

Epilepsy and Traumatic Brain Injury

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Objectives

- Review Epilepsy Centers of Excellence Organization
- Discuss a case of posttraumatic epilepsy
- Review epidemiology of posttraumatic epilepsy (PTE) after TBI
- Discuss therapy and evaluation of PTE and intractable epilepsy
- Review potential research strategies

VA Epilepsy Centers of Excellence (ECoE)

Congressional Mandate for ECoE

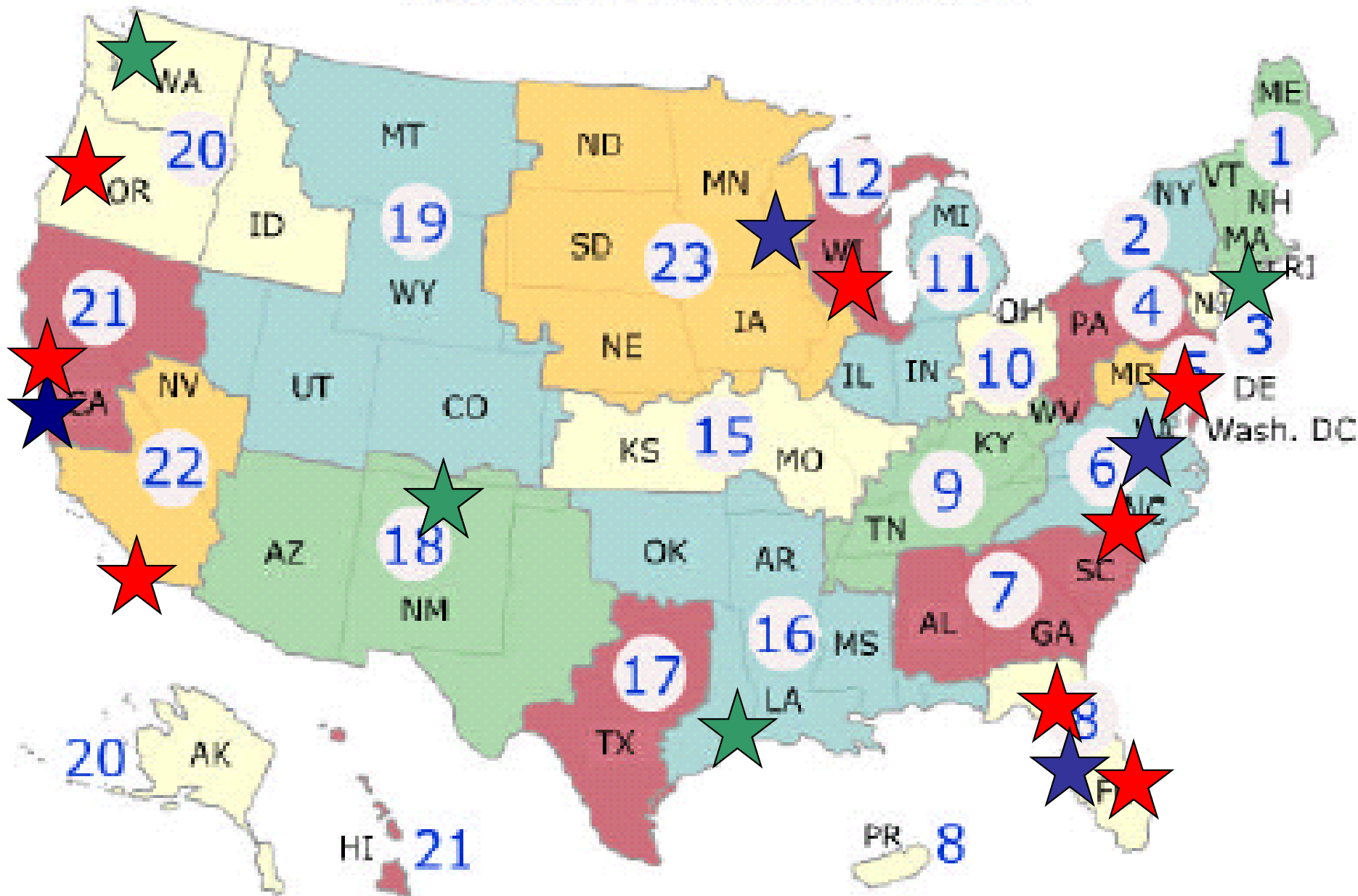
- Section 404 of Public Law 110-387, Veterans' Mental Health and Other Care Improvements Acts of 2008
- Spurred by support from John Boos, former National VA Chief of Neurology, with AAN, AES, EF, CURE support
- Largely lobbied with references to traumatic brain injury (TBI) and OIF/OEF conflicts
- Need to serve polytrauma needs
- \$6 million/year up to 6 centers

