand - middle/superior motor strip ▪ legs/feet - mesial motor strip
Occipital lobe		visual patterns ▪ complex patterns - visual association areas ▪ simple patterns (spots/colors) - primary visual areas

Focal Seizures (old Partial Complex Seizures)

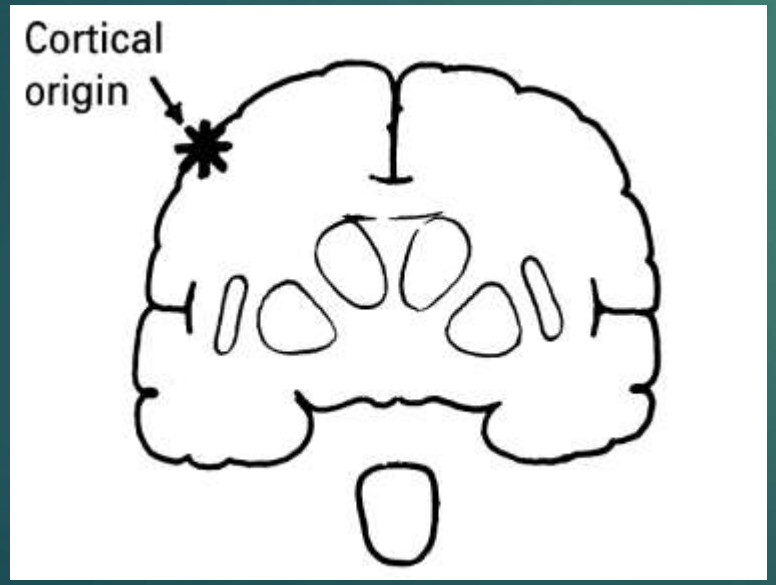
- Characterized by 1 or more features: Aura, Motor, Autonomic, Awareness/Responsiveness altered (dyscognitive) or retained
- May evolve to bilateral convulsive seizures
- New classification: avoid terms “simple partial” & “complex partial”): describe on basis of:
  - (1) focal or generalized in onset,
  - (2) if csness is lost during ictal period

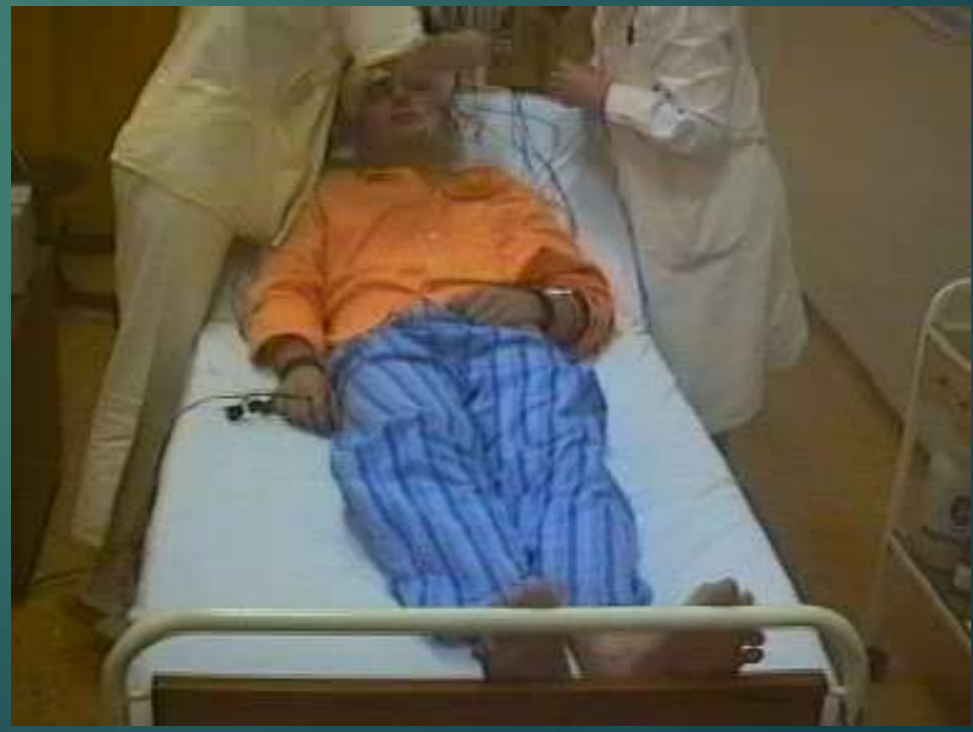
Focal (partial) seizures

- Focal (Simple partial) seizures

  Motor, sensory, vegetative or psychic symptomatology

  Typically consciousness is preserved





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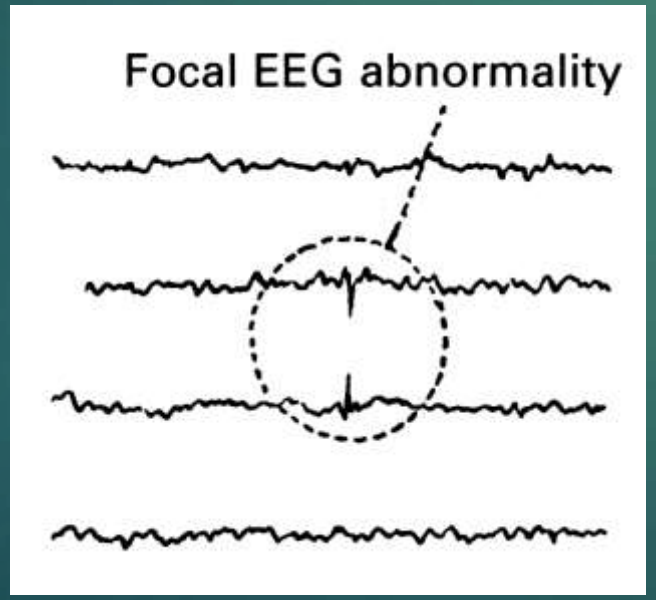

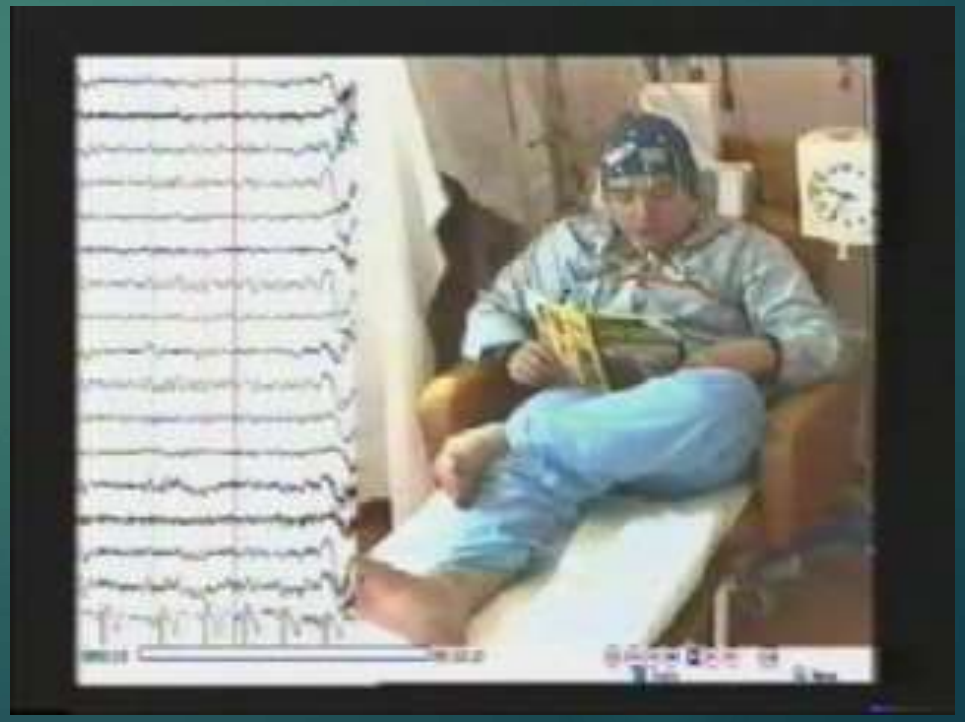

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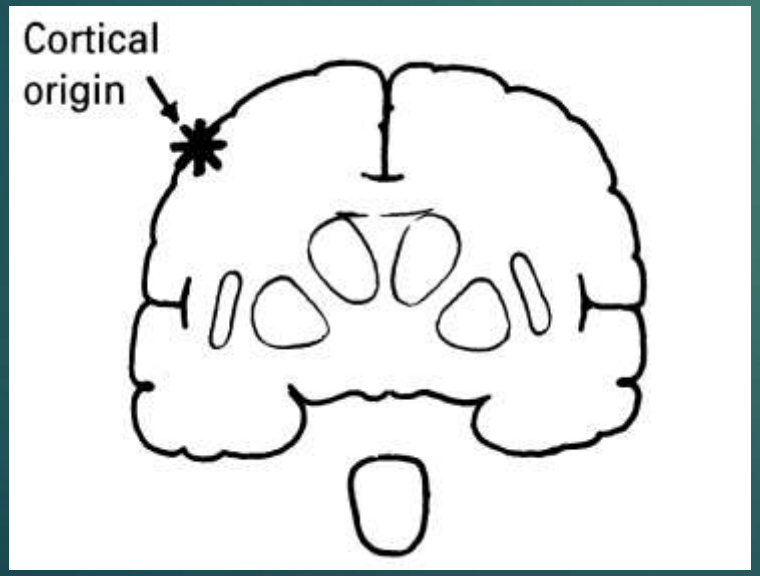
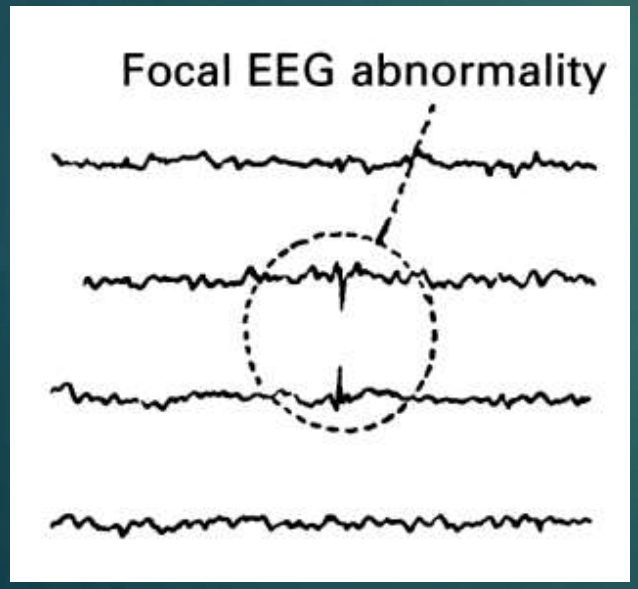


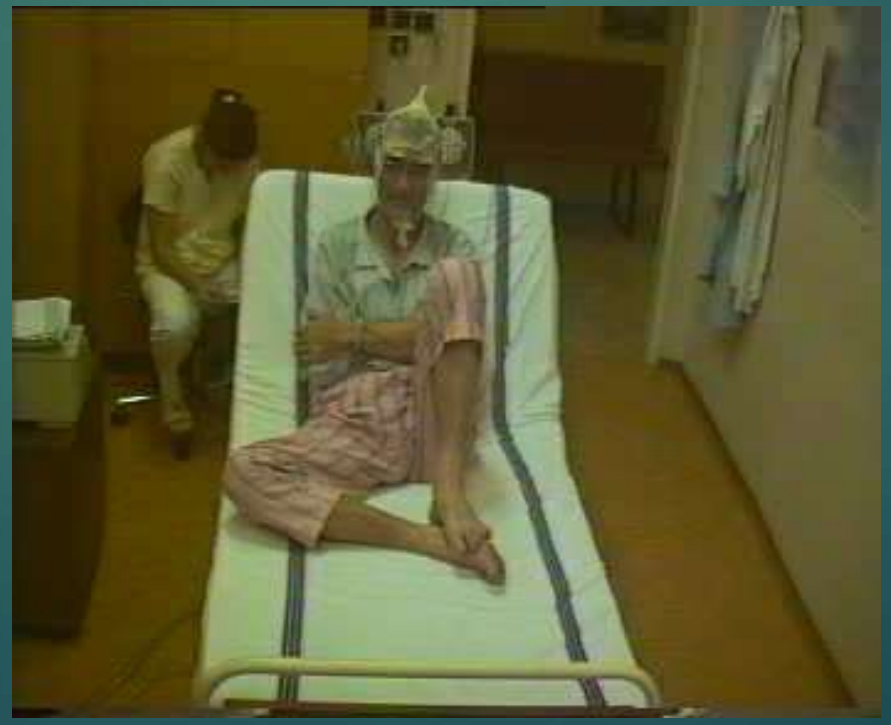
Focal (partial) seizures - LOC

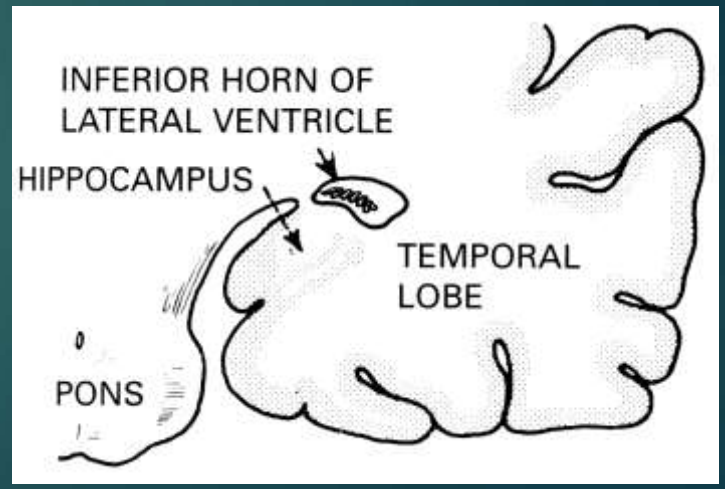
- Focal (Complex partial) seizures (= psychomotor seizures)

  Initial subjective feeling (aura), loss of consciousness, abnormal behavior (perioral and hand automatisms)

  Usually originates in TL

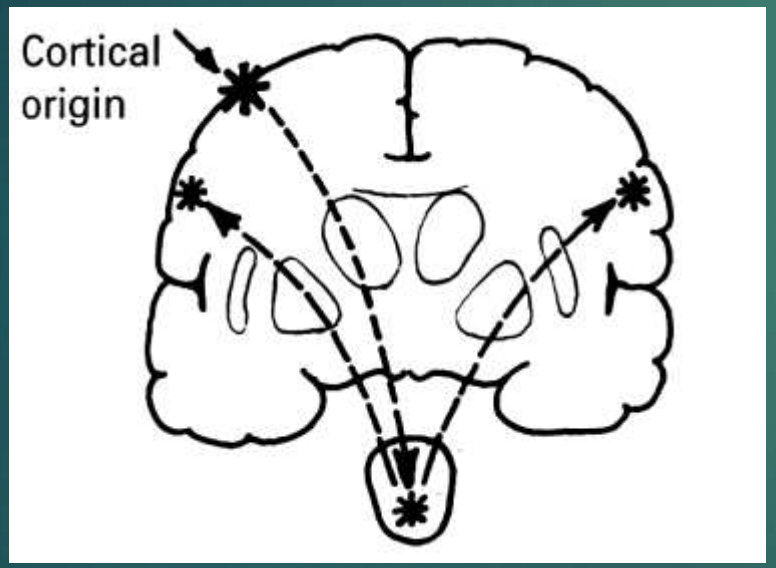


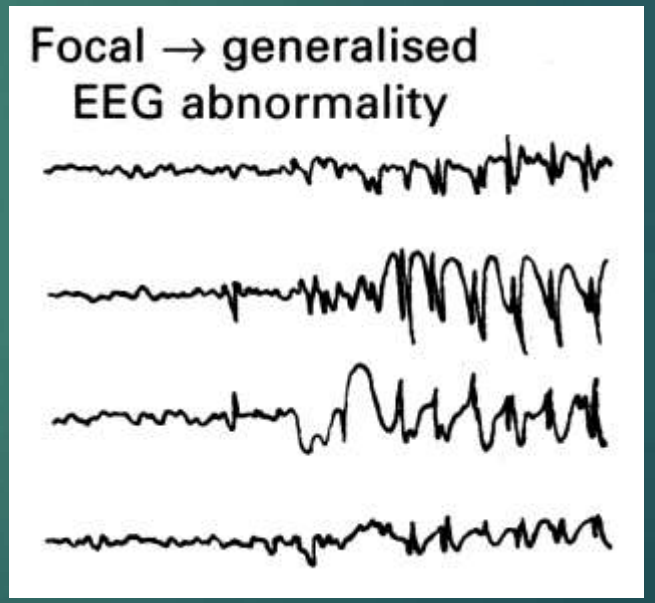




Focal (partial) seizures

- Focal (Partial) seizures evolving to Generalized tonic/clonic convulsions – secondary generalised tonic/clonic seizures (sGTCS)





Focal Seizures 2

- A. Focal (Simple Partial): 1 focal area and do not impair csness (no LOC):
  - (Old Simple Partial, Focal motor, Jacksonian, versive, postural, aphasic)
  - Sensory, motor, autonomic, or psychic phenomena
  - Lasts a few seconds (or minutes)
  - Historically, non-motor simple partial szs referred to as auras.

