Seizures & Epilepsy: Diagnosis and Treatment Options

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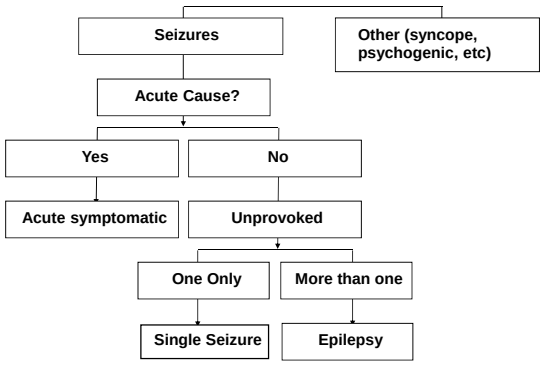
Objectives

- **Understand the basic diagnosis of spells and seizures**
- **Learn basic medication treatment for epilepsy**
- **Review advanced treatment options for refractory epilepsy including epilepsy surgery and devices.**

Evaluation of Spells



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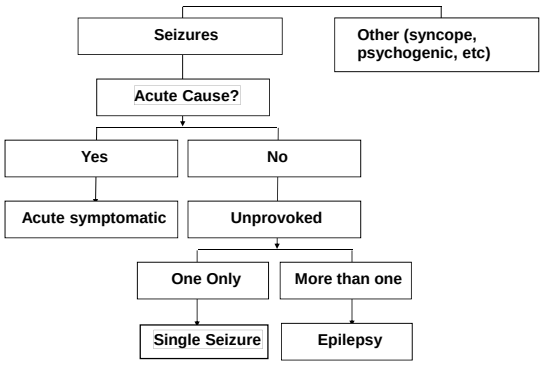
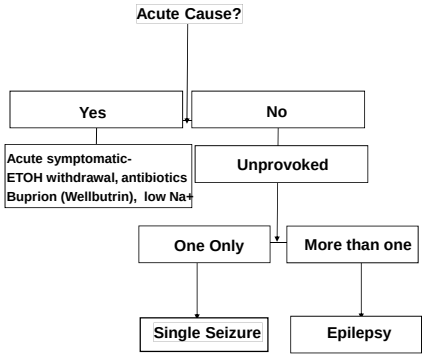


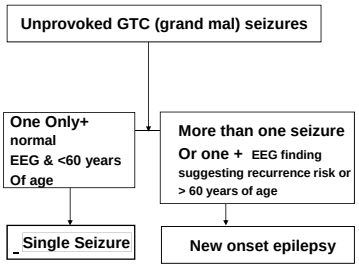
Major Spell Categories

- Seizures, epileptic
- Syncope
- Migraine
- Psychogenic
- Vestibular disorder
- Transient ischemia
- Transient global amnesia

Evaluation of Seizures



One seizure versus Epilepsy



Seizure and Spell Diagnosis

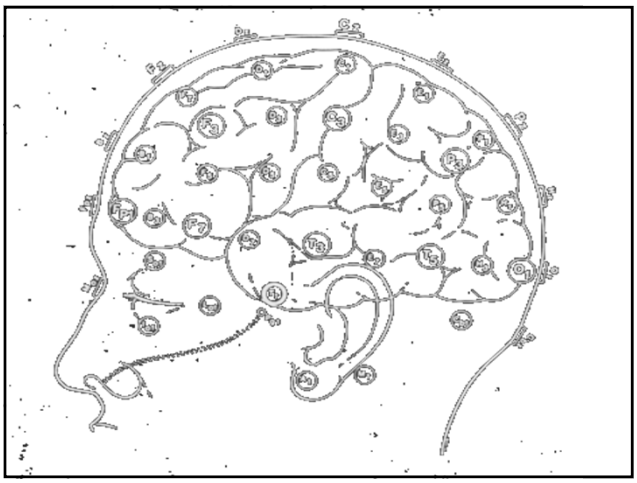
A. History
   - patient
   - witness
B. Physical and Neurological Examination
C. Electroencephalogram (EEG)
D. Imaging-
   - CT
   - MRI
E. Video-EEG monitoring

Seizure and Spell Diagnosis

A. History
- patient &/or witness
- define terms- “black out”
- postictal amnesia?
- circumstance?
- staring spells, myoclonic