Objectives for ECoEs

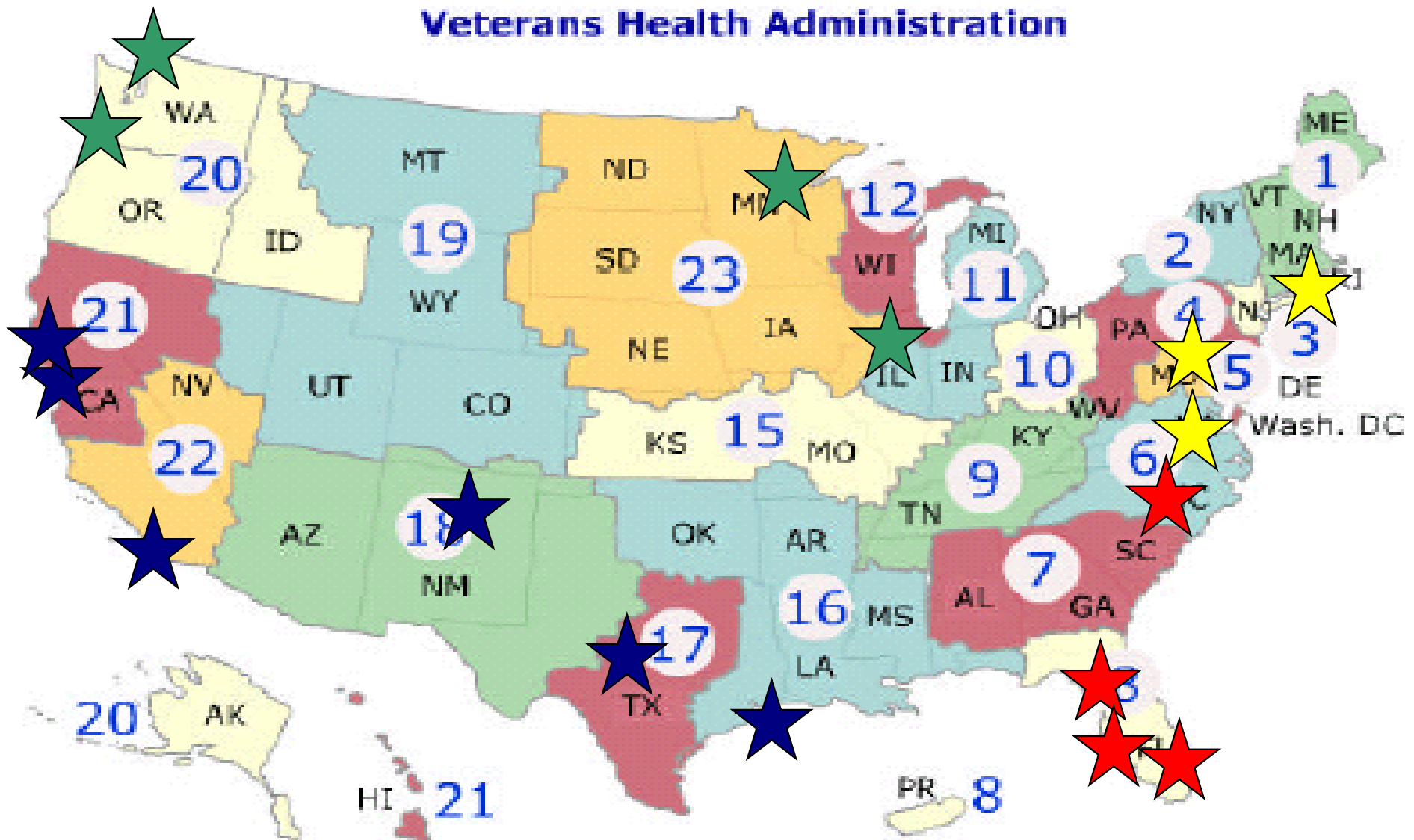
- To improve quality of care for veterans with epilepsy
- To improve availability of care for veterans with epilepsy
- To anticipate need for post-traumatic epilepsy care

Sites of Epilepsy Strength – Red Sites Surgical & Monitoring Capacity, Green Sites have Monitoring Capacity Existing Polytrauma Centers in Blue

Veterans Health Administration



Linking Sites of Strengths in Epilepsy Care with Polytrauma Centers to form 4 Multisite Centers: Northwest, Southwest, Southeast and **Atlantic**



ECoE Northwest Goals

- Improve care for veterans with epilepsy
 - Focus on post traumatic epilepsy
- Leverage technology
 - Telemedicine
 - Tele-EEG
- Educational core
- Research infrastructure
 - Epidemiology of post traumatic epilepsy

Where do we go from here?

- Implementation of a real network
 - Web page <http://www.epilepsy.va.gov/ecoe.asp>
- Identification of patients with epilepsy and their needs, particularly post traumatic epilepsy
- Develop research
 - Post traumatic
 - Surgery
 - Standard of care

Case Presentation

- 48 yo LH man was hit with a baseball bat at age 24
- Hospitalized and in coma for 1 week, had a left frontal hemorrhage evacuated
- Made slow but complete recovery
- One year after injury had first generalized tonic-clonic seizure