- B. Focal (Complex Partial)
  - (Old Partial seizures with complex symptomatology)
  - CP szs involve 1 focal area & impairs csness
  - Starts either as simple partial or aura & evolves into CP sz with impaired csness or starts as CP
  - Impaired responses to environmental stimulus;
  - Lasts from few seconds to few minutes (ave = 83 seconds)
  - Most common sz; 50-60% of all szs
  - Sz semiology provides major clues as to localization onset

Focal Seizures (Partial Complex Seizures) 3

- C. Secondarily generalized seizures: evolves from focal (simple (aura) to complex) to 2ndarily generalized sz
  - Generalized tonic-clonic szs (old Grand Mal), with warning
  - First involve epileptic cry, followed by generalized stiffening, then bilateral jerking of extremities; lasts less than 3 minutes

- LOC and fall; tonic-clonic muscular event

- **Ictus**:

  A. **Tonic**: Tonic extension of all 4 limbs, rigidity, stop breathing, arch back

  B. **Clonic**: rapid alternating relaxation of muscles, incontinence

- **Postictal**: Conscious immediately or stupor, confusion

- Most frequent in sleep; amnestic for seizure; apneic (stop breathing) and cyanotic (blue)

Features Suggesting Focal seizures

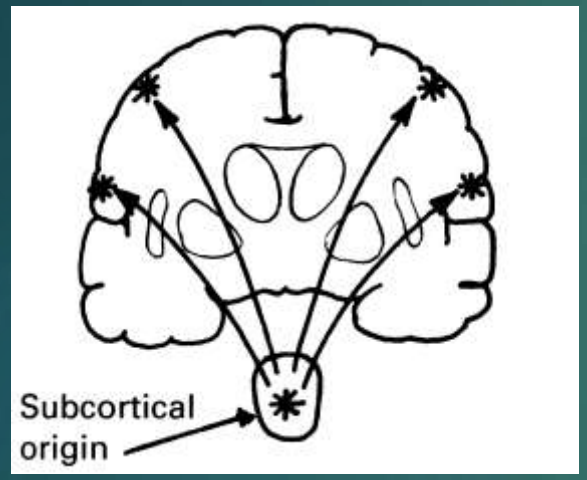
- Auras (déjà vu, epigastric sensation, fear)
  - Thought to arise from amygdala and insular cortex
- Unilateral automatisms/ Head or eye deviation
- Contralateral arm posturing/Asymmetric limb movements
- Brief Ictal event (1-2 minutes) or secondary generalization
- Impaired consciousness/long postictal period (amnesia, aphasia, disorientation, fatlgue, etc.)
- Postictal hemiparesis (Todd’s paralysis)
- Postictal nose wipe (secretions)

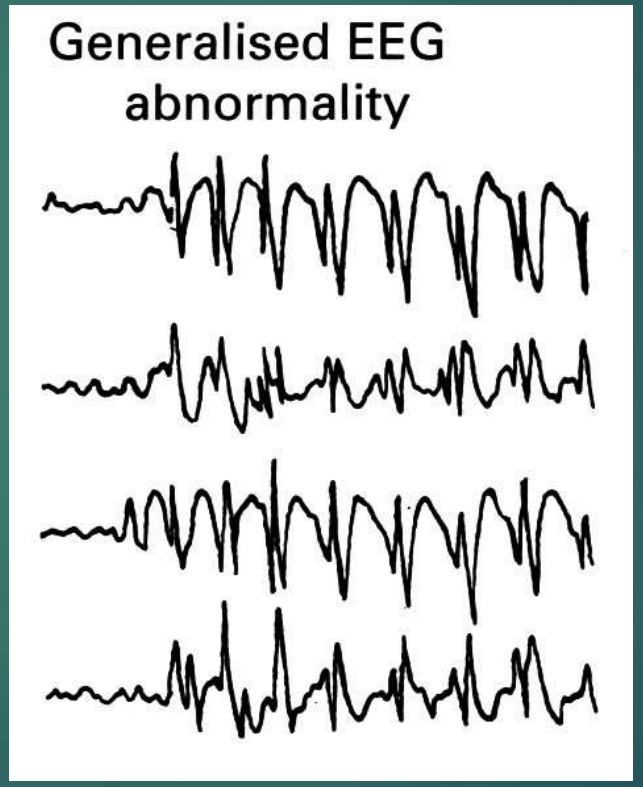
Focal Seizures

- **Focal**: 4 components, Amnestic

1. Sensory: vague giddiness, auditory, visual, gustatory sensations
2. Autonomic: palpitations, goose bumps, nausea, dry mouth
3. Psychic: impending doom, altered state of awareness, dreamy, twilight states, forced thoughts, hallucinations, deja or jamais vu
4. Somatomotor: automatisms (blink, grimace, lip smack, chew, gesturing); aggression very rare

Generalized seizures
(convulsive or non-convulsive)





Generalized Seizures

- Arising within and rapidly engaging bilaterally distributed networks
- Bilaterally symmetrical and without local onset

- 6 Types:
  - Absence (Petit Mal) (or Absence with special features (myoclonic, eyelid)
  - Clonic (rigidity)
  - Tonic (rhythmic jerk)
  - Atonic (drop)
  - Myoclonic (jerks)
  - Primary generalized tonic-clonic

- 30 percent of all seizure patients

- Brainstem and thalamic start

- Evidence for genetic basis

Case Study 1

- A 5 y/o female is brought to your office because of episodic “ blanking out” which began 1 month ago. The patient has episodes in which she abruptly stops all activity for about 10 seconds, followed by a rapid return to full consciousness. The patient’s eyes are open during the episodes and she remains motionless with occasional “ fumbling” hand movements.

Case Study 1

- After the episode the patient resumes whatever activity she was previously engaged with no awareness that anything has occurred
- She has 30 episodes per day
- No convulsions

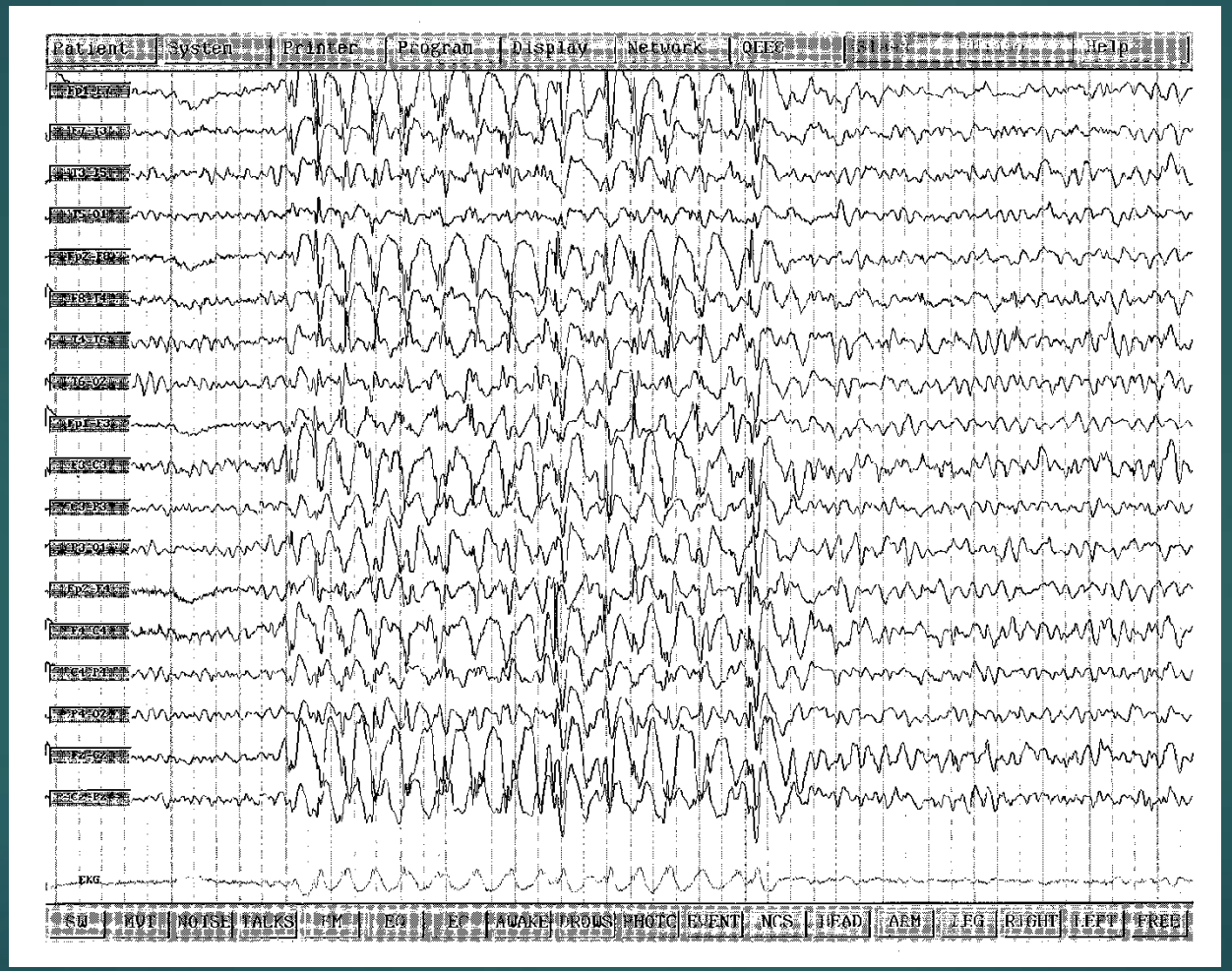
Case Study 1

- Past medical, physical and developmental histories are unremarkable.
- No history of previous or current medications; No allergies
- Family history is pertinent for her father having similar episodes as a child.

Case Study 1

- General physical and neurological examination is normal.
- Hyperventilation in your office replicates the episodes.

Case Study 1



EEG for Case Study 1

Case Study 1

- What is the diagnosis?

Generalized: Absence (Petit Mal)

- Primary generalized sz; 15% of childhood szs; idiopathic, but GABA genes may be involved
- Brief episode of impaired csness; 5-10 second blank staring spell; some minor motor automatisms (eyelid flutter); brief disorientation; may look like daydreaming
- Childhood (3-8 year onset; peak is 6), cease at puberty; rare in adults; 50% genetic; szs can persist into adulthood; 15% develop juvenile myoclonic epilepsy
- MRI typically normal
- EEG: 3 Hz spike-wave discharges, begin suddenly, last 5-10 seconds
- If untreated, very frequent seizures (100+ per day)
- Best treatment: Ethosuximide (Zarontin) – best sz relief & least side effects

Staring: Absence vs. CP Seizure

- **Absence**
  - multiple/day
  - brief: 10-20 sec
  - minor automatisms
  - EEG: 3 Hz
  - Meds:
    - Ethosuximide
    - Valproate

- **Complex Partial**
  - less frequent
  - 30 sec to 3 min
  - common automatisms
  - EEG: N1 or focal spike
  - Meds:
    - Carbamazepine
    - Phenytoin
    - Valproate

Case Study 2: Nervous disorder?

- 25 year-old right-handed marketing executive for a major credit card company, began noticing episodes of losing track of conversations and having difficulty with finding words.
- These episodes lasted 2-3 minutes.
- At times, the spells seemed to be brought on by a particular memory from her past.
- No one at her job noticed anything abnormal.

Case Study 2

- Patient had no significant past medical history, and took no medicines except for the birth control pill.
- She was in psychotherapy for feelings of depression and anxiety, but was not taking medications for mood or anxiety disorder
- Her therapist notes that she has been under significant stress from the breakup with her boyfriend.

Case Study 2

- What is your differential diagnosis at this point?

Case Study 2

- A careful medical history revealed that she had one febrile seizure at age three; no family members had epilepsy.
- The psychiatrist prescribed a benzodiazepine sleeping pill to be used as needed, and scheduled her for an electroencephalogram (EEG).

Case Study 2

- Prior to the EEG, the patient had an episode while on a cross country business trip, in which she awoke on the floor near the bathroom of her hotel room.
- She had a severe headache and noted some blood in her mouth, along with a very sore tongue. She called the hotel physician and was taken to the local emergency room.

Case Study 2

- What is your differential diagnosis now?
  - How would you classify her event?
-

Case Study 2

- In the ER, a diagnosis of nocturnal convulsion was made.
- A head computerized tomographic (CT) scan was normal.
- Laboratory tests including a CBC, chemistries and toxicology screen were normal.

Case Study 2

- She was given fosphenytoin 1000 mg PE intravenously and observed.
- She was discharged home on phenytoin 300 mg per day and referred to a neurologist.
-

Case Study 2

- Neurologist took a complete neurologic and medical history and found patient had an uncomplicated febrile seizure as a toddler, but no other seizures.
- There was no family history of epilepsy in her immediate family members.
- Medical history is otherwise benign and she has no medication allergies. She had regular menstrual periods since age 13 and has never been pregnant, although she wants to have children.
- General and neurologic examination was normal.

Case Study 2

- EEG showed right anterior temporal spike and wave discharges.
- An MRI of the brain was normal.
- Complaint of persistent sedation led to change from phenytoin to lamotrigine, at a dose starting at 50 mg BID increasing by 50 mg/day every two weeks to reach a target dose of 300 mg/day.

Generalized seizures

- Atonic: brief loss of muscle tone of postural muscles, i.e. simple head drop, or drop to floor if legs involved
- Clonic: brief rhythmic jerking movements of muscles, often of both upper & lower extremities; csness impaired; EEG: bilateral discharges
- Tonic: sudden onset of bilateral tonic extension or flexion of head, trunk, or extremities for several seconds; drop to ground; usually during drowsiness or just after falling asleep or waking up; EEG: high frequency discharge with low amplitude
- Myoclonic: lightning fast-like jerks, involving symmetric movements of head, limbs or axial muscles; cluster over period of several minutes; no LOC; can evolve to generalized; can be present in neurodegenerative disorders
- Primary generalized tonic-clonic: (Grand Mal) tonic extension of extremities for ~20s, then clonic synchronous rhythmic muscle movements for ~45s; post ictal confusion; no warning

Generalized: Febrile seizures

- Seizure associated with fever (no intracranial infection, or cause)
- Must occur in child, aged 1 m to 5 years
- Generalized or focal
- 2-5% of children prior to 5;
- 50% genetic
- 2 types: simple & complex
  - Simple: generalized sz lasting less than 15 minutes, non-focal, no recurrence in 24 hrs; no higher risk for later szs
  - Complex: focal in onset &/or more than 15 minutes, or recurs in 24 hrs; increased risk for developing TLE epilepsy (27%)
  - No benefit from AEDs

Unknown Seizures

- Insufficient evidence to classify as focal, generalized or both

Severe Epileptic Syndrome

- Some epilepsy syndromes are known to be associated with more adverse cognitive consequences than others.
  - Idiopathic Benign syndromes—e.g., BECTS (Rolandic), absence
  - Adverse syndromes—e.g., Lennox-Gastaut
  - Variable syndromes—Localization related epilepsies

Idiopathic Syndromes: mild deficits

	Deficit	**Outcome**
Juvenile Myoclonus Epilepsy	Mild executive deficits	Presumed favorable
Generalized with absence or GTCS	Mild attentional deficits	Unknown
Centrotemporal spikes benign	Mild Heterogeneous	Mostly favorable (interictal abn)
Occipital epilepsy	Mild Heterogeneous	Unknown

Elger et al. (2004)

Adverse Syndromes: more severe outcomes

	Deficit	**Outcome**
CSWDS	Variable (diffuse or executive)	Variable - duration dependent
Landau Kleffner	Auditory agnosia, Expressive Language	Variable – early onset worse
West Syndrome	Retardation, regression	Poor, retardation
Lennox-Gastaut	Retardation, decline	Poor, retardation worse early onset

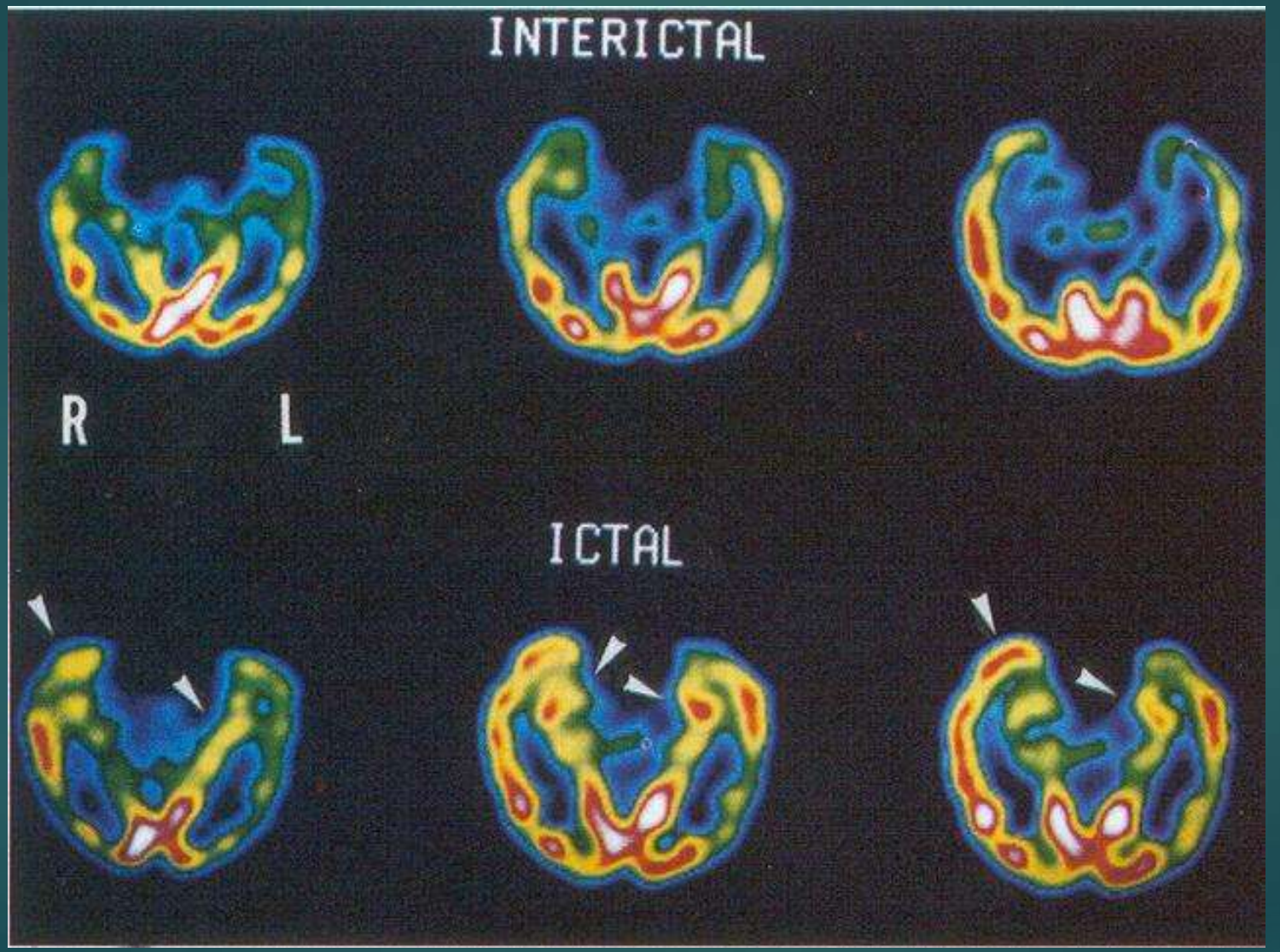
Elger et al. (2004)

Localization Related Syndromes

	Deficit	**Outcome**
Frontal	Executive function, attention, speed	Unknown
Temporal	Material-specific memory (executive 2º gen), naming, achievement	Very slow deterioration
Parietal Occipital	Unknown (variable)	Unknown (heterogeneous)

Elger et al. (2004)

Interictal Hypoperfusion; Ictal Hyperperfusion



Causation

- Primary:

  Idiopathic, no known etiology, 70% of patients

- Symptomatic:

  - Brain Trauma
  - Tumor is most common in adult onset
  - Knowledge of cause correlates with lower functioning

- ETOH withdrawal seizure:

  - 12-36 hours, tonic-clonic, 1/3rd go to DT's
  - Delirium Tremens – 4-7 days: confusion, delirium, delusion, tremor, hallucinations

- Seizure Threshold decrease: ETOH, drugs, fatigue, stress

Etiology of Seizures and Epilepsy

- Infancy and childhood
  - Prenatal or birth injury
  - Inborn error of metabolism
  - Congenital malformation
- Childhood and adolescence
  - Idiopathic/genetic syndrome
  - CNS infection
  - Trauma

Etiology of Seizures and Epilepsy 2

- Adolescence and young adult
  - Head trauma
  - Drug intoxication and withdrawal*
- Older adult
  - Stroke: 5% increase in risk
  - Brain tumor
  - Acute metabolic disturbances*
  - Neurodegenerative

*causes of acute symptomatic seizures, not epilepsy

Questions Raised by a First Seizure

- Seizure or not?
- Focal onset?
- Evidence of interictal CNS dysfunction?
- Metabolic precipitant?
- Seizure type? Syndrome type?
- Studies?
- Start AED?