B. Physical and Neurological Examination
- orthostatic BP, neuro exam may be normal

C. Electroencephalogram (EEG)
- routine vs sleep deprived



Small (microvolt) electrical fields are generated by synaptic currents in excitatory cells

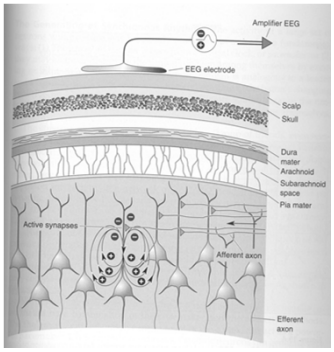
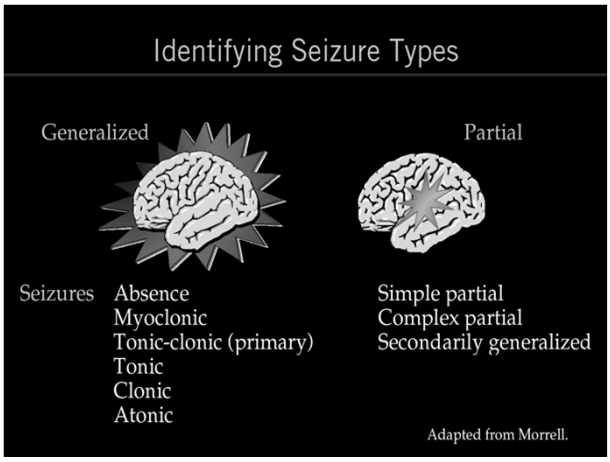


Figure: p609, Neuroscience, Connors et al., Eds

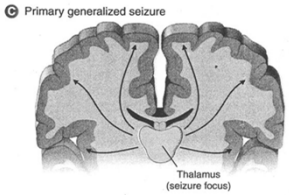
EEG measures this activity through the scalp but it can only detect it if thousands of neurons fire in synchrony.



Internatonal Classification: Generalized Seizures—primary generalized epilepsy

Non-focal, consciousness is impaired. No aura.

1. **Generalized Tonic-Clonic (e.g., grand mal)**
2. **Generalized Clonic**
3. **Absence (e.g., Petit Mal)**
4. **Tonic (Stiffness, tone)**
5. **Atonic (loss of muscle tone)**
6. **Myoclonic (brief jerk)**



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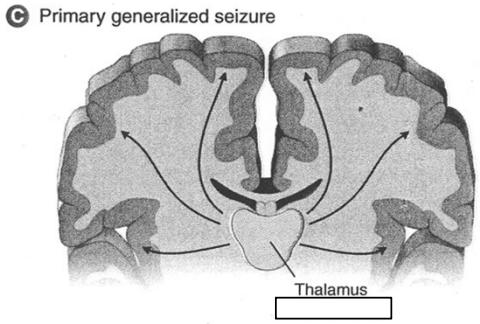
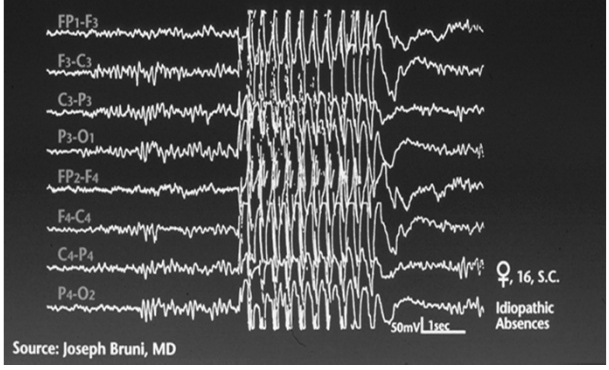


Generalized **refers to <u>mechanism</u>- cellular, synaptic, genetic**

EEG II: Idiopathic Absence Seizure



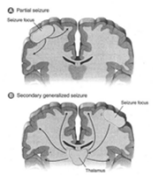
Source: Joseph Bruni, MD

International Classification: partial seizures-partial or focal epilepsy

Focal/partial/localization related.

Associated with an aura.