Case Presentation

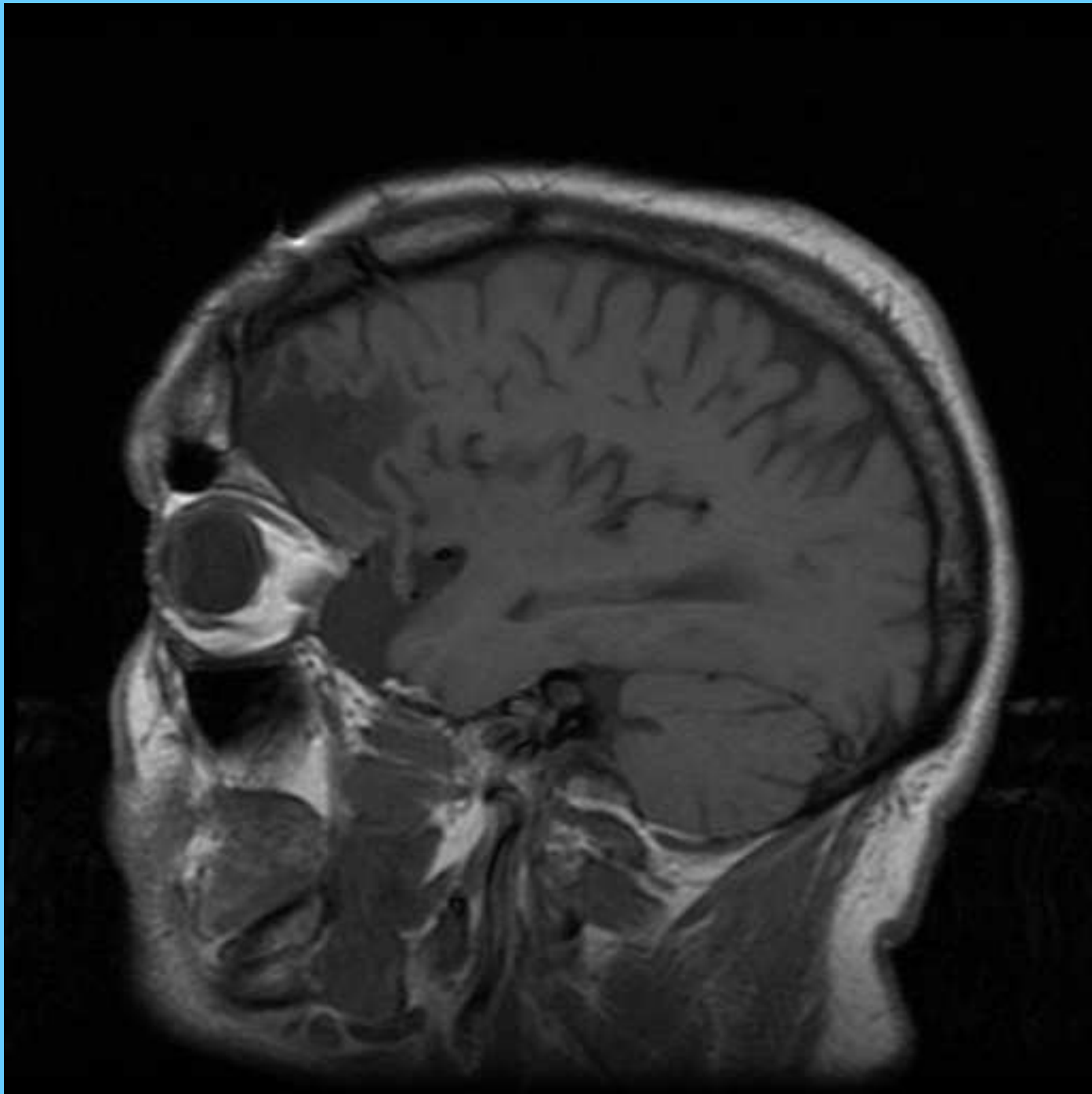
- Treated with phenytoin then carbamazepine
- Had “good” seizure control on carbamazepine for 20 years (2-3 seizures/yr)
- One episode of status epilepticus in the 90’s
- Social history positive for alcoholism and homeless