Seizure Precipitants

- Metabolic and Electrolyte Imbalance
- Stimulant/other proconvulsant intoxication
- Sedative or ethanol withdrawal
- Sleep deprivation
- Antiepileptic medication reduction or inadequate AED treatment
- Hormonal variations
- Stress
- Fever or systemic infection
- Concussion and/or closed head injury

Seizure Precipitants 2

Metabolic and Electrolyte Imbalance

- Low (less often, high) blood glucose
- Low sodium
- Low calcium
- Low magnesium

Seizure Precipitants 3

Stimulation/Other Pro-convulsant Intoxication

- IV drug use
- Cocaine
- Ephedrine
- Other herbal remedies
- Medication reduction

Evaluation of a First Seizure

- History, physical
- Blood tests: CBC, electrolytes, glucose, Calcium, Magnesium, phosphate, hepatic and renal function
- Lumbar puncture only if meningitis or encephalitis suspected and potential for brain herniation is ruled out
- Blood or urine screen for drugs
- Electroencephalogram
- CT or MR brain scan

Clinical evaluation

- The concern of the clinician is that epilepsy may be symptomatic of a treatable cerebral lesion.
- **Routine investigation:** Hematology, biochemistry (electrolytes, urea and calcium), chest X-ray, electroencephalogram (EEG).
- Neuroimaging (CT/MRI) should be performed in all persons aged 25 or more presenting with first seizure and in those pts. with focal epilepsy irrespective of age.
- **Specialised neurophysiological investigations:** Sleep deprived EEG, video-EEG monitoring.
- **Advanced investigations** (in pts. with intractable focal epilepsy where surgery is considered): Neuropsychology, Semiinvasive or invasive EEG recordings, MR Spectroscopy, Positron emission tomography (PET) and ictal Single photon emission computed tomography (SPECT)

Medical Treatment of First Seizure

Whether to treat first seizure is controversial

- 16-62% will recur within 5 years
- Relapse rate might be reduced by antiepileptic drug treatment
- Abnormal imaging, abnormal neurological exam, abnormal EEG or family history increase relapse risk
- Quality of life issues are important

Reference: First Seizure Trial Group. Randomized Clinical Trial on the efficacy of antiepileptic drugs in reducing the risk of relapse after a first unprovoked tonic-clonic seizure. Neurology 1993; 43 (3, part1): 478-483.
Reference: Camfield P, Camfield C, Dooley J, Smith E, Garner B. A randomized study of carbamazepine versus no medication after a first unprovoked seizure in childhood. Neurology 1989; 39: 851-852.

Epilepsy – Treatment

- If pt is seizure-free for three years, withdrawal of pharmacotherapy should be considered.
- Withdrawal should be carried out only if pt is satisfied that a further attack would not ruin employment etc. (e.g. driving license). It should be performed very carefully and slowly! 20% of pts will suffer a further sz within 2 yrs.

- The risk of teratogenicity is well known (~5%), especially with valproates, but withdrawing drug therapy in pregnancy is more risky than continuation.
- Epileptic females must be aware of this problem and thorough family planning should be recommended.
- Over 90% of pregnant women with epilepsy will deliver a normal child.

Epilepsy – Surgical Treatment

- A proportion of the pts with intractable epilepsy will benefit from surgery.
- Epilepsy surgery procedures: Curative (removal of epileptic focus) and palliative (seizure-related risk decrease and improvement of the QOL)
  - Curative (resective) procedures: Anteromesial temporal resection, selective amygdalohippocampectomy, extensive lesionectomy, cortical resection, hemispherectomy.
  - Palliative procedures: Corpus callosotomy and Vagal nerve stimulation (VNS).

Classification of Epilepsy

- Idiopathic
  - Benign history
  - Normal development
  - Normal neuro exam
  - Genetic
  - Good prognosis
- Symptomatic
  - History of brain insult
  - Abnormal development
  - Abnormal exam
  - Due to brain injury
  - Cautious prognosis

Anatomy

- Origin can be anywhere in brain
- Foci can spread along anatomic pathways to generalization
- Issue of Mirror Foci
- Sites: Most common is mesial temporal lobe (80%); frontal (15%), most uncommon is cerebellum

Diagnostic Methods

- Diagnosis is primarily through history and observation.

- EEG:
  - Normal in 20-30% of Seizure patients; 10-15% of Normals are abnormal
  - picks up in frequency and amplitude; sharp spike = proximal
  - subject to lots of random variation, artifacts
  - Absences: spike and wave pattern

- MRI: classification and prognosis

Electroencephalogram (EEG)

- Graphical depiction of cortical electrical activity, usually recorded from the scalp.
- Advantage of high temporal resolution but poor spatial resolution of cortical disorders.
- EEG is the most important neurophysiological study for the diagnosis, prognosis, and treatment of epilepsy.

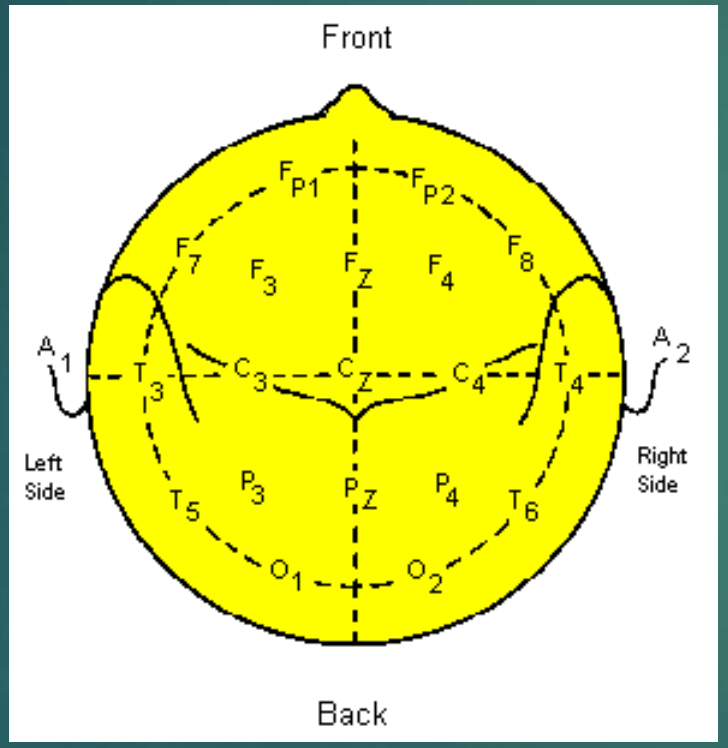
What EEG does Not do

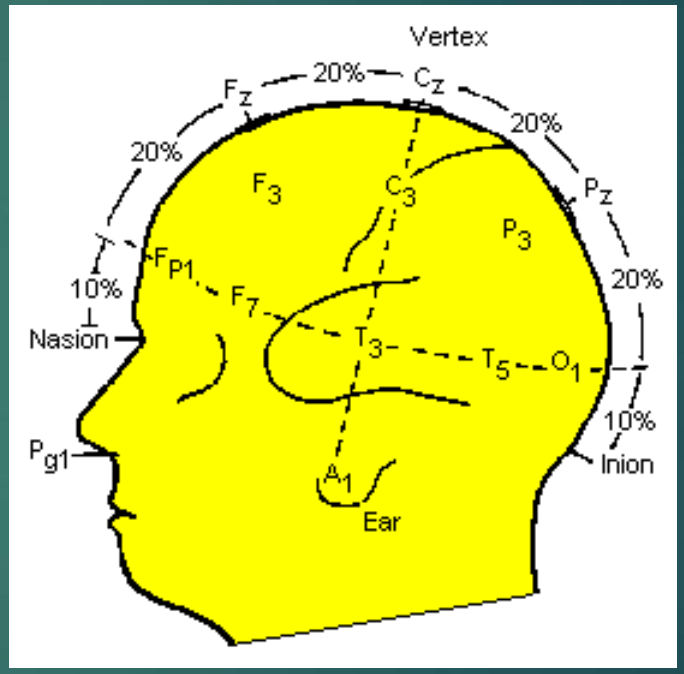
- The EEG does not “diagnose” or “rule out” the diagnosis of epilepsy
- A normal EEG does not preclude a diagnosis of seizure or epilepsy if history is convincing
- An EEG abnormality alone does not mean “epilepsy” if the history is not convincing

Special EEGs

- Ambulatory EEG
- Inpatient Telemetry: Video & EEG

10/20 System of EEG Electrode Placement

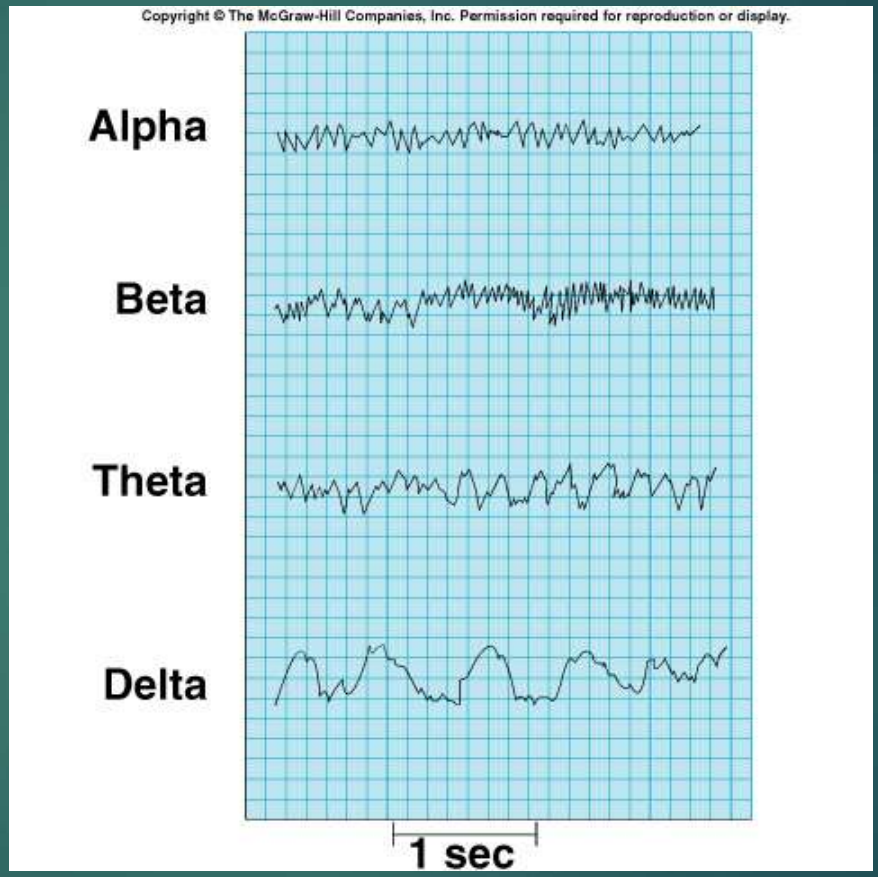




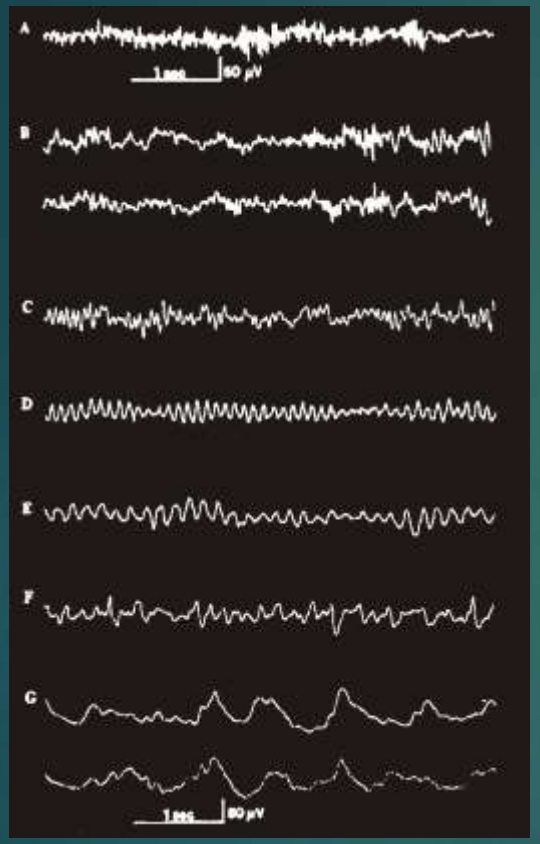
EEG Frequencies

- **Alpha: 8 to ≤ 13 Hz**
- **Beta: >13 Hz**
- **Theta:**

  4 to under 8 Hz
- **Delta: <4 Hz**



EEG Frequencies



EEG Frequencies

A) Fast activity

B) Mixed activity

C) Mixed activity

D) Alpha activity (8 to ≤ 13 Hz)

E) Theta activity (4 to under 8 Hz)

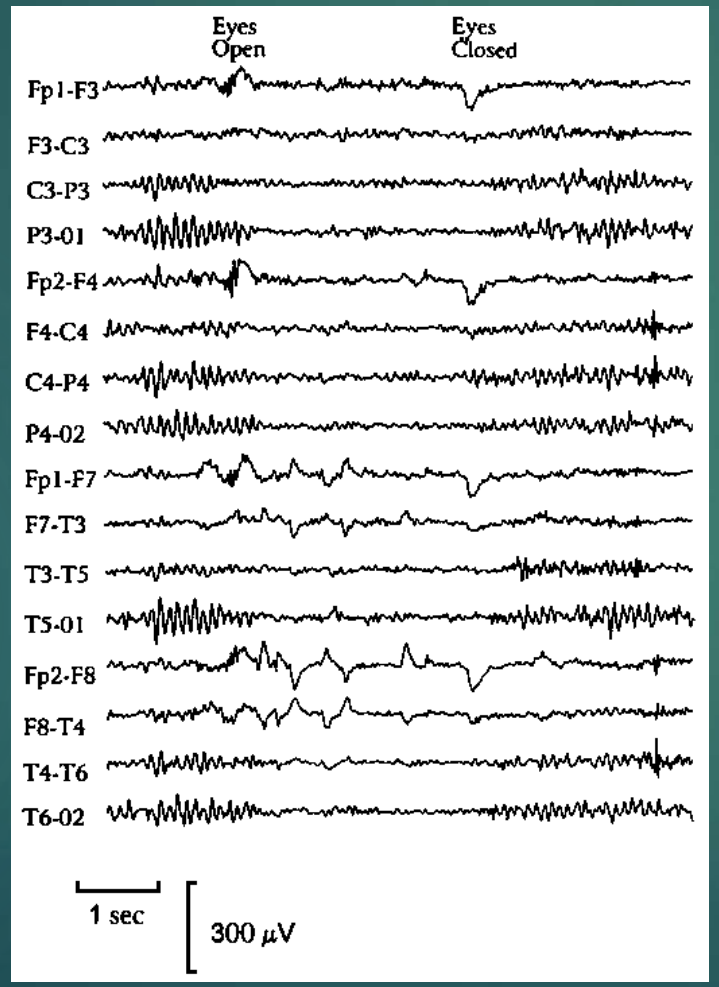
F) Mixed delta and theta activity

G) Predominant delta activity (<4 Hz)

Not shown: Beta activity (>13 Hz)

Niedermeyer E, Ed. The Epilepsies: Diagnosis and Management. Urban and Schwarzenberg, Baltimore, 1990

Normal Adult EEG

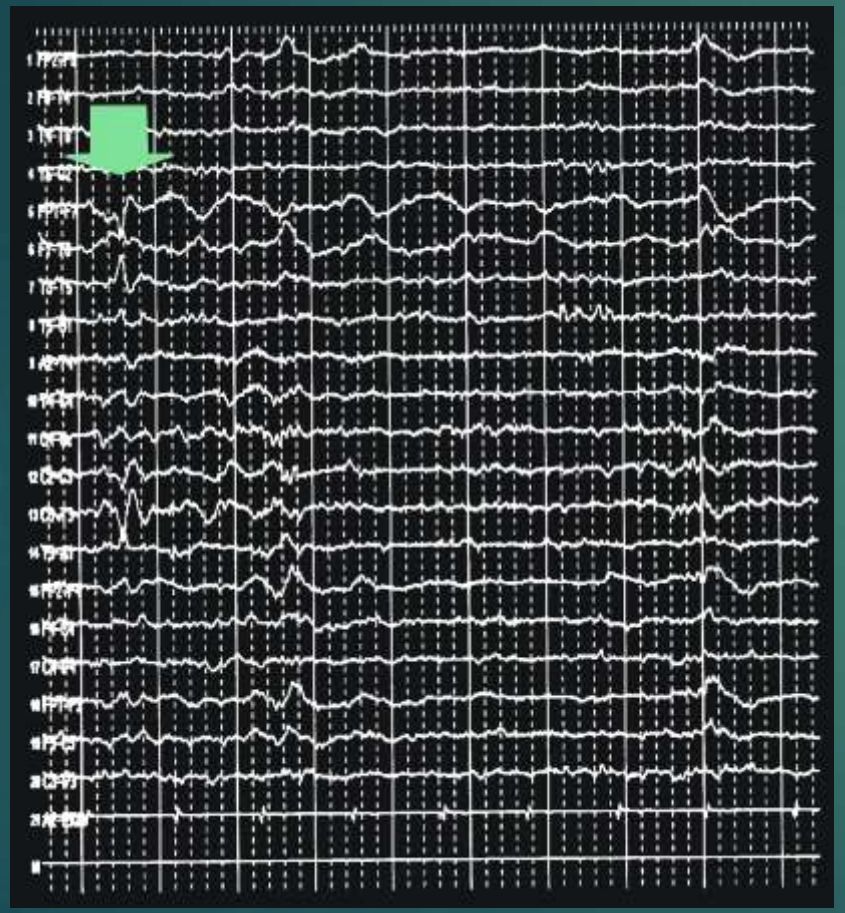


Normal alpha rhythm

EEG Abnormalities

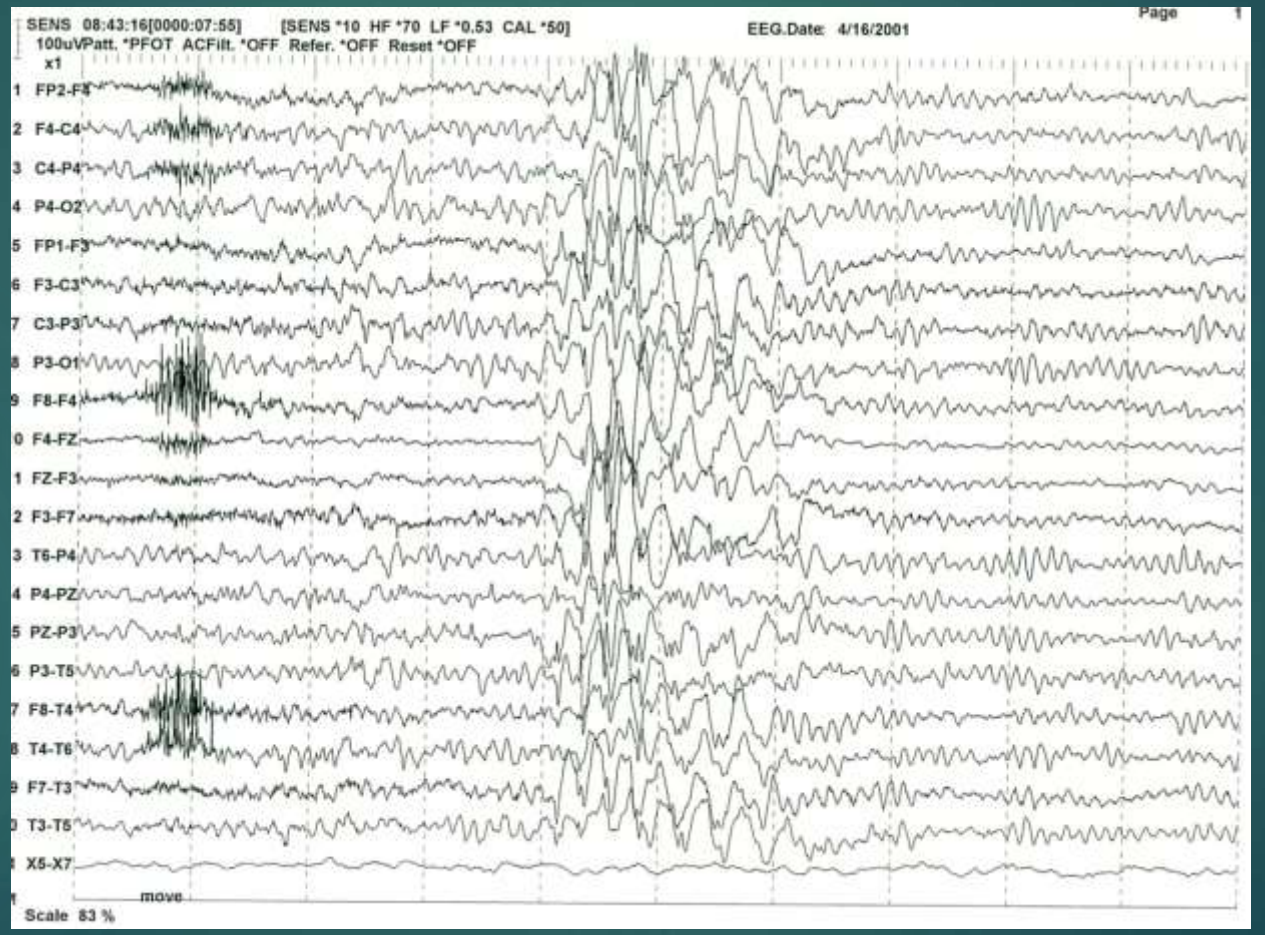
- Background activity abnormalities
  - Slowing not consistent with behavioral state
    - May be focal, lateralized, or generalized
  - Significant asymmetry
-
- Transient abnormalities / Discharges
  - Spikes
  - Sharp waves
  - Spike and slow wave complexes
  - May be focal, lateralized, or generalized