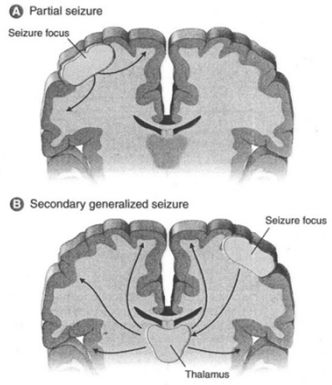
1. **Simple partial – consciousness not impaired**
2. **Complex partial – consciousness altered**
3. **Secondarily generalized seizures**
   - **grand mal seizure or GTC (generalized tonic clonic convulsion)**



International Classification: partial seizures-partial or focal epilepsy

Seizure focus often not apparent on imaging

Secondary *generalized* refers to <u>seizure spread</u> and not basic mechanism



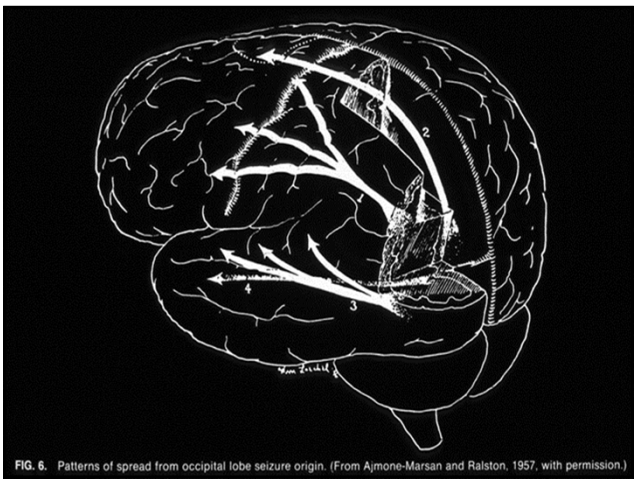


FIG. 6. Patterns of spread from occipital lobe seizure origin. (From Ajmone-Marsan and Ralston, 1957, with permission.)

Diagnosis of Staring Spells

Characteristic	Absence Seizures Generalized	Complex Partial Seizures
Aura (warning)	None	Common
Postictal confusion	No	Yes
Mean Duration	10 seconds	1-2 minutes
EEG	Generalized spike and wave	Focal spikes and sharp waves
Surgical treatment	No	Yes

Temporal Lobe Seizures

- Motionless stare common
- Oral automatisms-lip smacking, chewing
- Manual automatisms- eg. repetitive picking at clothes; ipsilateral to focus
- Hand dystonic posturing- contralateral to focus
- Postictal aphasia common if dominant temp lobe focus
- Easiest to localize seizure focus
- Best outcome for epilepsy surgery

EEG in Spell Diagnosis

A. Electroencephalogram (EEG)-30 min
B. Ambulatory EEG ±video
C. Video-EEG monitoring (epilepsy monitoring unit)
   1. 24 hours, inpatient
   2. elective (spell diagnosis or presurgical) versus nonelective (emergency department for spell diagnosis, seizure management)
   3. most patients elective

Misconception

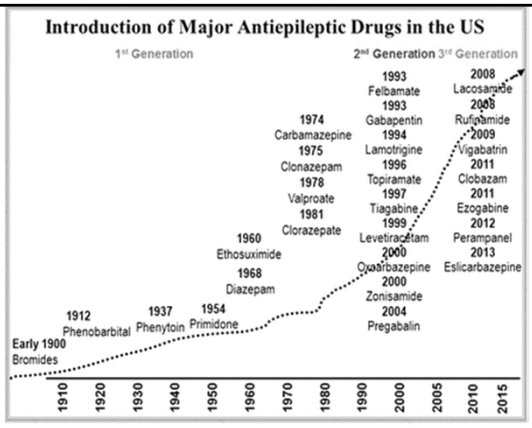
Spells ➔ LOC + Normal interictal EEG = <u>not</u> epilepsy

Comments:

- Single routine EEGs often (50%) normal in partial epilepsy
- Multiple EEGs to ~3 increase the yield to 90% using routine and sleep-deprived recordings
- Only ictal (during seizure) recordings may be positive in some patients

Basic Spell Management

- Regardless of diagnosis, common trigger factors should be eliminated- stress, sleep deprivation, alcohol, caffeine, seizure triggering meds, recreational drugs
- Treat underlying medical problems
- Medication treatment may not be necessary
- Simple measures- e.g. hydration, elevating head of bed for orthostatic hypotension
- If epilepsy choose single medication at lowest therapeutic dose
- If no response to treatment, reconsider diagnosis