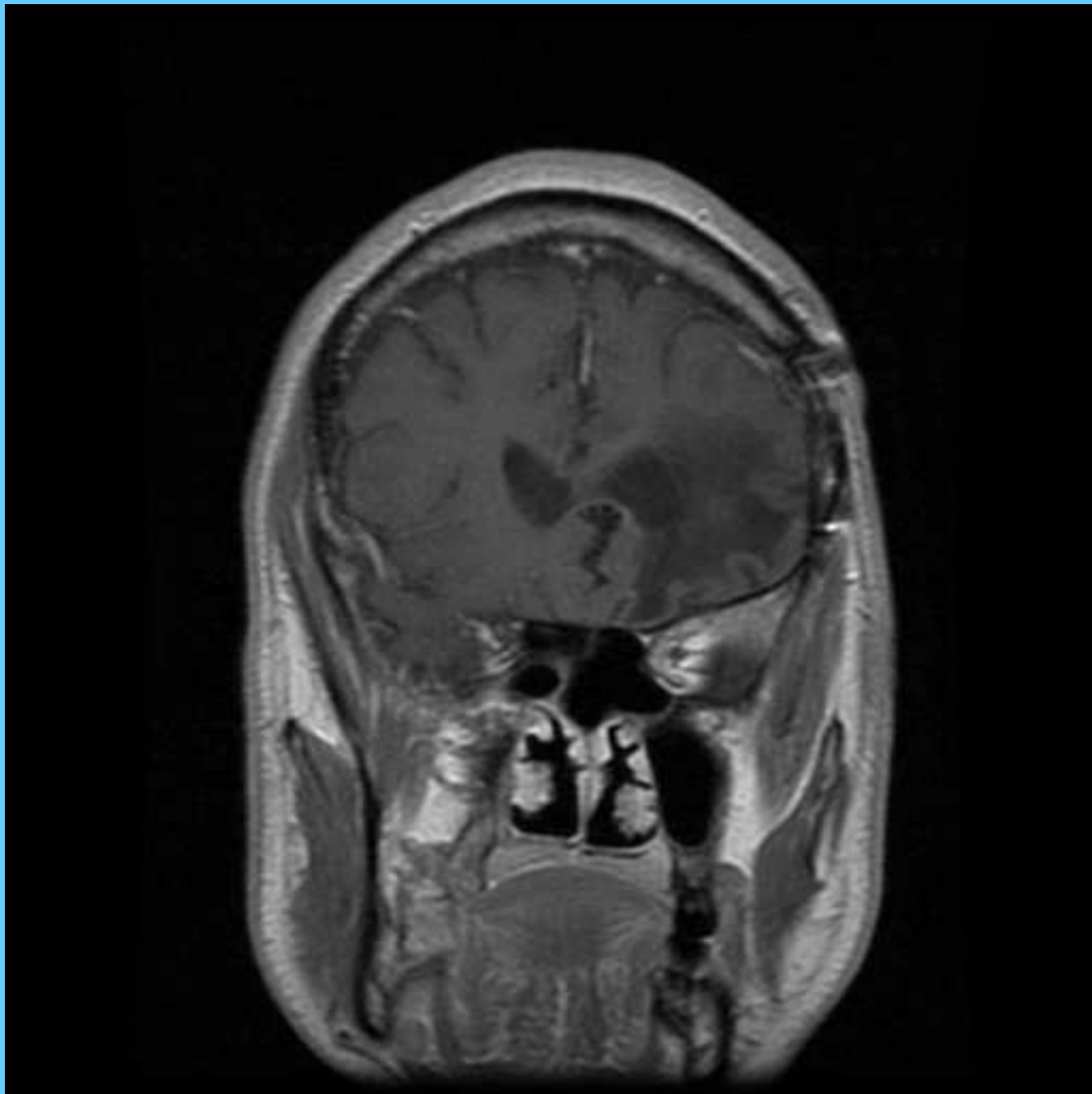
Case Presentation

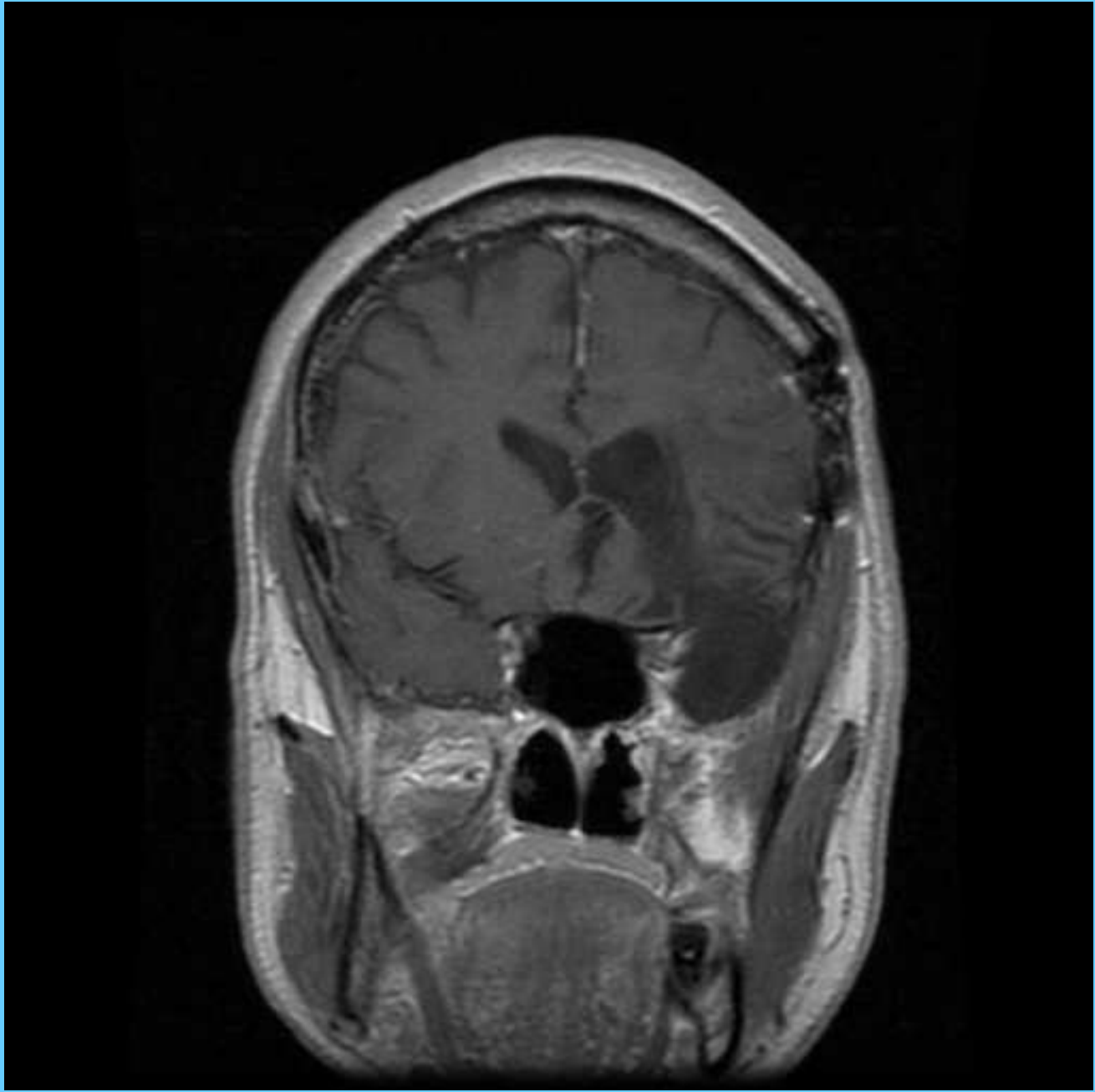
- 2 years ago began having 2-3 seizures a week described as generalized tonic-clonic in character. Usually occur during sleep. No aura. Wakes up sore.
- Failed topiramate, valproate
- Currently on gabapentin 600 TID and levetiracetam 1500 mg BID
- Referred for video-EEG monitoring