Sharp Waves

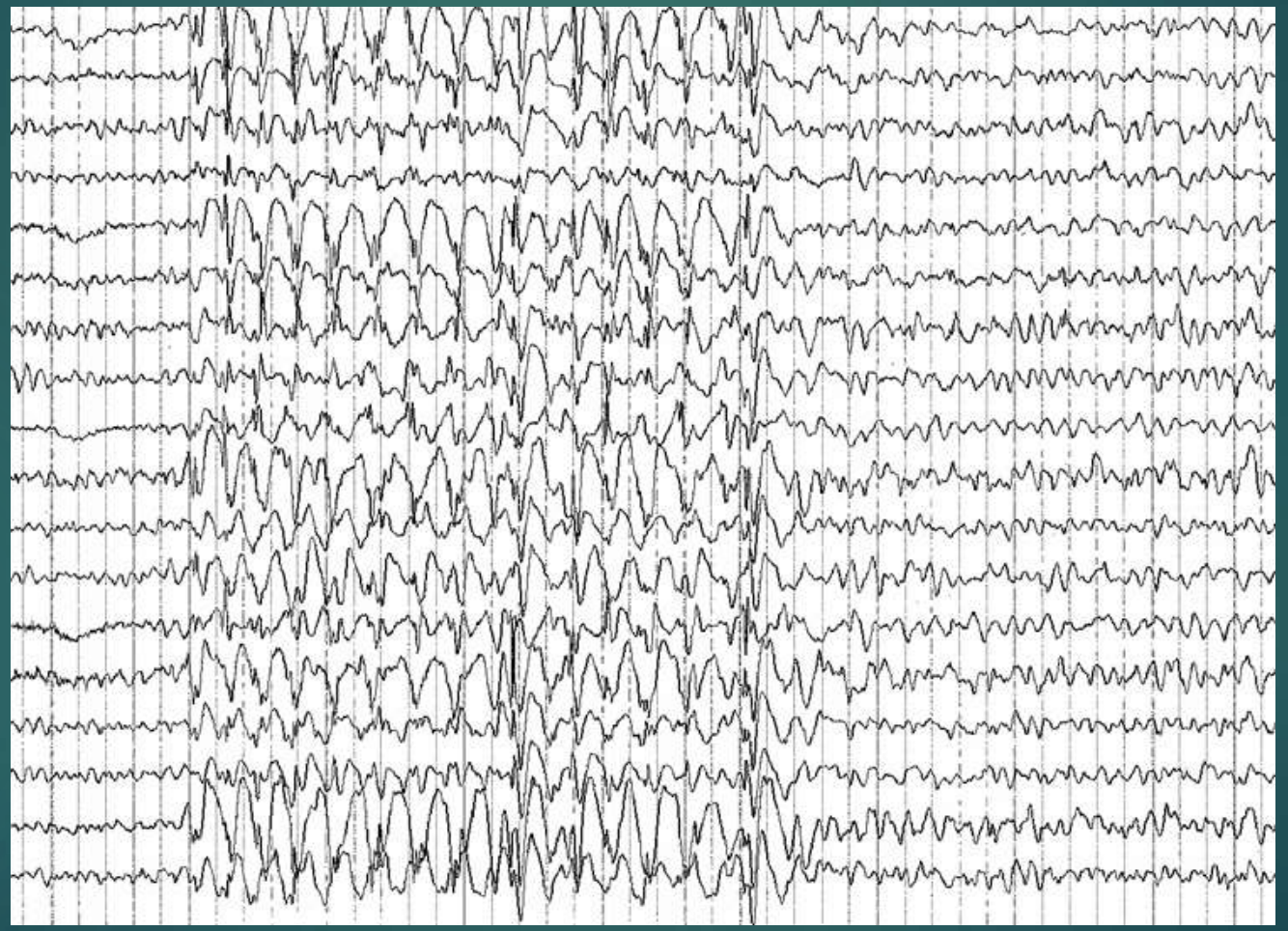


An example of a left temporal lobe sharp wave (arrow)

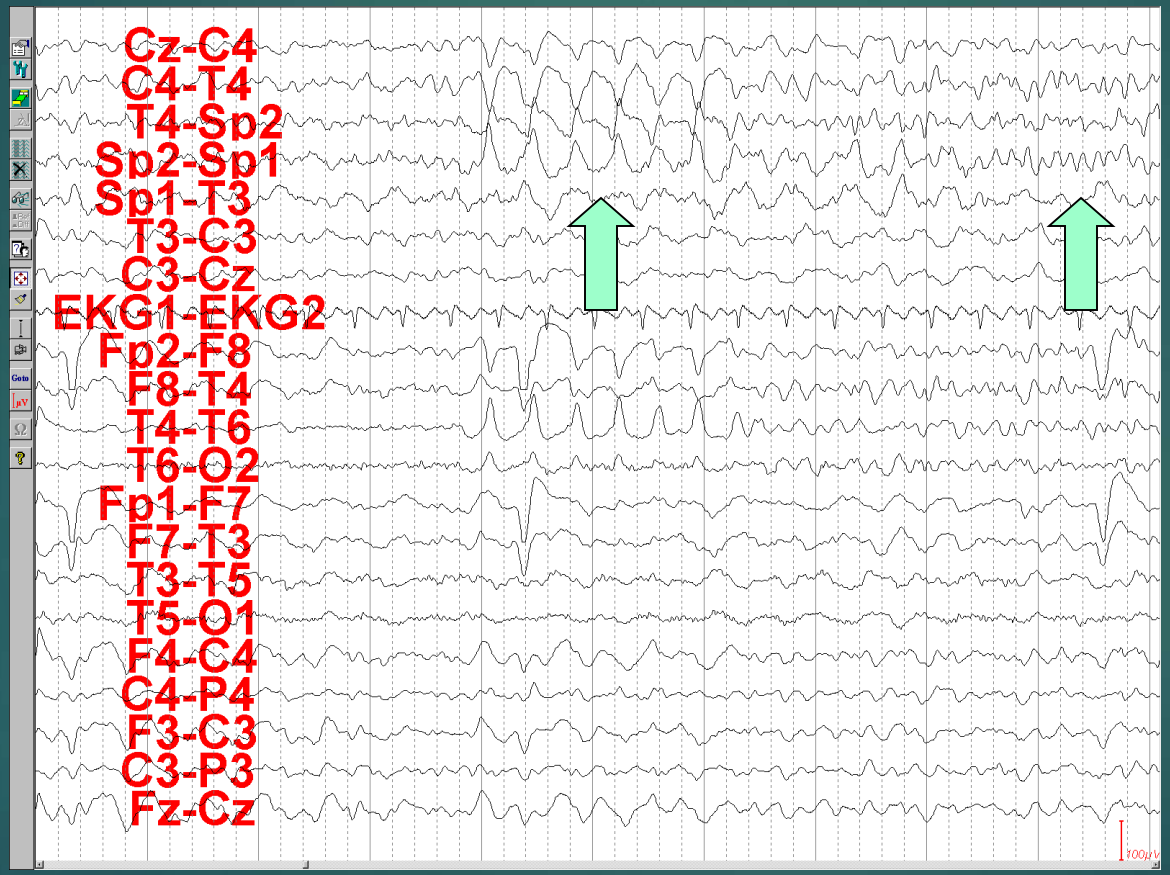
Generalize Spike Wave Discharge



EEG: Absence Seizure

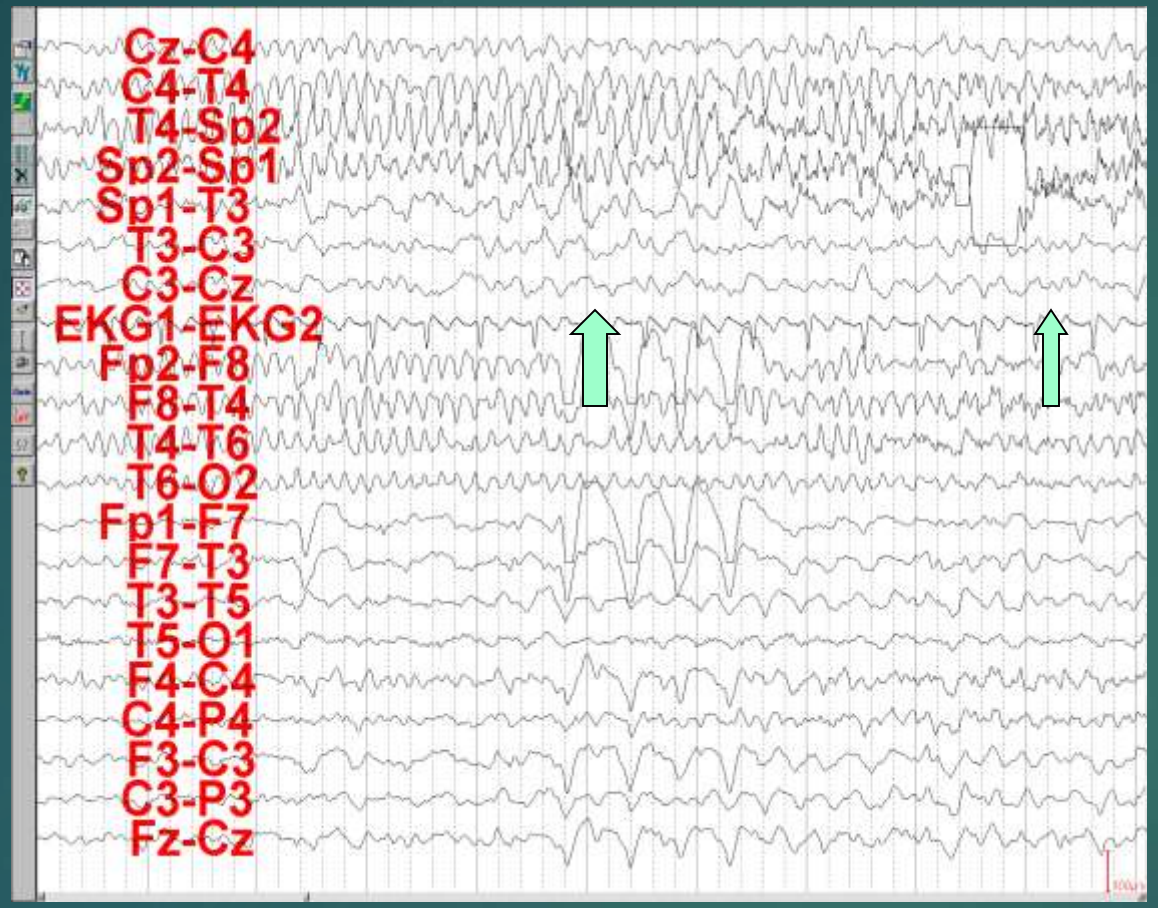


EEG: Simple Partial Seizure



Right temporal seizures with maximal phase reversal in the Right phenoidal electrodes

EEG: Simple Partial Seizure

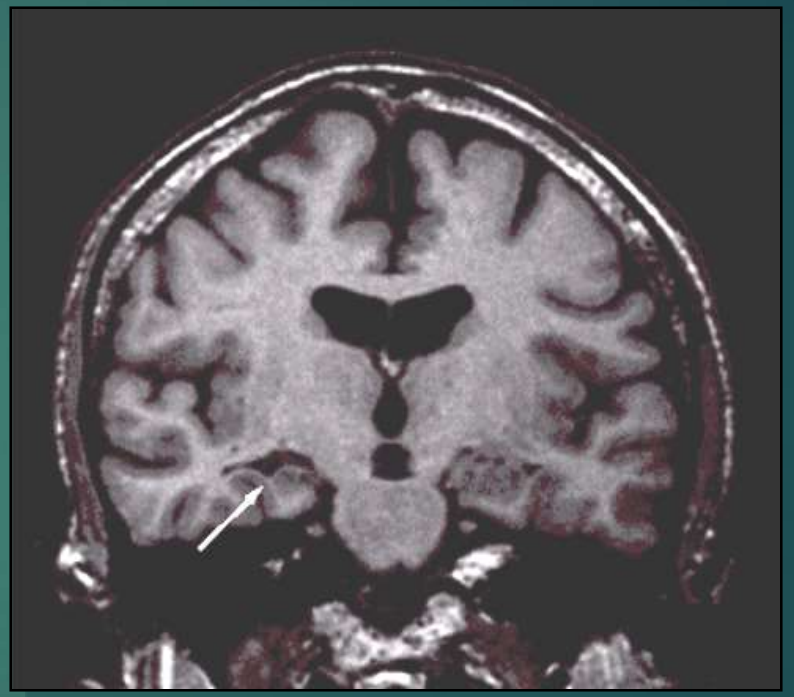


Continuation of same seizure

Right temporal seizures with maximal phase reversal in the right sphenoidal electrodes

Syndrome of Mesial Temporal Epilepsy

- Febrile seizure
- Early seizure onset
- Hippocampal sclerosis
- TLE seen without hippocampal sclerosis



Temporal Lobe

- Temporal lobe, esp. hippocampus, is the most common site of pathology in adults & adolescents with szs with alteration of csness (25% of kids; 50% of adults); of focal szs, 70-90% have szs arising from TL

- Most common pathology in adults is hippocampal sclerosis (65-75% of TLE); 40-60% had complicated febrile szs

- Hippocampal sclerosis = neuronal loss in hippocampal formation, esp. CA1 & CA 3; in addition, remaining neurons may become an “epileptogenic network” with synaptic reorganization; on MRI, atrophy (increased T2 signal)

- Mesial temporal sclerosis (MTS)(80%): neuronal loss & gliotic scarring of hippocampus/mesial temporal; often present with aura are often medication refractory; often ideal for surgery

Temporal Lobe Epilepsy (TLE)

- In pediatric cases, underlying pathology is much more variable; often unknown; 80% idiopathic; malformations of cortical development (MCD) & low grade tumors are majority of pathological substrates

- TLE with hippocampal sclerosis (HS) is associated with a hx of febrile seizures as infant or toddler. Febrile szs that are prolonged or recurrent are greater risk for TLE. Other risks: perinatal complications, hypoxic-ischemic injuries, CNS infections.

- Age of onset with hx of febrile szs is trimodal: age 5, 15, 26; greatest frequency in 2nd decade

- TLE can be difficult to treat; 30% develop intractable seizures; therefore more temporal lobectomies

Mesial Temporal Sclerosis (MTS) Epilepsy

- Present with aura (focal (simple partial) sz before LOC): often wide eyed stare, then oro-alimentary automatisms (lip smacking, swallowing, chewing) or upper extremities automatisms (pill rolling, picking movements)
- Associated with alteration of awareness & gradual clouding of csness, but not necessarily LOC
- Most frequent auras:
  - Rising epigastric sensation (butterflies in stomach)
  - Fear
  - Deja-vu
  - Pilorection (goose pimples)
  - Memory flashback
  - Olfactory hallucinations (uncinate fits)
  - Dreamy states

Lateral TLE

- Auras of lateral TLE:
  - Auditory hallucinations – unformed (buzzing, ring)
  - Visual hallucinations (unformed figures, objects , rarely faces)

- TLE often refractory to medication = 33%

- Seizure freedom in 60-80% after temporal lobectomy

Seizure Type: Temporal Loci 1

- Temporal lobe (most seizures: 25% of child; 50% of adults):

- Temporal Location:
  - Auditory sxs if superior gyrus;
    - more vestibular if posterior;
    - hippocampal produces strange, indescribable feelings and illusions;
    - amygdala produces epigastric, nausea, fear, panic, olfactory and gustatory hallucinations;
    - perisylvian associated with taste;
    - lateral and posterior, with auditory and visual hallucinations

Temporal Loci 2

- Behavior may be disorganized, include repetitive movements of hands (ipsilateral to side of seizure onset; opposite hand in forced tonic posture), tongue, mouth, lips
- Speech during seizure: speech associated with non-language dominant temporal lobe onset in majority of cases; aphasia after sz related to dominant lobe
- Postictal confusion or fatigue common
- Memory problems universal; but also naming, verbal fluency, attention, EF, VS
- Hallucinations often lack bizarre interpretation; more likely to test its reality
- Automatisms: stereotyped pattern, events invariant

Frontal Seizures

- Short seizures; many presentations; 20% of refractory focal szs; most DLPFC
- Jacksonian spread if precentral gyrus
- No post ictal period; no clear LOCD; clear quickly
- Forced thinking, yawning; olfactory hallucinations with automatisms; ictal sexual activity
- Bilateral motoric movements; bicycle motor movements; some look like PNES (pelvic thrusting, wild random limb movements)
- Vocalizations: roars
- Often nocturnal
- 30-100% sz free after surgery; best if lesion shows on MRI

Frontal Lobe Epilepsy

Neuropathologies:

- Ganglioglioma
- Cortical dysplasia
- Venous angioma
- AVM

Frontal Lobe Epilepsy 2

- 2nd most common location of seizures (25-30%)
- Cognition: standard executive dysfunction syndrome
- Often misdiagnosed as pseudoseizures
  - Normal/inconclusive EEGs
  - Motor/psychiatric manifestations
    - Hypermotor activity, brief in duration
    - Only mildly impaired consciousness/rapid recovery
    - Often nocturnal/fencer's posture

Frontal Lobe Epilepsy 3: Behavior via Locations

- Motor area
  - 1:1 manifestation with motor homunculus; unilateral clonic jerks; can have Jacksonian march
- SMA
  - Tonic posturing
- Premotor
  - Contraversive (away from sz focus) head and eye movements
- Prefrontal (loss of awareness; amnestic for events)
  - Explosive, hypermotor automations; bilateral automatisms (bicycling)
  - Bizarre and hysterical behavior (screaming)
  - 50-90% have aura of tightness or tingling of body parts, or fear
  - Aphasic szs
  - Mesial region: negative behaviors, loss of consciousness

Parietal Lobe Epilepsy

- Focal onset rare (6-8% of focal)
- Semiology: sensory, motor, vertigo, mood, before loss of awareness
- Can spread to frontal or temporal lobes & look like them
- Seizure freedom post surgery = 50-88%
- NP = language, praxis

Occipital Lobe Epilepsy

- Uncommon
- Localization by visual aura (60%) (hallucination of lights, colors); ictal blindness; can have formed hallucinations or illusions
- Contralateral eye movements, blinking
- NP = visual field defects and VS deficits