Rudzinski, L. A., Vélez-Ruiz, N. J., Gedzelman, E. R., Mauricio, E. A., Shih, J. J., & Karakis, I. (2016). New antiepileptic drugs: focus on ezogabine, clobazam, and perampanel. *Journal of Investigative Medicine,* (), jim-2016-000151

Medication for Epilepsy

- Become comfortable with 2-3 seizure medications
- New onset epilepsy
  - Levetiracetam (Keppra)- broad spectrum, easy to titrate, no interactions but irritability (20%)
  - Oxcarbazepine (Trileptal)- partial epilepsy, easy to titrate, avoid in elderly due to hyponatremia

Medication for Epilepsy

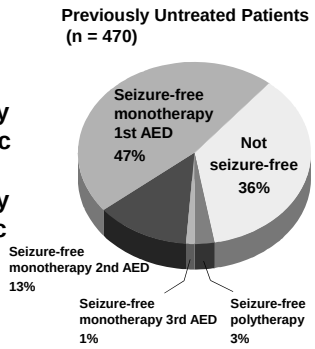
- Good add-on agents
  - Lamotrigine (Lamictal)- broad spectrum, slow titration to prevent rash, mood disorder treatment
  - Zonisamide (Zonegran)- broad spectrum, slow titration, weight loss
  - Lacosamide (Vimpat)- partial epilepsy, slow titration to prevent side effects

Medication for Epilepsy

- Good agents, But Be Careful!
  - Valproate acid (Depakote)- broad spectrum, may treat mood disorder, avoid in women of child bearing age, tremor
  - Topiramate (Topamax)- broad spectrum, useful for migraine, cognitive & language side effects, weight loss.

Success Rate of Antiepileptic Drugs

- 63% remained seizure-free
- Seizure-free rates were similar between those treated with monotherapy with an older antiepileptic drug (67%) and those treated with monotherapy with a newer antiepileptic drug (69%)



Kwan P, Brodie MJ. N Engl J Med. 2000;342:314-319.

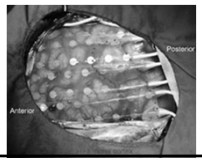
Surgical Management of Epilepsy

- Devices (approved)
  - Vagal nerve stimulation (Cyberonics)
  - Responsive neurostimulaton (Neuropace)
- Surgical resection
  - Lesionectomy*
  - Temporal*
  - Extratemporal
  - Hemispherectomy
  - Disconnection procedures

* Best success rate

Surgical Resection in Epilepsy

- Concepts
  - Refractory epilepsy
  - Best results when single cortical focus
  - Benefits outweigh risks
- Evaluation
  - Phase I- scalp video-EEG monitoring, neuroimaging (MRI, SPECT, PET)
  - Phase II- invasive video-EEG monitoring: depth and grid electrodes
    - Allows cortical mapping

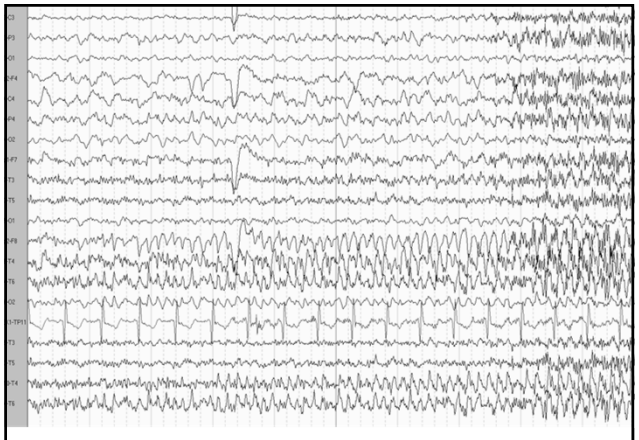


Presurgical Evaluation
Phase I

- Interictal EEG data
- Video-EEG monitoring
- Ictal SPECT
- Neuropsychological testing
- MRI scanning
- PET scanning

32 year old RH male with refractory complex partial seizures

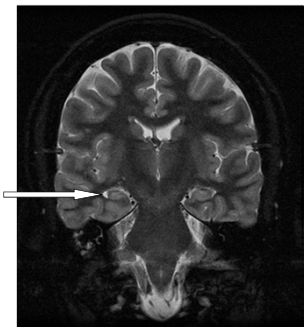
- Aura: sensation of abdominal bloating and interictal GI symptoms
- Episodes of staring, confusion and automatic movements of hand and mouth since age 10
- Rare secondarily generalized (grand mal) seizures
- Many different antiepileptic medications tried, but only able to go 2-4 weeks without seizures
- MRI brain scan was reported to be normal