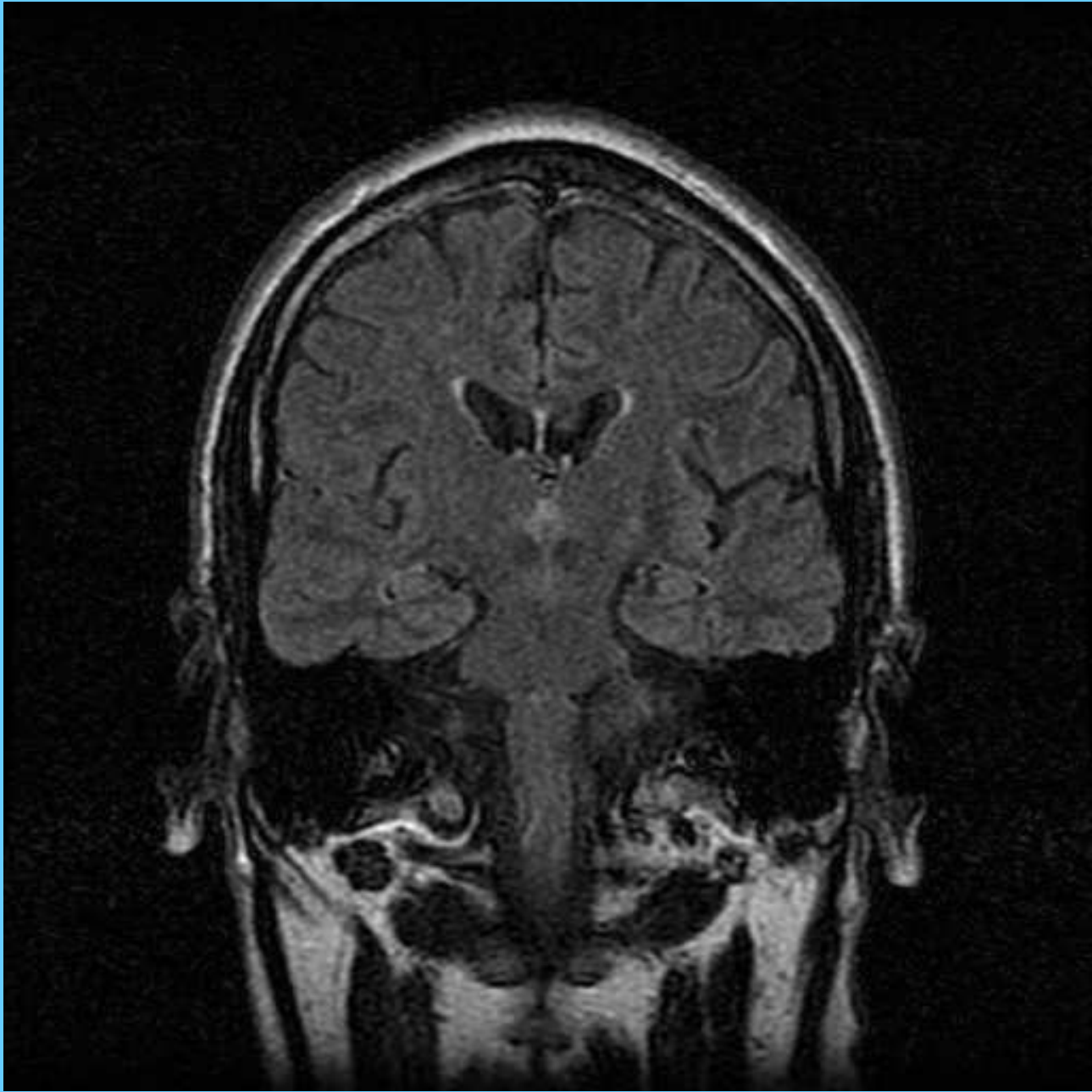
Case Presentation

- History of hypertension and hyperlipidemia
 - Rx metoprolol and simvastatin
- Exam remarkable for 1/3 memory and Right UE drift
- EEG showed left frontotemporal slowing in theta range with intermittent F7 spike/sharp waves
- MRI with left frontotemporal encephalomalacia, left temporal arachnoid cyst, microvascular changes in white matter