Seizure Induction/Triggers

Triggers:

Reading, writing, talking, math. calculation, music, eating, tooth brushing, tapping, moving, noises, hot water immersion, sensory stimuli, venetian blinds or pick fences, startles, video game

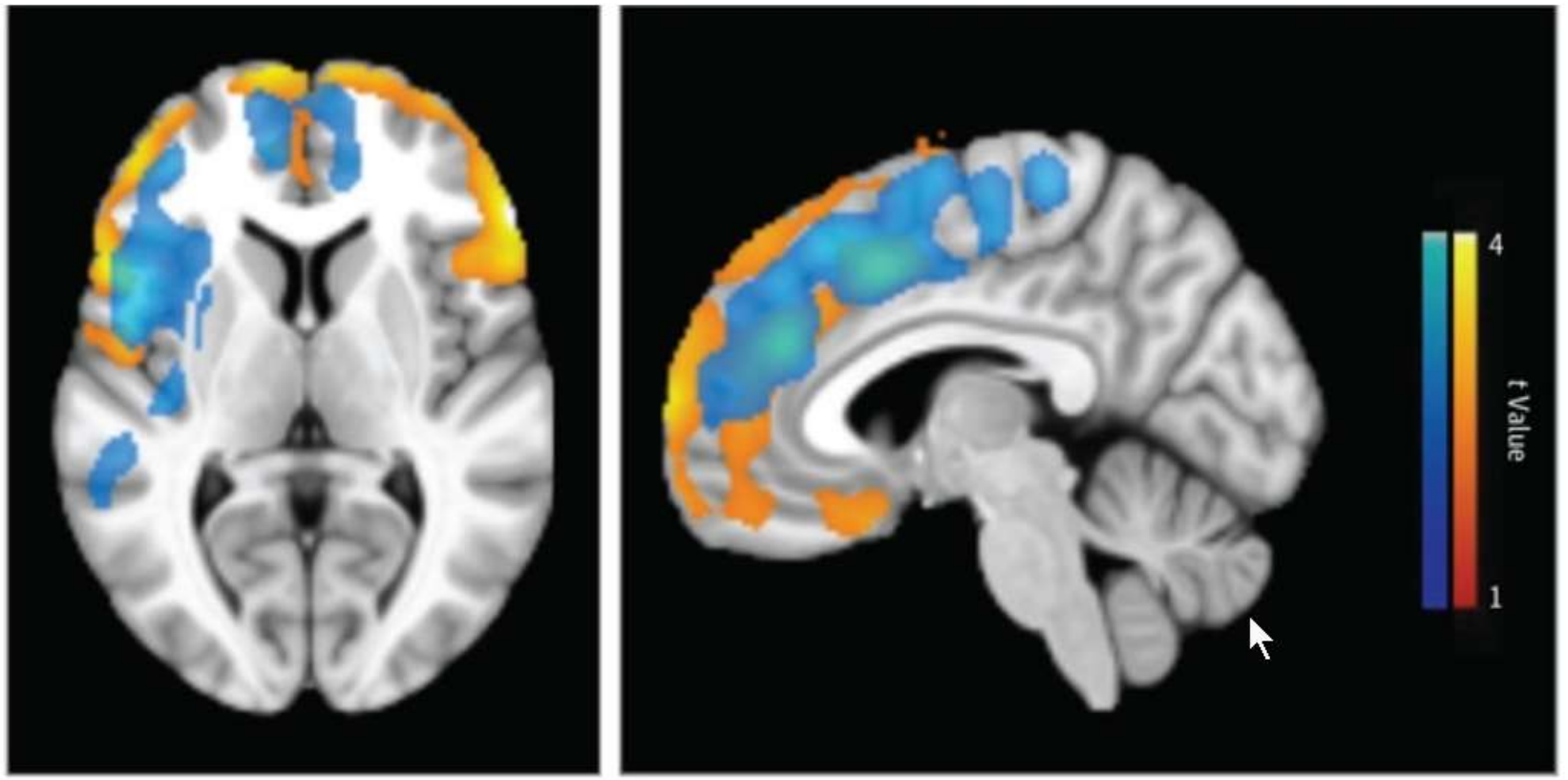
Epilepsy and Cognitive Impairment

- All patients with epilepsy are at increased risk for cognitive and/or behavioral impairment,

- Origin for this type of impairment appears to be multifactorial

Epilepsy and increased Beta Amyloid

- Early life differences shape the susceptibility to neurodegenerative disease later on.



***Amyloid in Epilepsy**: PiB uptake is higher in people who had epilepsy as children than in controls (orange scale). In ApoE4 carriers, the increase was more widely distributed (blue scale). [© 2017 American Medical Association. All rights reserved.]*

Epilepsy and AD 2

- Previous studies have reported a greater incidence of dementia and AD in people with epilepsy (see Breteler et al., 1991; Breteler et al., 1995). Vice versa, AD patients have an increased risk of seizures (Amatniek et al., 2006)
- The epilepsy-related plaques turn up in the default mode network, the target of AD
- Amyloid sticks around even in people whose epilepsy is controlled or in remission.
- People with epilepsy deposit Aβ at a younger age than the general population, carrying amyloid loads typical of people 10 years older
- Older epilepsy patients with ongoing seizures perform worse on tests of language, semantics, and visuomotor function (Karrasch et al., 2017). There is more brain atrophy and network abnormalities in patients with active epilepsy (see Garcia-Ramos et al., 2017)

Memory Impairment in TLE

- Verbal Memory impaired with left TLE
- Visual Memory impaired with right TLE
- Depends on degree of medial temporal sclerosis

Neuropsychological Correlates of Epilepsy

- Most common complaint: memory function
- No one complains of poor judgment
- Primary problem is neurological damage; secondary and tertiary problems are seizures, abnormal brain waves, neuropsychological deficits, emotional and social problems
- Neuropsychological assessment reflects neurological damage, not seizure

NP in Generalized & Focal Epilepsy

- Generalized szs more likely to impair cognitive functions; esp. with multiple episodes of status epilepticus
- Frontal lobes play significant role in generalized szs
- NP outcome is considered important marker of successful sz surgery outcome
- Variables that show reduce risk for cognitive morbidity following surgery: longer duration of szs, MTS, impaired pre-surgical memory scores, WADA test failure when testing sz focus side

NP in Temporal Lobe Epilepsy

- Preoperative:
  - Material-specific pattern of memory dysfunction in TLE; L -TLE auditory verbal & R-TLE – visual memory (latter less robust)
  - Confrontation naming, semantic verbal fluency impairment with Left TLE
  - Attention/Executive
  - IQ & achievement
  - Fine motor (grooved pegboard)
- Seizure lateralization prediction by naming deficits (BNT, Hamburg auditory naming) still questioned; but left TLE pts more likely to have these, even after ATL
- Postoperative:
  - Visual field defect (Meyers loop resection)
  - Decline in memory (10-50%) (25-50% of medically refractory pts)
  - Language/naming decline (40%), but not aphasia
- Improved NP function following ATL in seizure free; right ATL can show improvement in verbal memory; improved EF

NP in Frontal Lobe epilepsy

- Impaired attention and complex motor ability
- Impaired fluency, both verbal and design and action
- Impaired cost estimation, reasoning, temporal order, social cognition
- More behavioral problems
- Frontal memory problems: efficient encoding & retrieval, release of proactive interference, temporal order of memories

Posterior Cortical Epilepsy: Parietal & Occipital

- Visual processing deficits (field cuts, facial processing, color perception, object localization, object recognition, VS)

- Case 3: 51 year old female with frequent seizures

Case Study 3

- Seizure History: Her birth was unremarkable except that she was born with syndactyly requiring surgical correction.
- Early developmental milestones were met at appropriate ages.
- She had her first convulsive episode at age 2 in the setting of a febrile illness.

Case Study 3

- She began to develop a new type of episode in the third grade.
- The attacks consisted of her seeing a pink elephant that was sitting on various objects and waving to her.
- The patient has subsequently found a ceramic model of an elephant that was the same as the elephant that she saw during her seizures.

Case Study 3

- How are her symptoms different from most patients with schizophrenia?

Case Study 3

- She was not diagnosed with seizures until the age of 15.
- Initially, the seizures were controlled with medicine.
- After a few years, however, the attacks re-occurred despite treatment with anticonvulsants.

Case Study 3

- At age 20, the seizures changed in character to the current pattern.
- The seizures begin with an aura of “a chilling sensation starting at the lower back with ascension to the upper back over the course of 10-20 seconds”.

Case Study 3

- Observers then note a behavioral arrest.
- She tends to clench her teeth and breath heavily, such that her breathing sounds “almost as if she were laughing”.
- She is unable to fully respond to people for 5-10 minutes.
- Typically, she experiences 4-5 seizures per month.

Case Study 3

- She has had several EEGs in the past; the most recent available report is from seven years ago, which revealed mild, diffuse slowing of background elements with no abnormalities noted during three minutes of hyperventilation and photic stimulation.

- She had an MRI 13 years ago with no reported abnormalities.

Case Study 3

- She has tried several different medications, but is currently maintained on carbamazepine and lamotrigine. Her carbamazepine dose is 700 mg/day and Lamotrigine 125 mg/day with BID dosing.

- She feels excessively tired on higher doses.

- She has been on carbamazepine 32 years and on lamotrigine for four years.

- She states that she has had some success with the lamotrigine.

Case Study 3

- In the past, she has been unsuccessfully tried on phenobarbital, primidone, valproate, gabapentin, phenytoin and ethosuximide.
- She had marked weight gain while taking valproate.
- She hated having seizures in public and she “felt like a prisoner in my own home”.
- Upon hearing of seizure surgery, she requested a referral for evaluation.

Case Study 3

- When are seizures “medically refractory”?
- When should an inpatient video EEG evaluation be considered?
- What might you learn from such an evaluation?

Case Study 3

Social History:

- She currently lives with her mother.
- She works as a sales clerk.
- She completed twelve years of school and finished one semester of college.
- She has not driven a car after being reported to the DMV by her doctor 23 years ago.

Case Study 3

- She tells you that she still has her driver's license.

  1) What are your legal and ethical obligations as a psychologist?

  2) What are some of the employment issues experienced by people with epilepsy?

Case Study 3

- Family History: She has a cousin with a history of ”grand mal” seizures who died at age 12.

- Habits: She does not use of alcohol, tobacco, or illicit drugs.

- Medications: Carbamazepine 600/400 mg/day BID, Lamotrigine 50/75 mg/day BID, Conjugated estrogens 1.25 mg PO qd, thyroxine100 mcg PO qd, and sumatriptan PRN.

- Neurologic Examination: Normal

Case Study 3

- Impression
  - Possible Mesial Temporal Lobe Epilepsy
    - Auras of forced recall and rising autonomic experience
    - Complex Partial Seizure
  - Seizures refractory to multiple antiepileptic medications

- Recommendation
  - Epilepsy Surgery Evaluation

Case Study 3

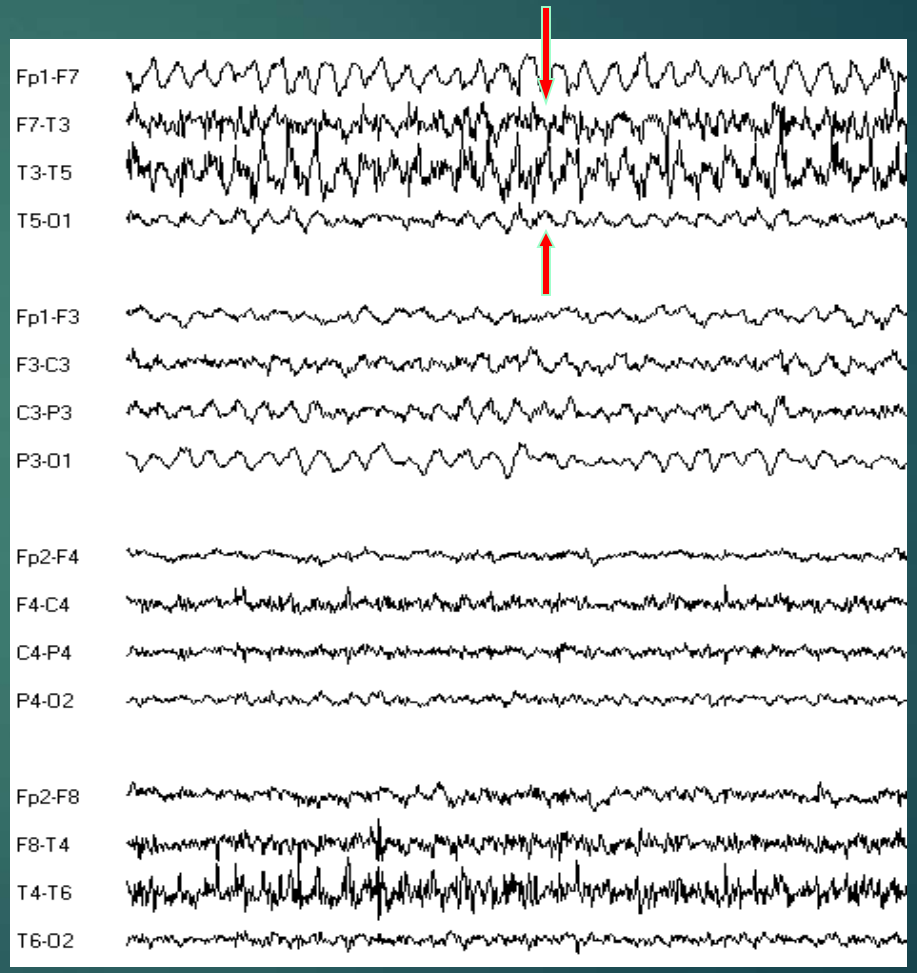
- The patient underwent video-EEG monitoring.

Case Study 3

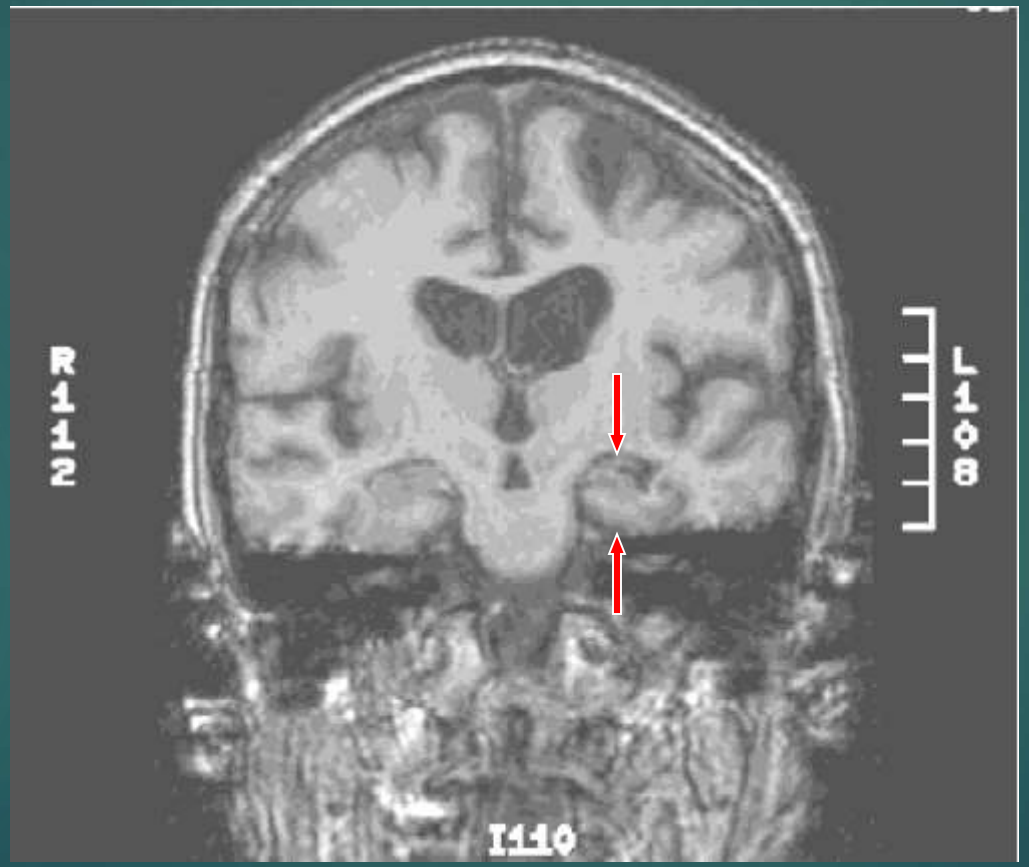
- During 5 days of video EEG, she had 3 typical CPS.
- Her seizures began with her typical aura followed by lip smacking and left hand automatisms. Right hand had tonic posture
- She had a brief post-ictal aphasia

Case Study 3

EEG onsets consisted of a rapid build up of rhythmic theta frequency activity over the left temporal region (Arrows)



Case Study 3



- MRI reveals an atrophic Left Hippocampus

Case Study 3

Pre-surgical Evaluation:

- Neuropsychological Testing
  - Performance and Verbal IQ normal
- Wada (Intracarotid amobarbital) test
  - Language on Left side only
  - No memory difference with left and right injections

Case Study 3

Pre-surgical Evaluation: Conclusions

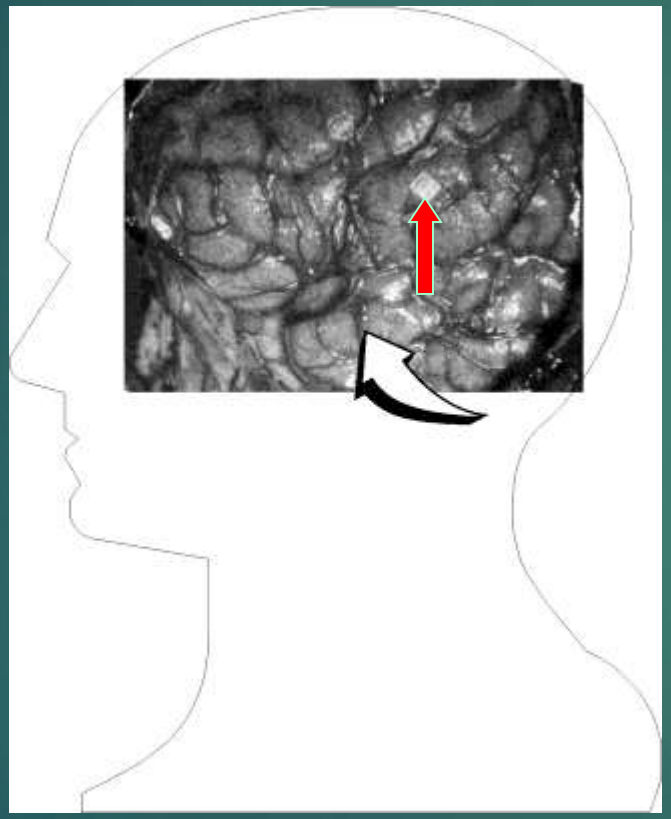
- She has complex partial seizures refractory to anticonvulsant treatment
- Clinical and EEG features are compatible with seizure origin from the left, language-dominant temporal lobe
- MRI suggests mesial temporal sclerosis is the underlying pathology
- She has an excellent chance for a seizure-free outcome with a left anterior temporal lobe resection

Case Study 3

Surgery

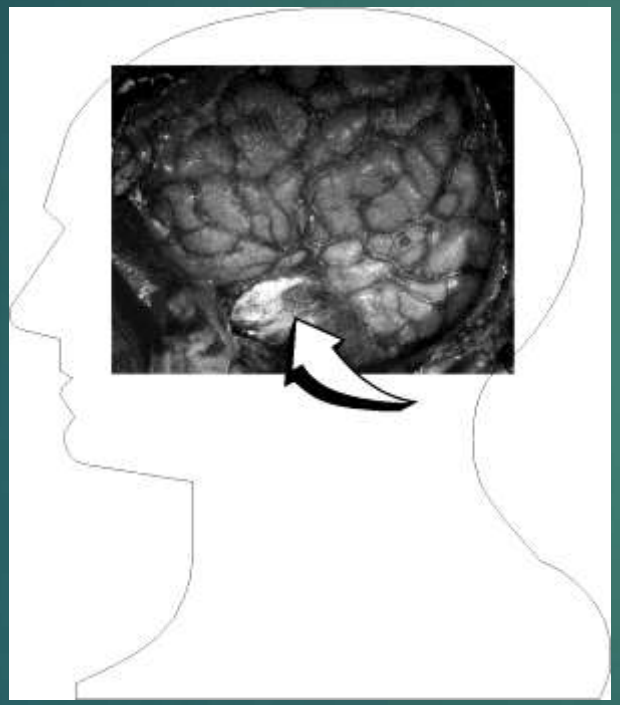
- Surgery under local anesthesia
- Language map determined by electrical stimulation
- Language areas (green arrow) and epileptogenic tissue (white arrow) labeled on next slide

Case Study 3



- MRI showing language areas

Case Study 3



Surgery

- Anterior temporal lobe resected (arrow)
- Amygdala and hippocampus also resected

Case Study 3

Follow-up

- Immediately following surgery she had mild dysnomia
- At three months post-op, cognitive testing confirmed no change from pre-op
- She has had no seizures for two years. She declines a trial off of anticonvulsants for fear of recurrent seizures. She drives to her appointment in a new car.
- She writes, “I’m now having a life I never knew was possible”

Why need for NP Testing

- NP data has value in predicting surgical outcome in adults with no currently identifiable lesion and TL seizure onset
- NP:
  - Predicts cognitive & psych. outcome: NP independently predicts post surgical cognitive outcome
  - Assess post-surgical cog and behav. functioning
  - Assist in lateralizing/or localizing presence of brain dysfunction
  - Provide baseline assessment of cognitive function
  - Assess effects of AEDs on cog/psych function
  - Treatment planning for PNES

Neuropsychological Correlates 2

- No identified NP profile exists for epilepsy. NP in epilepsy is multifactorial in origin.