32 WM with right temporal lobe focus

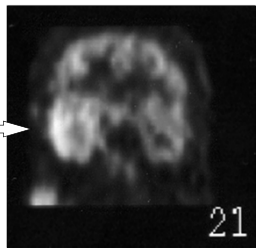
MRI

Smaller right hippocampus compared to left

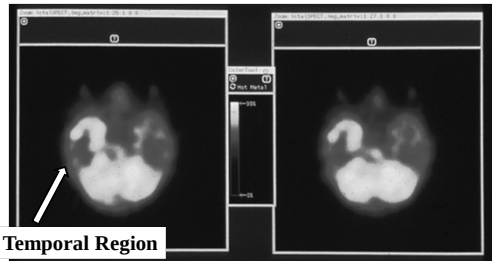


Ictal SPECT (Single Photon Emission Computed Tomography)

Right temporal hyperperfusion



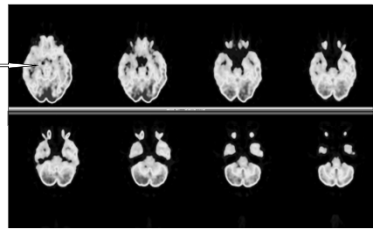
Ictal SPECT (single photon emission computed tomography)



Right Temporal Region

PET (Positron Emission Tomography)

Right temporal hypometabolism



32 year old RH male with refractory complex partial seizures

- On April 21, 2004, he had a right temporal lobectomy. Since surgery he initially had some rare auras, but otherwise has been seizure free.
- AED's have been streamlined. He is driving and working
- All GI symptoms ictal & interictal resolved

Source: Winston-Salem Journal

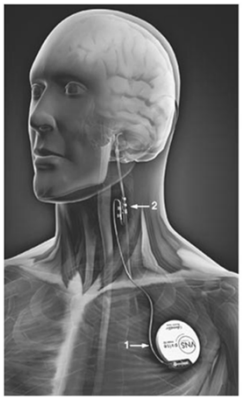
Presurgical Evaluation
Phase II- invasive electrode implantation

Randomized, Controlled Trial of Surgery For Temporal Lobe Epilepsy

	Surgical group	Medical group
Seizure-free for complex partial seizures	58% All	8%
Seizure-free for all seizures including auras	38% All	3%
Seizure-free for complex partial seizure	64% Actual surgery	
Seizure-free for all seizures including auras	42% Actual surgery	

Wiebe et al, 2001 (NEJM)

Vagal Nerve Stimulation



Vagal Nerve Stimulation

- Implanted on left side
- Change parameters with wand
- Generator battery changed every few years
- Early side effects and delayed efficacy
- Two modes of activation when first approved
  - Constant cycling
  - Magnet activated

VNS Therapy Clinical Trial: E03

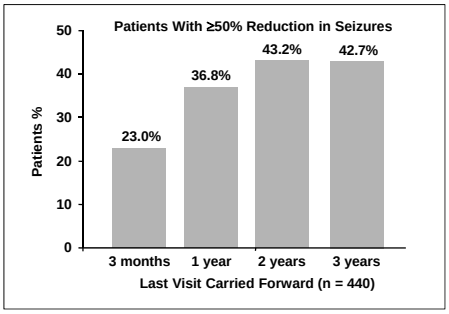
Adverse events (occurring in ≥5% of patients)

- Hoarseness 37%
- Throat pain 11%
- Coughing 7%
- Dyspnea 6%
- Paresthesia 6%
- Muscle pain 6%

Vagus Nerve Stimulation Study Group. *Neurology.* 1995;45:224-230.