- IQ: often proxy for outcome, disease severity & extent of pathology;
  - can have low IQ or normal IQ with specific deficits;
  - risk factor for low IQ is age of onset, with earlier onset correlating with lower IQ (but verbal/nonverbal ability is not lateralizing sign);
  - decline risk factors are sz severity and Tx with multiple meds;
  - MCDs & syndromic epilepsies (i.e. Lennox-Gastaut) often associated with low IQ

Neuropsychological Correlates 3

- Attention: 30-40% of children have inattentive ADHD; combined type associated with severity of epilepsy (earlier onset, more intractability); absence szs tend to be highly associated with attention problems; methylphenidate does not increase szs

- Reduced processing speed: either due to epilepsy or meds (common because they reduce excitatory potential)

Neuropsychological Correlates 4

- Language: commonly reported in children; not necessarily just in epilepsy of dominant hemisphere; development of language networks disrupted; often in early onset epilepsy; dominant hemisphere epilepsy will produce language deficits (word finding & semantic klg deficits are as robust as verbal memory deficits); these can also be found in right hem. epilepsy

- Visuospatial: highly variable, associated with generalized type & focal type of nondom. Hemisphere; large, early onset lesions that provoke reorganization of language may crowd out VS abilities (weak VS in early left hem injury & are R hem dominant for lang)

Neuropsychological Correlates 5

- Memory: material specific deficits dependent on hemisphere effected (verbal-left; nonverbal-right); directly related to amount of HS; list learning most affected (story recall less sensitive)
- Executive Functions: early age of onset and longer duration of szs correlate with more deficit; also involvement of subcortical structures; word & nonverbal/figural fluency-list generation correlate.
- Sensorimotor: frontal or parietal involvement: hemiparesis to incoordination
- Emotional/Personality: high frequency of affective sxs
- Effort: 25% perform suboptimally

Neuropsychological Correlates 6

- Poor judgment of their own cognitive abilities; -.3 correlation; 1/3 cannot self report

- History taking: etiology, onset age, duration, seizure type and frequency:

- Onset age:
  - longer seizure hx, IQ effect;
  - lifetime number of tonic-clonic has highest effect;
  - IQ lower in known etiology cases; 5-10 IQ points;
  - affects education

Neuropsychological Correlates 7

- Frequency of seizures: greater the number, more the NP impairment
- Frequent tonic-clonic seizures have most cognitive effect

Dodrill Battery

- Dodrill Battery: Category, TPT, Tapping, TMT, Tonal Memory, Stroop, Name Writing, WMS, IQ test (best predictors: Tap, WMS-Visual, TPT-Total, TMT-B; strong motoric)

- Dodrill: cognitive findings beside memory deficit are distraction to question of surgery; verify the memory disorder!!

Effort: WMT & interictal spiking

- D. Drane: We found that over 70% of the documented epilepsy patients on the epilepsy monitoring unit experienced interictal spikes during some portion of their NP testing.

- 80% of the patients experiencing left basal temporal spikes (not clinical seizures) during or before the oral WMT produced a genuine impairment profile.

- Basal TL discharges are disrupting some aspect of memory consolidation.

Effort 2

- The profile the patients are producing during these episodes looks left temporal (e.g., deficits on some aspects of auditory/verbal memory - e.g., list learning, word pair deficits)- but usually completely normal story recall - which may be less dependent on medial TL structures; decreased visual confrontation naming and semantic fluency).

- Most of these epilepsy patients are on disability or applying for it, etc. However, failure on SVT and incentive still do not equate to malingering in these individuals. It reflects the impact of epileptiform discharges and the financial incentive is simply coincidental.

Age of Onset and Neuropsychological Outcome

	Early (7.8 yr)	*Late (23.3 yr)*	*Healthy Controls*
N	37	16	62
FSIQ	90*	100	107
Naming	47	52	55
Verbal Mem	44	51	52
NV Mem	46	55	62
WCST PE	13	8	8

Hermann et al, *Epilepsia* 2002;43:1062-71

Seizure Burden

- Individuals with poorly controlled and severe seizures often have more detectable cognitive consequences than individuals with well-controlled and/or minor seizures

- Even with treatment: higher unemployment, less occupational success, lower education, less likely to marry and have children

Cumulative Seizure Effects?

- Cognitive and behavioral impairments are present at first seizure and prior to treatment

- Newly diagnosed Left TLE patients have verbal memory impairment

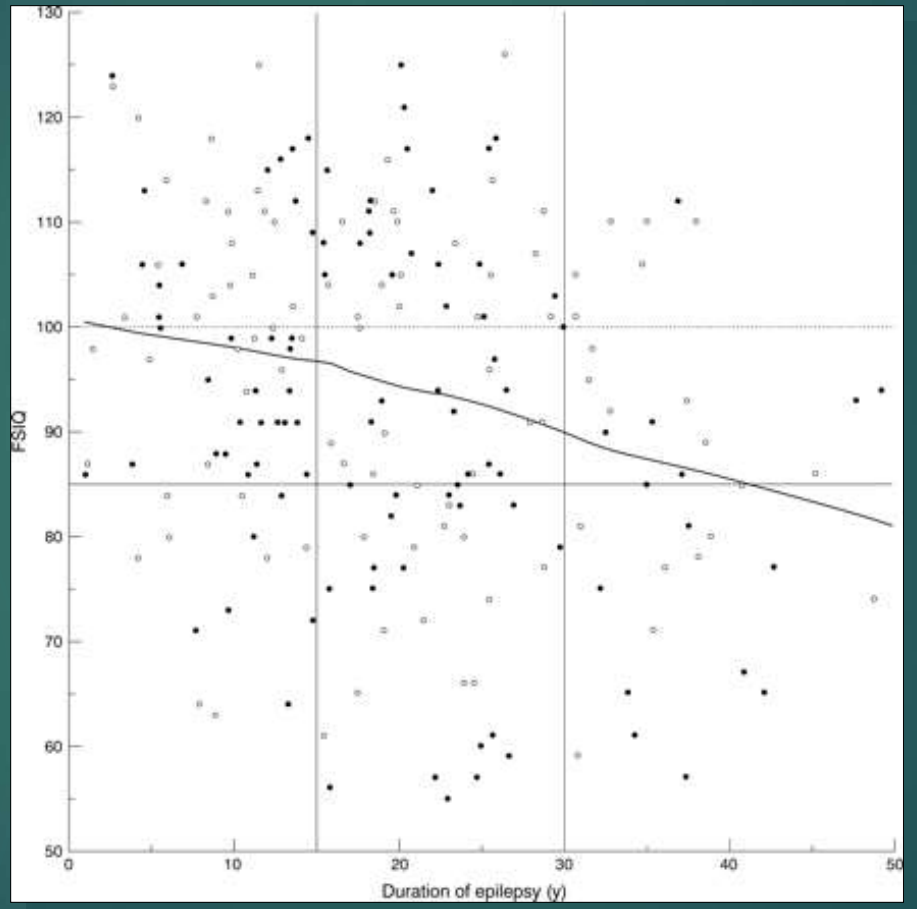
Äikiä , *Epilepsy Research* 1995;22:157-164

Neuropsychological Effects of Seizures

- Decreased scores with higher number of seizures
- IQ lower with increased seizure frequency
- Losses seen beyond “memory”

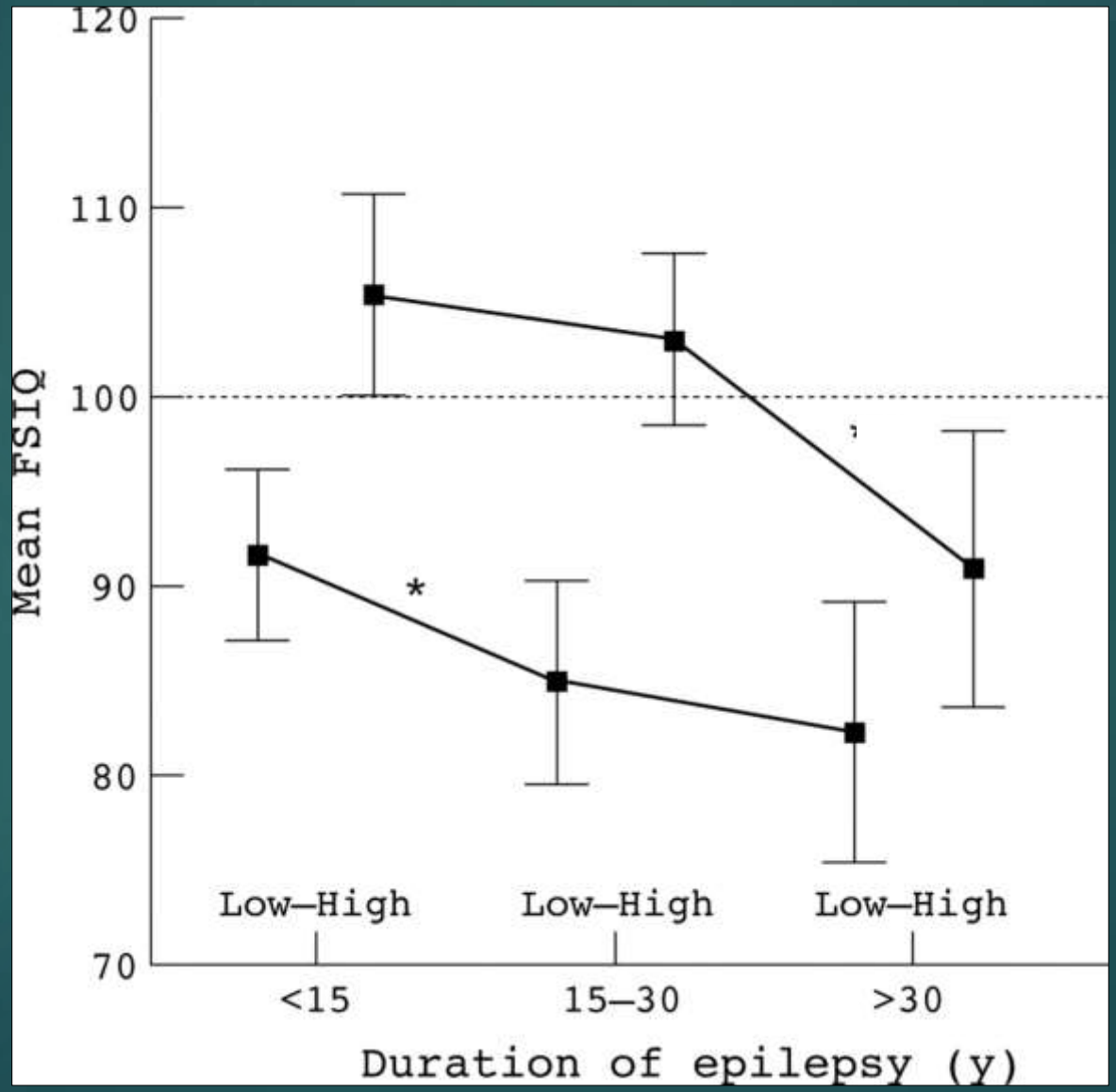
Dodrill, *Epilepsy & Behavior* (2004)

Cross-sectional Neuropsychological Outcome of TLE



Jokeit et al, *JNNP* 1999;67:44-50

Educational Attainment and Seizure Duration



Jokeit et al, *JNNP* 1999;67:44-50

Language Localization Reorganization

Early onset L Temp Sz	→	Displacement of Language – alt. hemisphere
IQ 80+	→	Language in Wernicke's Area
IQ < 80	→	Language outside Wernicke's Area

Distribution of Lang Sites ↑ ↓ IQ, Lang, Verbal memory, education ↓↓

44 patients with L Hemisphere Language and L Temporal CPS

Age 30.6 (7.2); Education 13.4 (2.1); FSIQ 88.6 (12.8)

Onset of sz 13.4 (2.1) RH 84%; M 48%.

Other than MTS 30%; Hx feb sz 36%; 20 Gen 57%

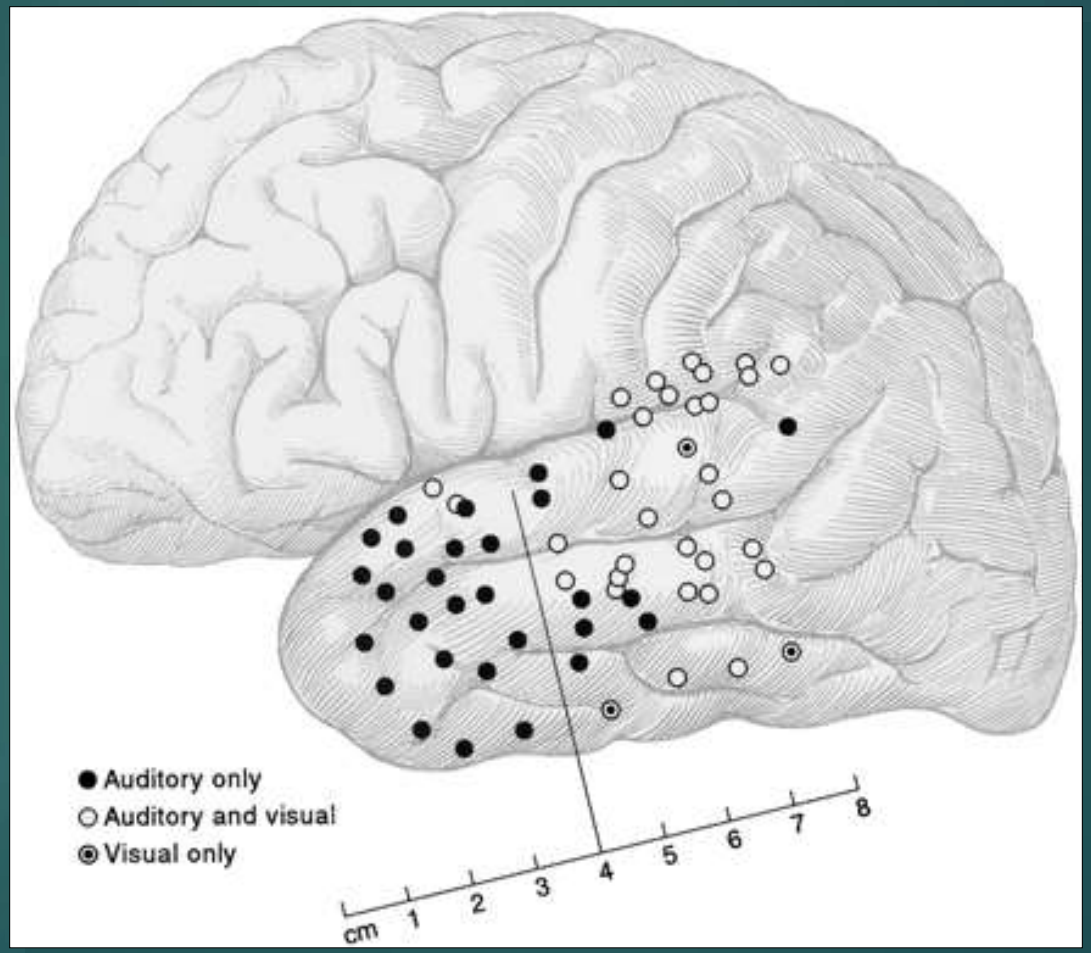
Devinsky et al. *Epilepsia* 2000; 41:400-404

Confrontation Naming

- Left TL volume related to Boston Naming Test
- Left TL white matter and L hippocampal volume related to BNT
- Left TL white matter (not hippocampus) related to BNT recognition

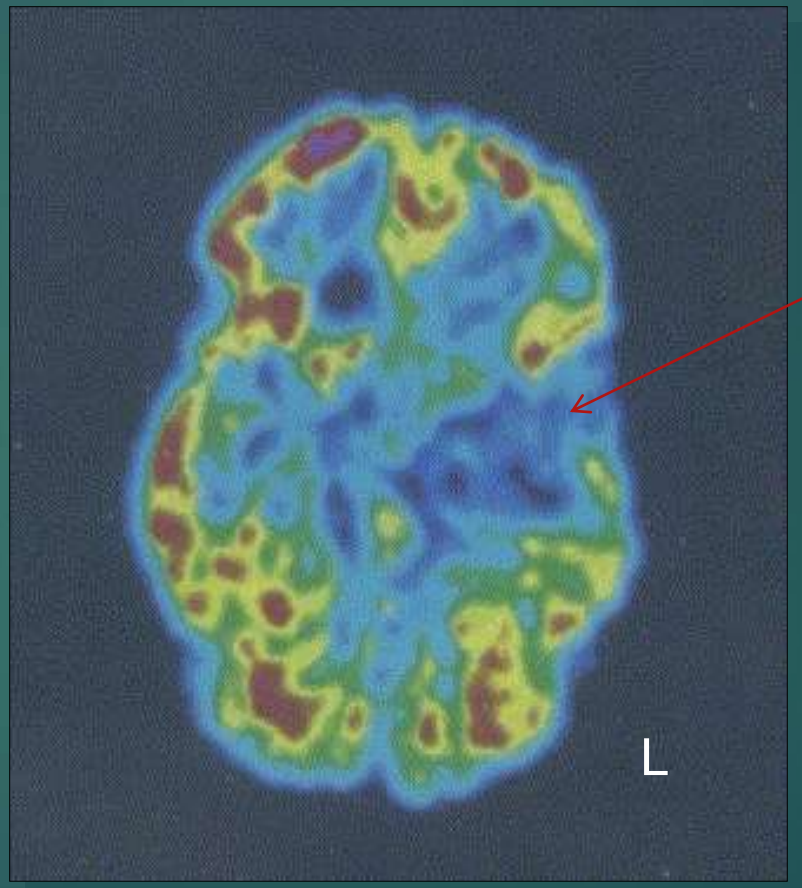
Seidenberg et al., *JINS* (2005)

Visual Naming vs. Auditory Naming: Why Naming is nonspecific symptom



Hamberger et al. *Neurology* 2001;56:56-61

PET Scan trumps MRI
Left TLE with Med Temp Szs
Had normal MRI

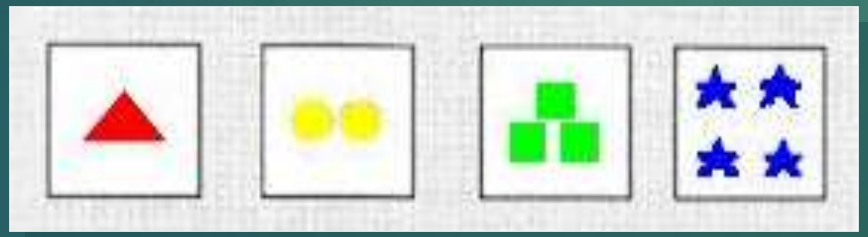


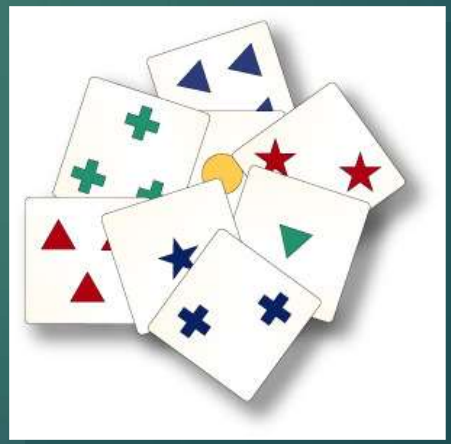
Left hypometabolic

Jokeit & Schacher, *Epi & Beh* 2004;5(Suppl 1):14-20

Cognitive Impairment in TLE

- Decreased Full Scale IQ
- Diminished academic achievement
- Poor performance on WCST





Hermann & Seidenberg, *JCEN* 1995;17:809-819

MRI Volumetrics in Chronic TLE: Atrophy

- Generalized and diffuse cortical volume reduction 60-80% of TLE pts
  - Ipsi hippocampus greatest
  - Ipsi & contra temporal, frontal, and parietal
  - Cerebellar volume loss (devel. Pathology, meds (Dilantin), GTC szs)
  - FMRI has 91% correct lateralized classification
- Progressive Cortical Thinning both proximal and distant from sz focus
- White matter volume loss> gray matter
  - Present with or without MTS

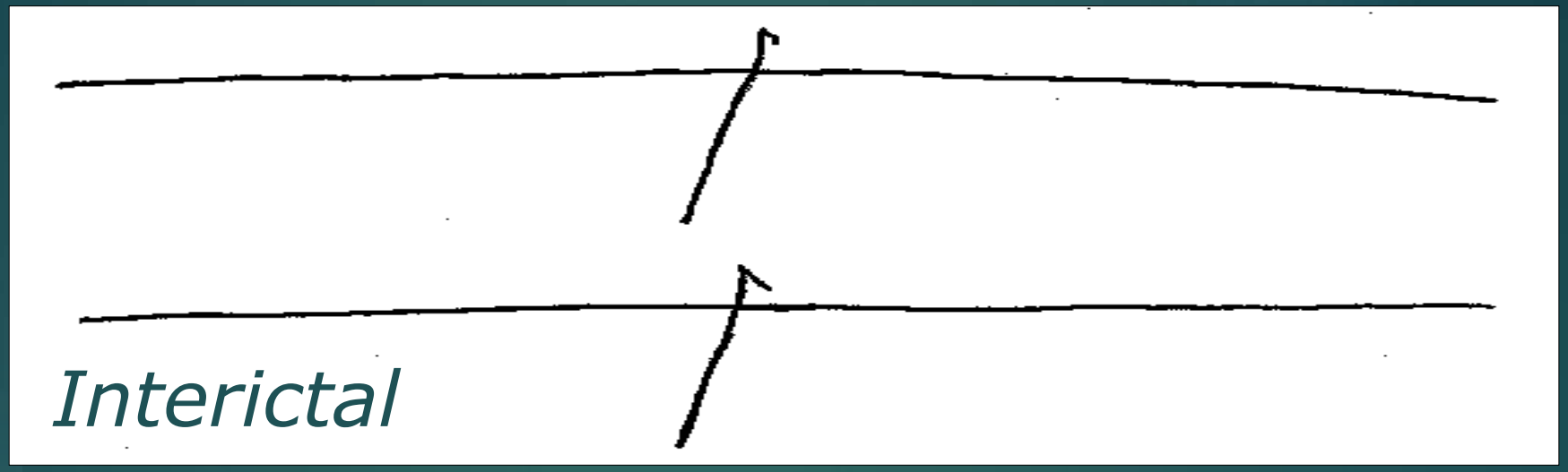
  (L=15, R=19, control=65)

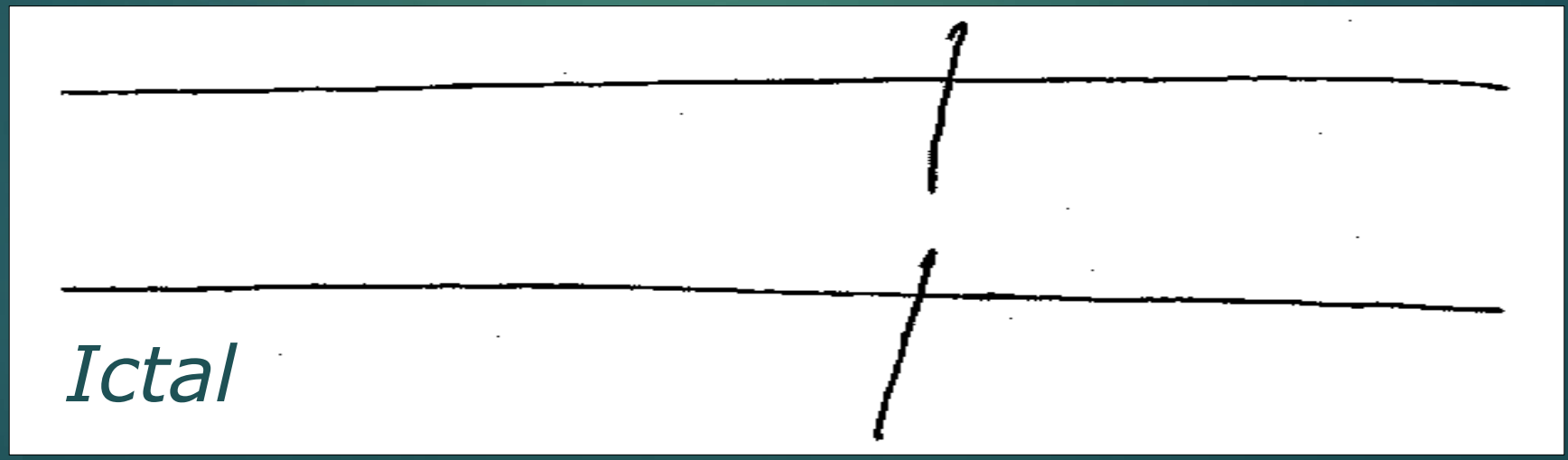
Seidenberg et al. *Epilepsia.* 2005;46(3):420-430.
McDonald, 2008

Memory and seizures

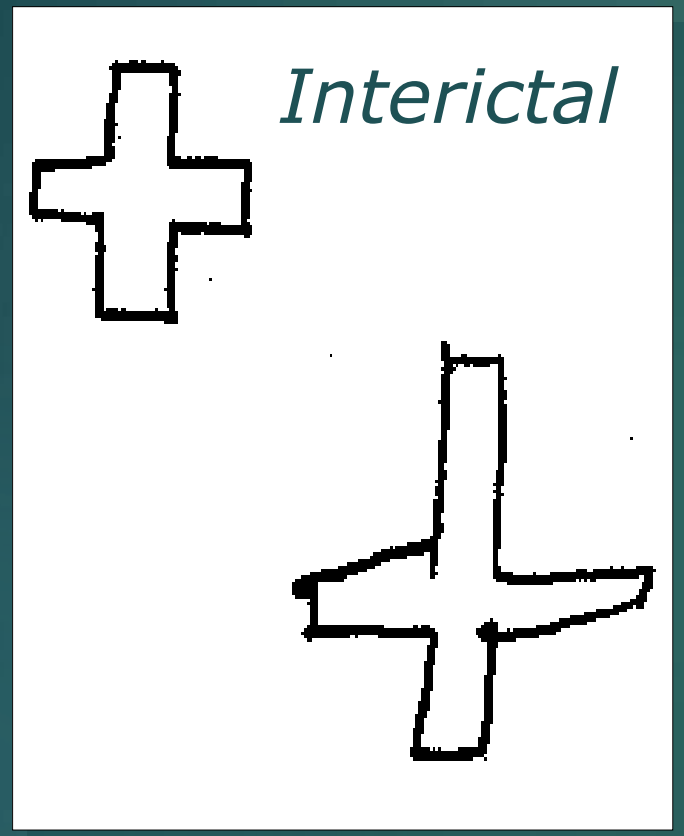
- Bringing these patients back and testing them when they are not spiking, they sometimes perform completely normally.
- Studies by Bert Aldenkamp out of the Netherlands demonstrate that even children with well-controlled epilepsy frequently experience spikes even when their seizures are well-controlled on anti epileptic medications.
- Kids with epilepsy could really be at risk of compromised learning due to epileptiform discharges

Ictal Neglect

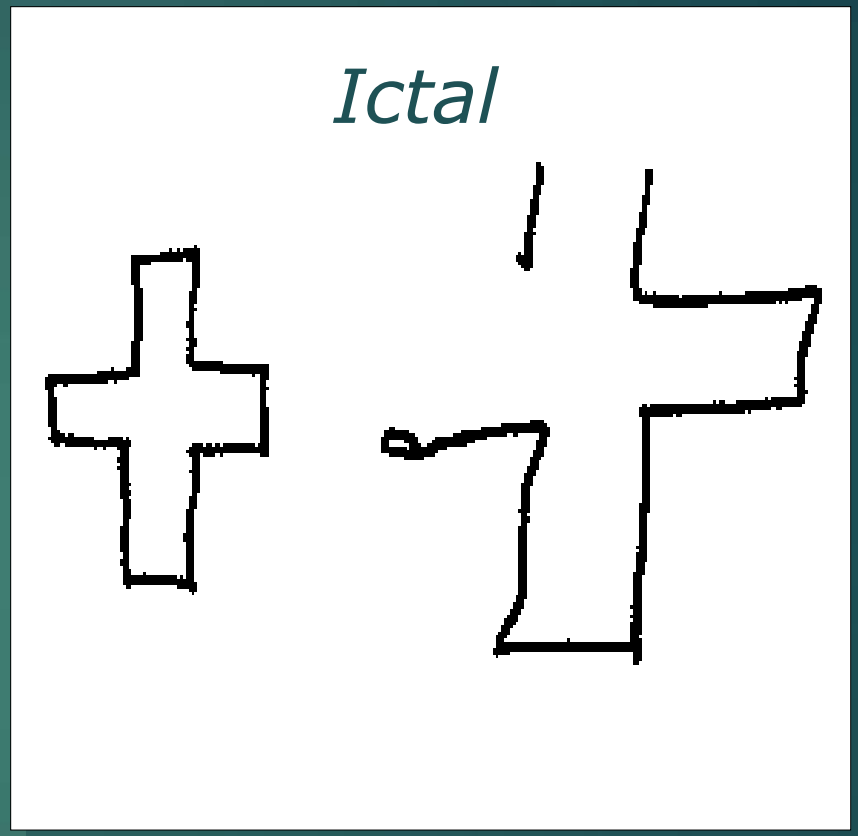




Meador & Moser, *JINS* 2000;6:731-733



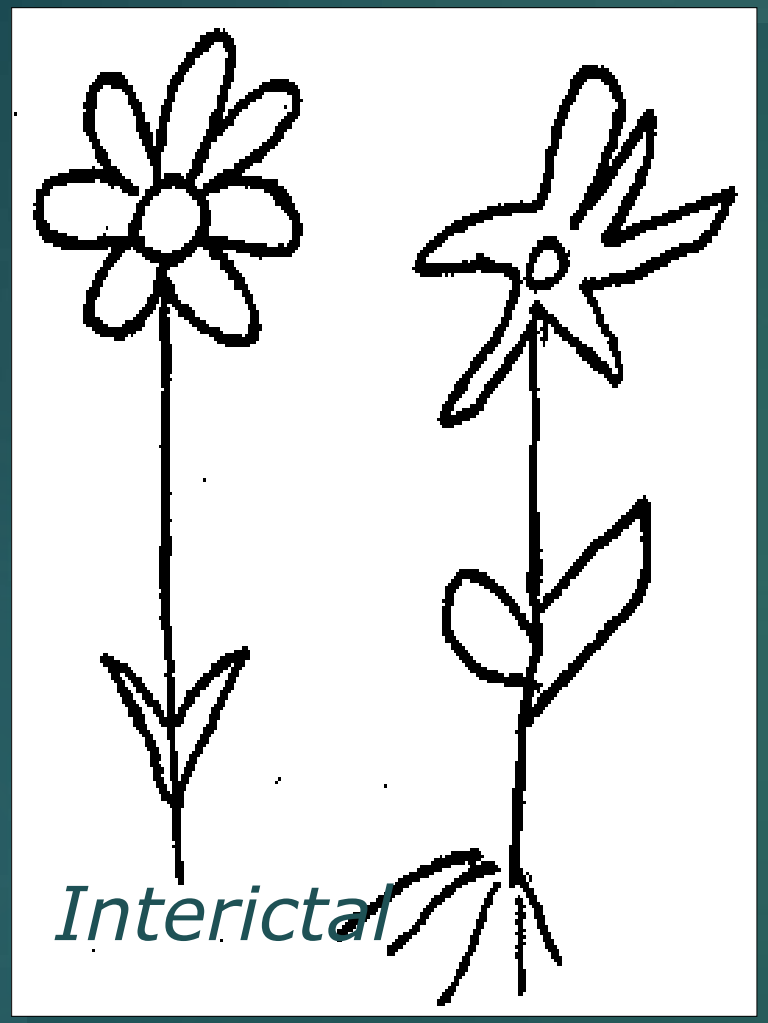
Target Response



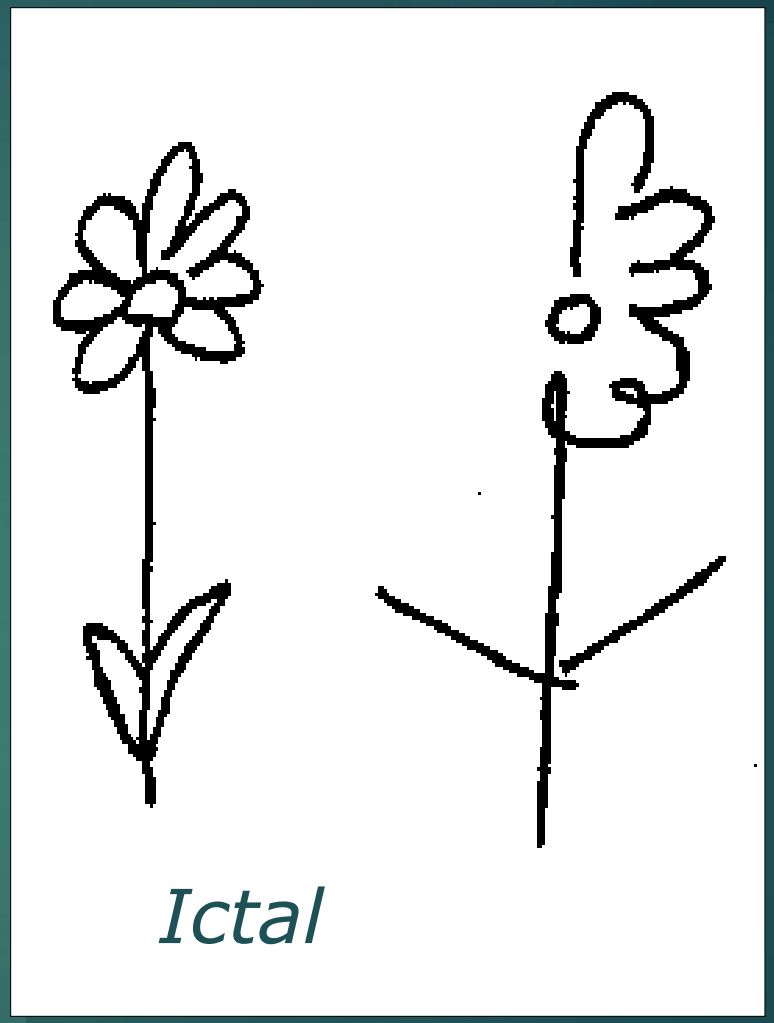
Target Response

February 6, 2006

Meador & Moser, *JINS* 2000;6:731-733



Target Response



Target Response

Meador & Moser, *JINS* 2000;6:731-733

Patients with epilepsy can still have seizures due to:

- Failure to take medication correctly
- Variation in medication effectiveness
- Sleep deprivation
- Stress/ Illness
- Hypoglycemia/dehydration
- Alcohol/drug use or withdrawal
- Hormonal fluctuations
- Flashing lights or other triggers

Treatment

- Controlling seizures (seizure freedom) is strongly correlated with decreasing cognitive deficits.

- Medication refractory epilepsy: majority have focal szs of symptomatic origin; esp. MTS; at risk for death 2ndary to sz, progressive NP deficits, poor academic & work outcomes

- Treatments:
  - AED medications: 60-70% sz control; different side effect profiles; if fail 3 meds, only 3% chance of 4th being effective
  - Surgery: for refractory szs; seizure freedom with surgical resection in 80%; highly effective Tx for refractory epilepsy; 5-10% complication rate (death, stroke, infection)

Established Medications (neg. cog. Effects = ++)

- Phenytoin (Dilantin): approved in children; +++
  - GTC, CPS
- Carbamazepine (Tegretol, Carbatrol): approved in children
  - GTC, CPS
- Ethosuximide (Zarontin): approved in children
  - Absence epilepsy; not for partial szs
- Valproate (Depakote, Depakene): approved in children (>10)
  - GTC, CPS, Absence, myoclonic, infantile spasms
- Phenobarbital: approved in children; +++
  - GTC, CPS (exacerbates absences)
- Benzodiazepines (Klonopin, Tranxene, Valium, Lorazepam); +++; mood ++
  - GTC, CPS, myoclonic, absence, infantile spasms

Newer Anti-seizure Medications

- Felbatol (Felbamate) (liver failure, bone marrow suppression)
- Gabapentin (Neurontin) (worsens myoclonic szs)
- Lamotrigine (Lamictal)
- Levetiracetam (Keppra)
- Topiramate (Topamax): good for wgt loss, bad for cognition; +++
- Oxcarbazepine (Trileptal)
- Tigabine (Gabitril)
- Zonisamide (Zonegran)

Marijuana: cannabidiol (CBD) as AED

- Existing seizure medications fail about one-third of all sufferers, either because the drugs don't stop the seizures or because the side effects are too severe.
- National Academy of Sciences report—the most in-depth analysis of marijuana research to date—concluded that there was not enough evidence to say that cannabis oil could actually treat epilepsy,
- Just three clinical studies where doctors treated patients with CBD and measured whether and by how much those patients' seizures were reduced. The largest of those studies included a total of 162 patients, treated with 99 percent CBD oil extract for 12 weeks; it found that CBD worked about as well as existing anti-epilepsy medications do in treatment-resistant sufferers.
- CBD reduced seizures by a monthly average of 36.5 percent; only five patients saw their motor seizures completely disappear during the study period, and only two patients became completely seizure-free.
- But no placebo control and were taking other anti-epilepsy drugs.