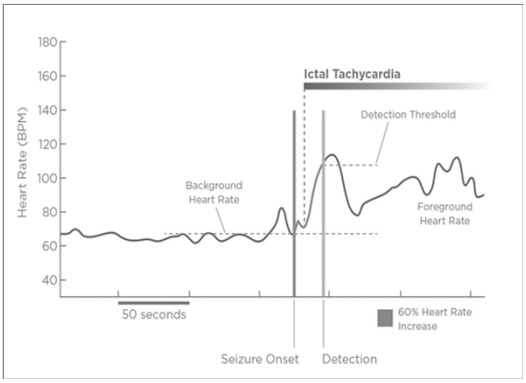
VNS Long-Term Seizure Control

Response Rates Increase Over Time (E01-E05)

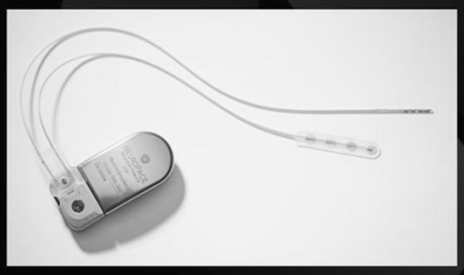


Morris GL III and Mueller WM. *Neurology.* 1999;53:1731-1735.

AspireSR Device with 3rd Activation Mode



RNS™ Neurostimulator with Leads



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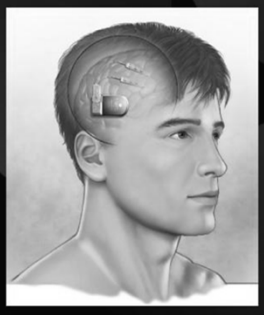
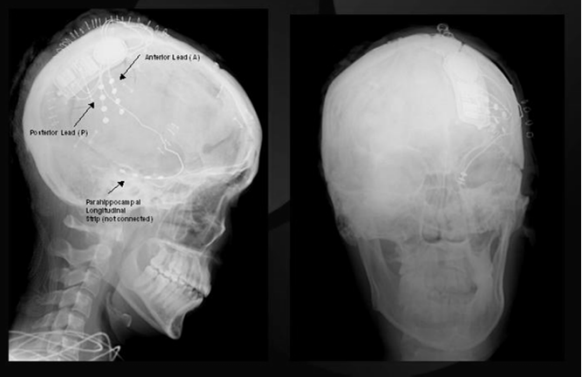
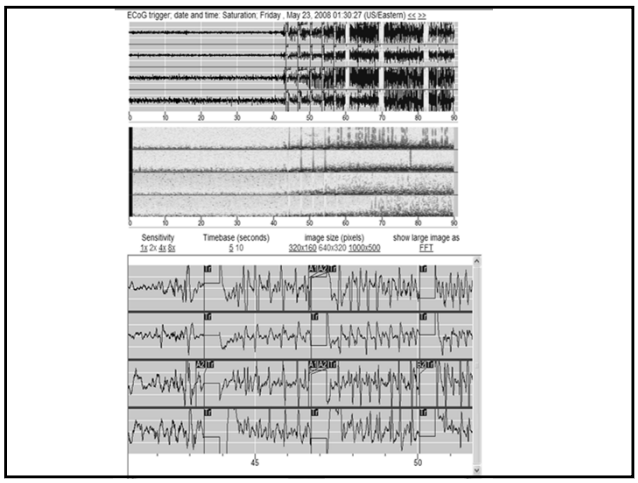


Implanted RNS™ System



RNS™ System Programming

- **Detection sets**
  - Detection algorithms selected by physician according to specific electrographic onset pattern
- **Stimulation settings**
  - Parameters modified by physician according to electrographic response
    - Frequency
    - Duration of stimulation
    - Pulse width
    - Current intensity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Patient Data Transmitter
2007-12-12, Rev 6
NeuroPace Inc. CAUTION-Investigational device. Limited by United States law to investigational use.
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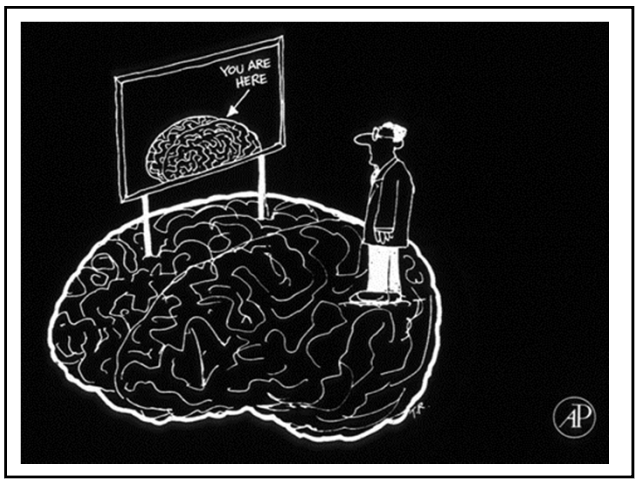
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