Ketogenic Diet

- Diet to initiate ketosis (energy from ketone bodies, not glucose)
- Indicated for medically refractory epilepsy
- Mechanism: unknown, like AED
- Three main components
  - High fat content as % of calories
  - Low calories
  - Fluid restriction

Vagus Nerve Stimulator

- Intermittent programmed electrical stimulation of left vagus nerve
- Option of magnet activated stimulation
- Adverse effects local, related to stimulus (hoarseness, throat discomfort, dyspnea)
- Mechanism unknown
- Clinical trials show 26% effective and <10% seizure free
- May improve mood and allow AED reduction
- FDA approved for partial complex seizures

Surgical Treatments

- Anterior Temporal Lobectomy: left 3-5 cm; right 4-8 cm
  - Amygadalohippocampectomy (some or all of hippocampus)
- Hemispherectomy
- Corpus callosotomy
- Multiple subpial transection (horizontal axonal fibers transected)
- Vagus Nerve Stimulator implantation
- Deep Brain Simulator implantation
- Stereotaxic gamma-knife radiation treatment

Anterior Temporal Lobectomy

- Temporal lobe epilepsy most common: Focal szs
- Cognitive morbidity: memory and language (naming)
  - Verbal memory deficits – L medial TL onset
  - Non-verbal memory impairment and R TLE less consistent
    - Related to age of seizure onset
    - Pathologic status of hippocampus
- Risk of superior quadrantanopia (pie shaped visual loss)
- 80% of medically refractory TLE can become sz free (but need AED)

Risk Factors for Surgery Failure

- Continue Uncontrolled Seizures post surgery:
  - Bilateral EEG abnormalities
  - Secondarily generalized tonic-clonic szs with TLE
  - No structural pathology on MRI
  - Contralateral memory function intact on Wada's test (TLE only)

Postsurgical memory

- 10% of TLE pts undergoing ATL experience a significant memory decline
- Individuals with MTS & lower presurgical memory scores are significantly less likely to have decline than individuals with average or better scores.
- 30% of right ATLs have improved verbal memory, but 59% have impaired visual memory; and possible impaired facial emotional recognition
- 53% of left ATLs have impaired verbal and visual memory & 47% have only impaired verbal
- Improvement in memory for up to 2 to 6 years after surgery

Predicting post-surgical NP Outcome

- Presence of hippocampal/mesial TL sclerosis:
  - Risk for material specific memory decline decreases
  - Decreased neuronal density (sclerosis) of CA1/3 associated with worse verbal memory
  - Significant dysnomia decreases in MTS
- Presurgical NP immediate & delayed memory scores:
  - Better memory scores prior to surgery, greater risk for decline after, esp. for left TLE
  - 10 pt decline with verbal memory index scores of 90+; with greater index score, 5x greater chance of decline
  - Visual memory decline likely in those with better prior
  - Higher IQ have better outcomes

Predicting post-surgical NP Outcome 2

- Duration of epilepsy:
  - Longer duration are at less risk for cog decline
- Age at onset of seizures:
  - Early age of onset are at less risk for BNT decline after left ATL
- Type of surgery:
  - Amygdalohippocampectomy has less memory decline?
  - BNT & fluency often decline in left ATL

NP prediction

- Predicting sz freedom from epilepsy surgery
  - Seizure-free rates: 1 year sz free rates of ATL is 70%; MTS, 90%
  - Seizure remission: unilateral EEG abnormalities, single pathology, MTS, duration of szs, age of onset
  - Brain pathology in predicting sz freedom: best predictor = MRI lesion or histopathology are 2.5x more likely to be sz free; as were TLE pts; MTS is esp. good for outcome (80% at 10 y)

Neurological & demographic variables predicting Sz remission & failure

Remission

- 1 – unilateral EEG with focus in 1 hemisphere
- 2 – Exclusively ipsilateral temporal inter-ictal EEG discharges
- 3 – Presence of structural lesion (cortical dysgenesis, cyst, MTS) ipsilateral to sz focus
- 4 – Younger pt (<30 y) (66% at 10 y); middle aged (30-59) similar
- 5 - Shorter duration of pre-op epilepsy

Failure

- 1 – bilateral EEG abnormalities
- 2 – Secondarily generalized tonic-clonic szs in TLE
- 3 – No structural pathology on MRI
- 4 – Contralateral memory function intact on Wada

NP variables

- NP data usually not helpful in prediction of sz outcome; but impaired verbal memory associated with sz free outcome for left ATL

Side of Seizure

- Ictal EEG is gold standard for side of sz onset; MRI helps, then PET and MEG
- NP data provide significant prediction of lateralizing side of onset: logical memory scores in bilateral hippocampal atrophy; verbal/visual memory for hemisphere, as well as BNT, WCST
- Wada test

Predicting memory impairment following ATL

- NP presurgical memory test scores: risk for post surgical memory deficit is 5 x greater for memory scores above 90 (100 mean), compared to those below 90
- Functional adequacy of ipsilateral hippocampus (one to be resected) better predicts material specific memory declines after ATL; pts with left TLE with intact memory function are likely to experience more verbal memory decline after ATL; high pre-surgical memory functioning is at greater risk for decline than low average pre memory
- 10% of ATL pts experience significant decline in memory; pts with MTS and lower presurgical memory are less likely to have decline; less decline in visual memory in right ATL, with some improving

Predicting memory impairment following ATL 2

- Study: Following left ATL, 53% showed impaired verbal and visual memory; other 47% had impaired verbal, ok visual; after right ATL, 59% had poor visual, ok verbal; other 42% had poor verbal and visual memory; right ATL associated with impaired facial emotional recognition
- Left ATL exhibit decline in verbal memory for up to 2 years post surgery; right ATL, increase in verbal at 6 months, but lost this at 2 years; at 6 years, side of surgery, pre-op verbal scores (higher worse), and age at surgery; older worse) were best predictors

Variables predicting post-surgical NP outcomes

- 1. Presence of MTS – risk of decline decreases with HS; HS associated with worse verbal memory; also risk of dysnomia decreases (80% of those without MTS had BNT decline)
- 2. Pre-surgical NP immediate & delayed memory scores – better pre surgery memory, greater risk for memory decline; esp. true for left TLE pts with average or better memory (WMS score of 90+ is a risk; 10 pt decline); right ATL less consistent, but same effect; better cognitive reserve/higher IQ have better outcomes
- 3. Duration of epilepsy – longer duration at less risk for post surgical cognitive decline (but have poorer NP to begin with)

Variables predicting post-surgical NP outcomes 2

- 4. Age at onset of seizures – early age of onset have decreased risk for BNT decline

- 5. Type of surgery – post surgery verbal memory decline less with more focused resection; change in language function not significantly affected by extent of resection, but decline in left language dominant who have left ATL; extent of superior temporal gyrus resection correlations with decline in BNT in left ATL

- 6. Many pts experience transitory period of more diffuse cognitive dysfunction following ATL, which resolves

Predicting NP outcome: good prognostic features (less memory/language decline)

- Presence of lesion (MTS) on same side as sz focus
- Unilateral EEG abnormalities
- Presurgical NP data: memory impaired for ipsilateral TL (left TLE has poor verbal memory, good visual)
- Presurgical memory scores below 90
- Longer duration of epilepsy

Predicting NP outcome: good prognostic features (less memory/language decline) 2

- Higher presurgical IQ
- Asymmetric functional neuroimaging findings (PET hypometabolism ipsilateral to sz focus
- Asymmetric Wada results: ipsilateral injection memory is good, contralateral impaired

Patient Selection Criteria for Surgery

- Epilepsy syndrome not responsive to medical management
  - Unacceptable seizure control despite maximum tolerated doses of 2-3 appropriate drugs as monotherapy

- Epilepsy syndrome amenable to surgical treatment

Diagnostic Tools in epilepsy

- Neurological exam: lateralize/localize
- EEG – interictal:
- Ictal Video-EEG: in hospital, sz monitoring
- MRI: lesion identification
- Interictal PET: decreased blood flow at sz focus
- Ictal SPECT: blood flow increase with sz
- Wada Test: amobarbitol – lateralize language and memory function
- MEG: inter ictal activity from focus
- MSI: Magnetic Source Imaging – functional mapping of language, motor/sensory, memory; Wada alternative
- fMRI
- NP testing: cognitive functions

Evaluation for Surgery

- History and Exam: consistency, localization of seizure onset and progression
- MRI: 1.5 mm coronal cuts with sequences sensitive to gray-white differentiation and to gliosis
- Other neuroimaging options: PET, ictal SPECT
- EEG: ictal and interictal, special electrodes
- Neuropsychological battery
- Psychosocial evaluation
- Intracarotid amobarbital test (Wada)

Surgical Treatment

- Potentially curative
  - Resection of epileptogenic region (“focus”) avoiding significant new neurologic deficit
- Palliative
  - Partial resection of epileptogenic region
  - Disconnection procedure to prevent seizure spread — corpus callosotomy
  - Multiple subpial transection – see next slide

Multiple subpial transection (MST)

- Relatively new treatment for epilepsy that may be an option when seizures begin in an area of the brain that cannot be removed; for example, areas associated with vital brain functions such as movement, sensation, language and memory.

- MST is based on the fact that normal electrical impulses in the brain generally move in an up-and-down pattern. Seizure impulses, on the other hand, mostly spread in a horizontal (side-to-side) fashion.

- MST stops the seizure impulses by cutting horizontal nerve fibers in the outer layers of the brain (gray matter), sparing the vital functions concentrated in the deeper layers of brain tissue (white matter).

Reason for Surgery

- Continued seizures triples your chance of dying early
- N = 245, 40 year Finnish Study, 2010
- 6 drowned, 9 by seizure, 18 epilepsy related

Epilepsy Surgery Outcomes: Good

	Temporal	Extra Temporal	Lesional	Hemispheric	Callosotomy
Seizure Free	68%	45%	66%	45%	8%
Improved	23%	35%	22%	35%	61%
Not improved	9%	20%	12%	20%	31%
Total	100%	100%	100%	100%	100%

Reference: Engel, J. *NEJM*, Vol 334 1996, 647-653

Status Epilepticus

- **Definition**
  - More than 30 minutes of continuous seizure activity

    or
  - Two or more sequential seizures spanning this period without full recovery between seizures

Status Epilepticus

- A medical emergency
  - Adverse consequences can include hypoxia, hypotension, acidosis and hyperthermia
  - Know the recommended sequential protocol for treatment with benzodiazepines, phenytoin, and barbiturates.
  - Goal: stop seizures as soon as possible

Nonepileptic Seizures

- Nonepileptic seizures (pseudoseizures, psychogenic seizures)
- Imitation of tonic-clonic; no electrophysiological event
- 5-20% in outpt, 40% in Epilepsy Centers; women 3:1; overlap with real epilepsy
- Refractory to medication
- Issues of secondary gain, repression, conversion disorder
- Use of MMPI, Word Memory Test failures (18-48% fail, for disability)

Differential Diagnosis

The following should be considered in the diff. dg. of epilepsy:

- Syncope attacks (when pt. is standing; results from global reduction of cerebral blood flow; prodromal pallor, nausea, sweating; jerks!)
- Cardiac arrhythmias (e.g. Adams-Stokes attacks). Prolonged arrest of cardiac rate will progressively lead to loss of consciousness – jerks!
- Migraine (the slow evolution of focal hemisensory or hemimotor ssymptoms in complicated migraine contrasts with more rapid "spread" of such manifestation in SPS. Basilar migraine may lead to loss of consciousness!
- Hypoglycemia – seizures or intermittent behavioral disturbances may occur.
- Narcolepsy – inappropriate sudden sleep episodes
- Panic attacks
- PSEUDOSEIZURES – psychosomatic and personality disorders

Differential Diagnosis of Non-epileptic Events

- Delirium
- Cerebral ischemia or TIAs
- Movement disorder
- Sleep disorder
- Metabolic disturbance
- Psychiatric disturbance
- Breath-holding spells

*** Need good history

Psychogenic Nonepileptic Seizures

- 10-45% of patients referred for intractable spells
- Females > males
- Szs frequent, intractable; psych/pain hx
- Convulsions non-clonic
- Psychiatric mechanism — disassociation, conversion
- Common association with physical, emotional, and sexual abuse
- Spells with non-epileptic etiology
- Non-ictal pattern on EEG
- Arching back, pelvic tilting

Psychogenic Nonepileptic Seizures 2

- Represents psychiatric disease
- Once recognized, approximately 50% respond well to specific psychiatric treatment
- Cognitive-behavioral therapy is more effective than standard medical care alone in reducing seizure frequency in PNES patients.
- Epileptic and nonepileptic seizures may co-exist
- Video-EEG monitoring often required for diagnosis

PNES is heterogeneous

- Epilepsy and Behavior (Magaudda, 2011) suggesting that "PNES" is actually heterogeneous, comprised of
  - patients whose problems are epilepsy related (classical conditioning?),
  - patients who develop PNES in response to cessation of seizures with pharmacotherapy (author suggested 'continued dependency'),
  - and patients whose PNES episodes seemed to conform to 'conversion' phenomena. Only the latter group had significant histories of psychological or physical trauma.
- The lesson is that "PNES" is not a homogeneous category.

Psychogenic Nonepileptic Seizures (PNES)

- PNES events occur in under 5% of patients with documented epilepsy
- 20 to 30 % of patients who are seen in epilepsy centers actually suffer from PNES as opposed to epilepsy.
- They exhibit a higher incidence of symptoms such as anxiety and depression than patients with epilepsy, along with a reduced quality of life.
- Cognitive behavioral therapy (CBT) can reduce the frequency of “seizures”.

CBT & PNES

- Study: Need to identify precursors, precipitants and perpetuating factors of the seizures. Based on the tendency of patients with PNES to somatize (to manifest mental pain as pain in one's body), hypothesized that identifying and modifying cognitive distortions and environmental triggers for PNES would reduce PNES.

- 50 percent reduction in seizure frequency, and 11 of the 17 who completed the CBT reported no seizures per week by their final CBT session.

- Higher rates of SVT failure in PNES (>40%) vs. epilepsy

Syncope (Fainting)

- Characteristic warning, usually gradual (except with cardiac arrhythmia)
- Typical precipitants (except with cardiac arrhythmia)
- Minimal to no postictal confusion/somnolence
- Convulsive syncope — tonic>clonic manifestations, usually < 30 sec; usually from disinhibited brainstem structures (only rarely from cortical hypersynchronous activity)

Pregnancy and epilepsy

Most pregnancies in mothers with epilepsy produce normal children

- Fetal anomalies (up to 10% of pregnancies) are multifactorial
  - Drug effects
  - Consequences of the mother's underlying diseases
  - Consequence of maternal seizures during pregnancy
- All antiepileptic drugs carry teratogenic risks
- Polytherapy increases risk

Phenobarbital (PB)

- Decreased IQ – improvement after PB discontinuation
- IQ changes - slowed mental growth rather than loss of previously acquired information or cognitive regression
- Decreased academic achievement
- Academic achievement impaired 3-5 years after PB discontinuation
  - Children do not fully “catch up”
- Concern for cumulative effects of other AEDs with milder cognitive side effect profile

Farwell et al. *NEJM* 1990;322:364-369
Sulzbacher et al. *Clin Pediatrics* 1999;38:387-394

Carbamazepine (CBZ)

- Slower RT
- Decreased EEG alpha rhythm (~ .5 Hz)
- EEG effect related to 1 year WISC-R performance
- Some children appear at disproportionate risk of cognitive decline

Mandelbaum et al. *CNS* abstract 2003.
Frost et al. *J Clin Neurophysiol* 1995;12:57-63.
Seidel & Mitchell. *J Child Neurol* 1999;14:716-723.

Older AEDs in Young Adults

- Neuropsychological impairment usually dose dependent
- May be individuals at unusual risk
- Memory and Quality of Life may be affected with serum concentrations in standard therapeutic range

Effects of Antiepileptic Drugs (AEDs) on Cognition

- Older AEDs can cause adverse cognitive side effects.
- Newer AEDs typically have more favorable cognitive side effect profile but may still have some cognitive side effects
- Of the newer AEDs, greater concern is for effect of topiramate (TPM, Topamax); “Dopamax”
- Side effects are typically dose dependent and greater when treated with more than one drug (polytherapy)

Higher Psychiatric Comorbidities in Epilepsy

	Epilepsy (range)	General Pop. (range)
Depression	11%–60%	2%–4%
Anxiety	19%–45%	2.5%–6.5%
Psychosis	2%–8%	0.5%–0.7%

Mood/Behavior in Epilepsy

- Incidence of depression: 4-5x greater
- Depression contributes more to reduced quality of life than ongoing seizure activity

- Depression, esp. with left sided foci vs activation with right focus unsupported

- Self-reported cognitive complaints are more strongly correlated with mood than with actual cognitive dysfunction

Emotional/Social Factors

- Psychological issues are most important in lives of epileptics:
  1. Do epileptics differ in emotional maladjustment?
  2. Normal least > medical > neurological (epil or not) most
  3. Epileptics have lower marriage and offspring rates.
  4. Do CP patients differ from other epileptic pts? No.
  5. Depression? Yes
  6. Aggression? No.

Emotional/Social Factors 2

- Washington Psychosocial Seizure Inventory:
  - Emotional Adjustment
  - Interpersonal Adjustment
  - Vocational Adjustment

Workplace issues

- High rate of unemployment & underemployment
- Discrimination against people with epilepsy
- Safety issues
  - Heights
  - Climbing
  - Balance
  - Dangerous equipment

Americans with Disabilities Act

The ADA, Public Law 101-336, prohibits discrimination on the basis of disability in employment, activities of state and local governments, public and private transportation, public accommodations and telecommunications. The purpose of the law is to provide uniform protection against discrimination throughout the United States.

Driving

- Laws are not specific to epilepsy, but to seizures and AMS
- Limit recurrent altered consciousness
- 3, 6, 12 months seizure free for license
- Compliance with medical regime
- CA is a “mandatory reporting” state

Driving

Regulation varies state by state regarding:

- Reporting requirements
- Required seizure-free period
- Favorable/unfavorable modifiers

- Insurance issues
- Employment issues

First Aid for Tonic-Clonic Seizure

- Turn person on side with face turned toward ground to keep airway clear, protect from nearby hazards
- Transfer to hospital needed for:
  - Multiple seizures or status epilepticus
  - Person is pregnant, injured, diabetic
  - New onset seizures
- DO NOT put any object in mouth or restrain

Books

- A Guide to Understanding and Living with Epilepsy, Devinsky, O, F.A. Davis Company, 1994.
- Anticonvulsant Prescribing Guide, PDR second edition, 1998, Ortho-McNeil.
- Clinical Epilepsy, Duncan, J.S., Shorvon, S.D., Fish, D.R., Churchill Livingstone, 1995.
- Core Curriculum for Neuroscience Nursing, third ed., American Association of Neuroscience Nursing.
- Epilepsy A to Z: A Glossary of Epilepsy Terminology, Kaplan PW, Loiseau P, Fischer RS, Jallon P, Demos Vermahde, 1995.
- Epilepsy in Clinical Practice: A Case Study Aproach, Wilner, A., Demos, 2000.
- Managing Seizure Disorders: A Handbook for Health Care Professionals, Santilli, N., Lippincott-Raven, 1996.