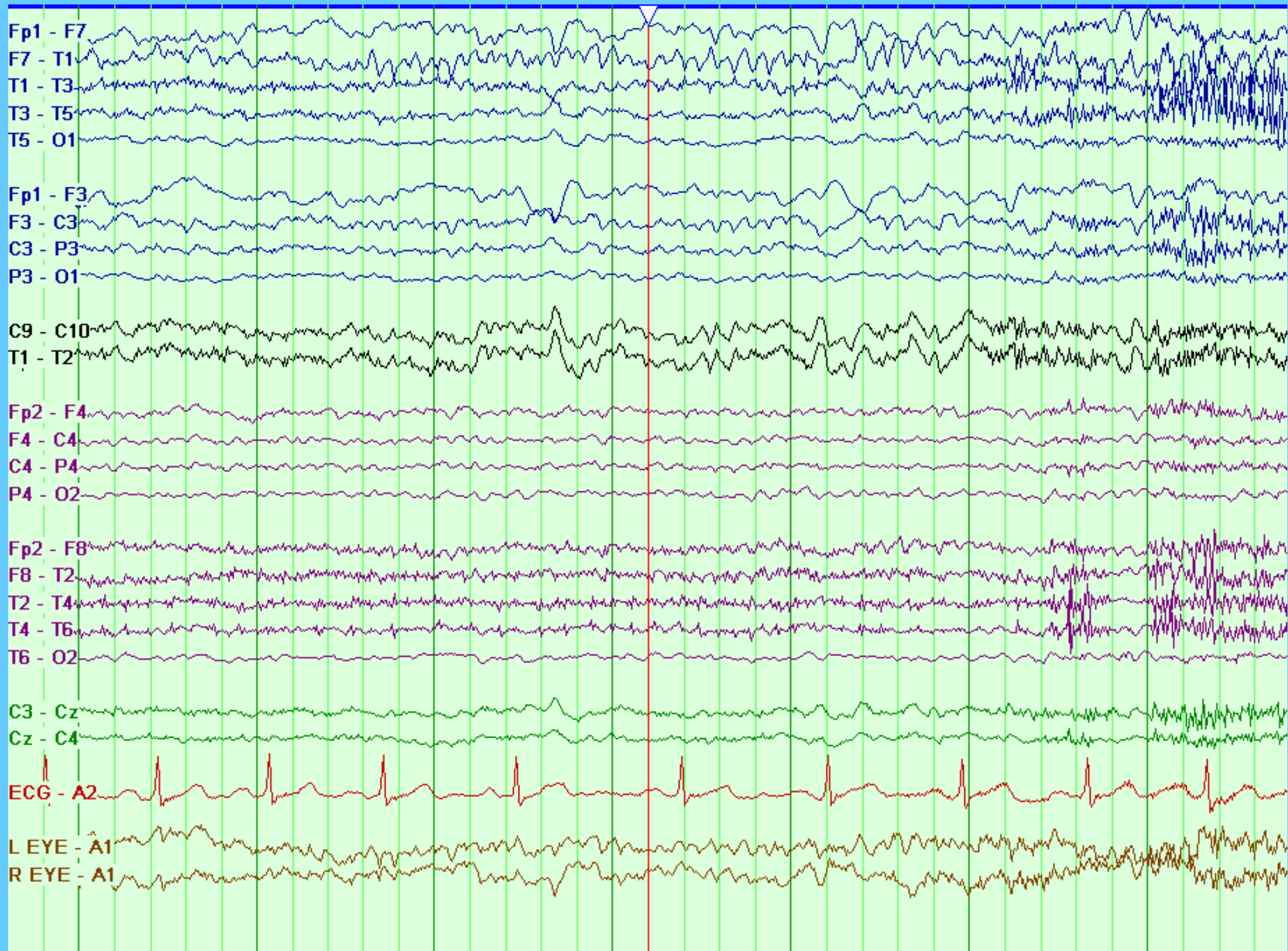


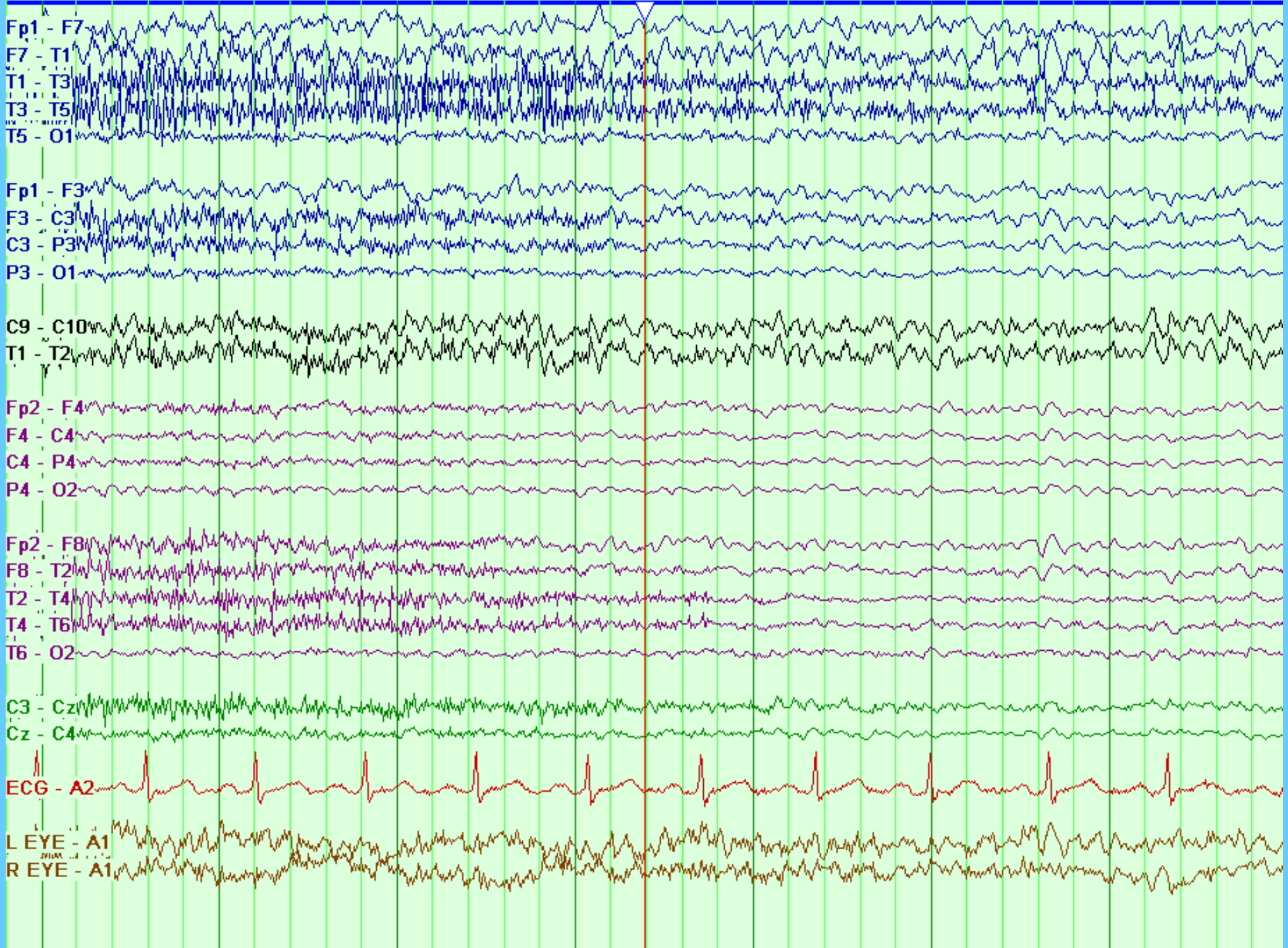


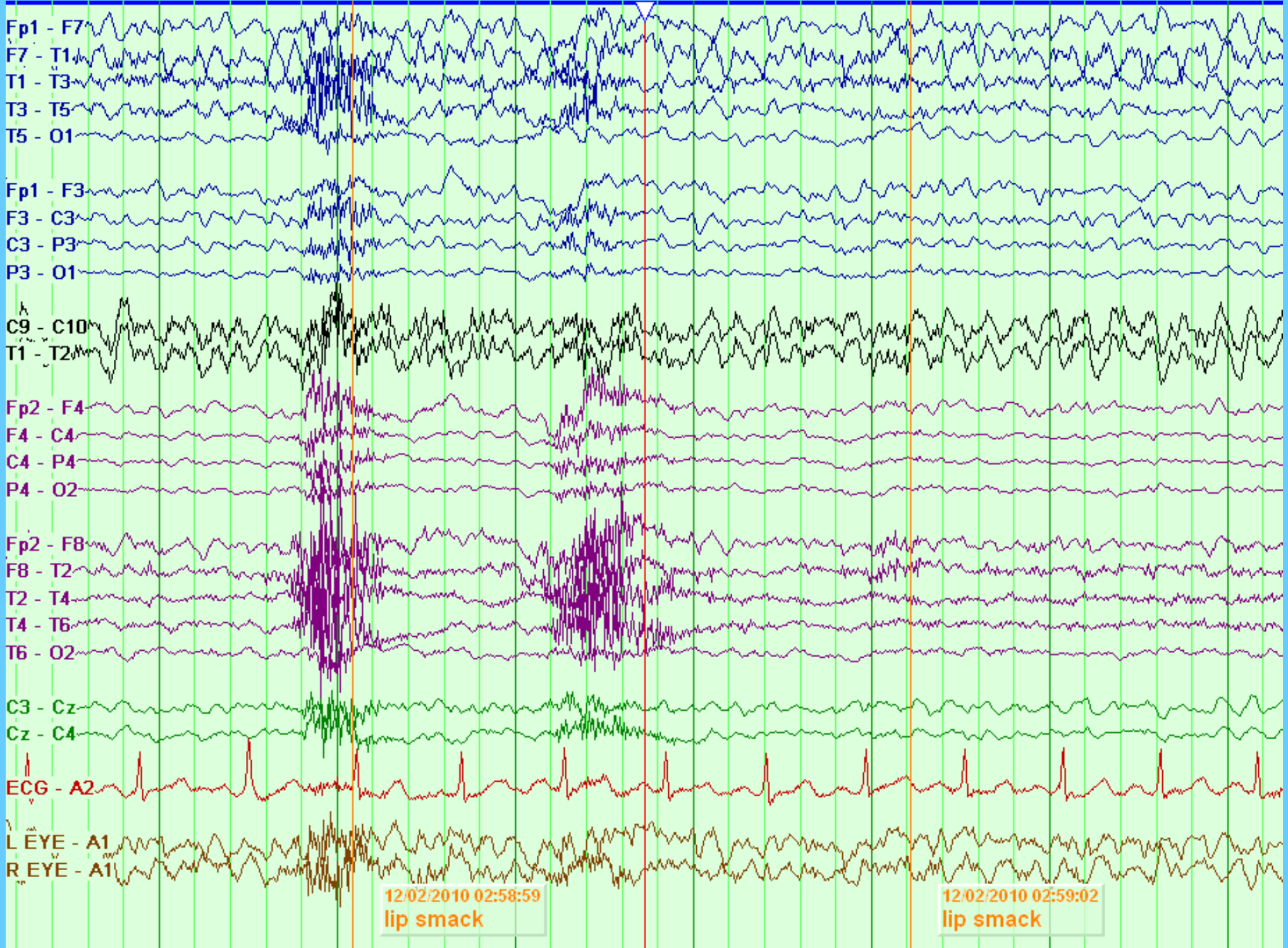


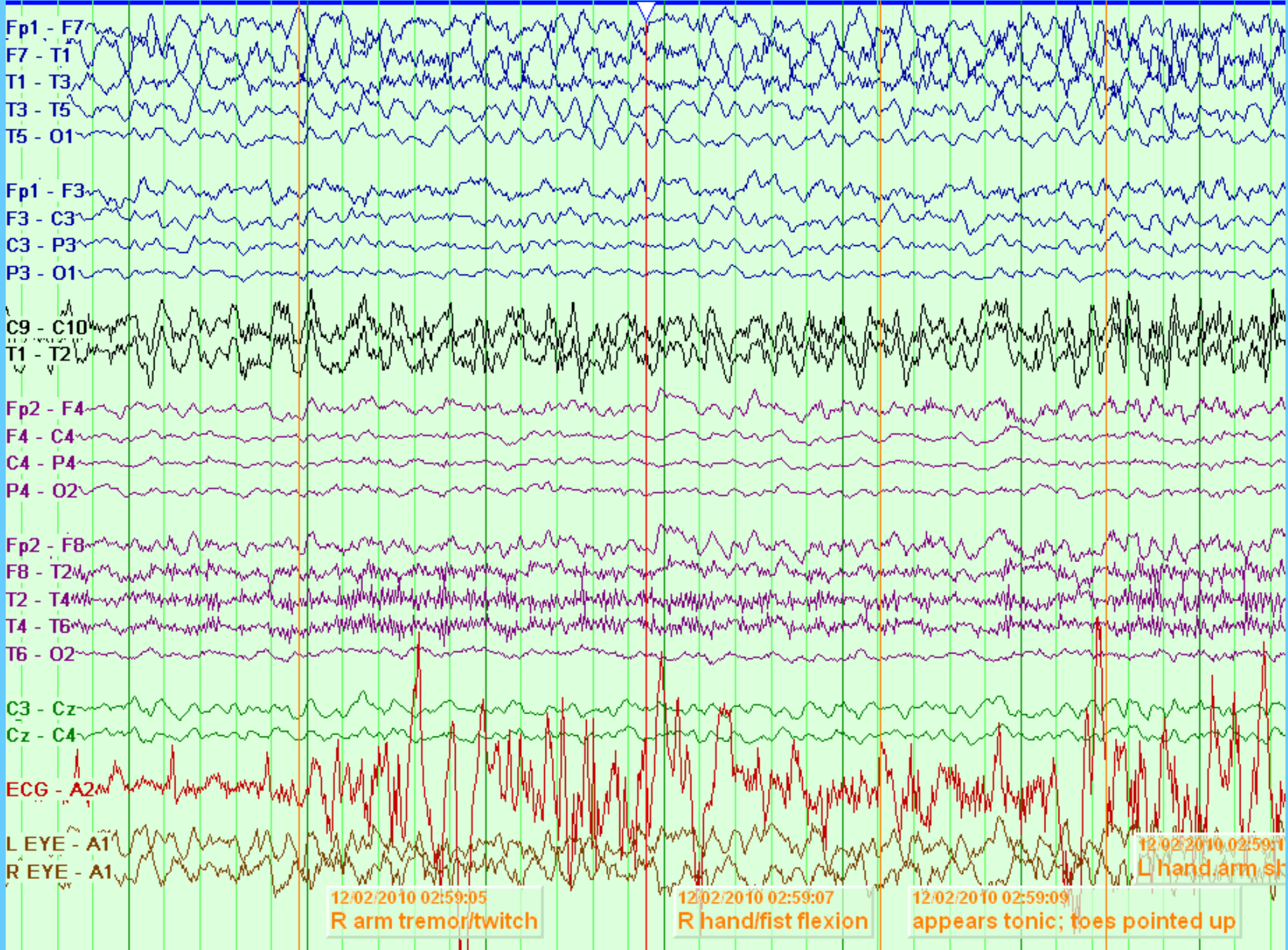
Video-EEG Study

- 3 partial seizures of left frontotemporal onset that secondarily generalized
- All began in sleep and appeared to have an apnea that awoke patient
- Opened eyes, staring, oral-buccal automatisms, then rhythmic right hand movements with secondary generalization





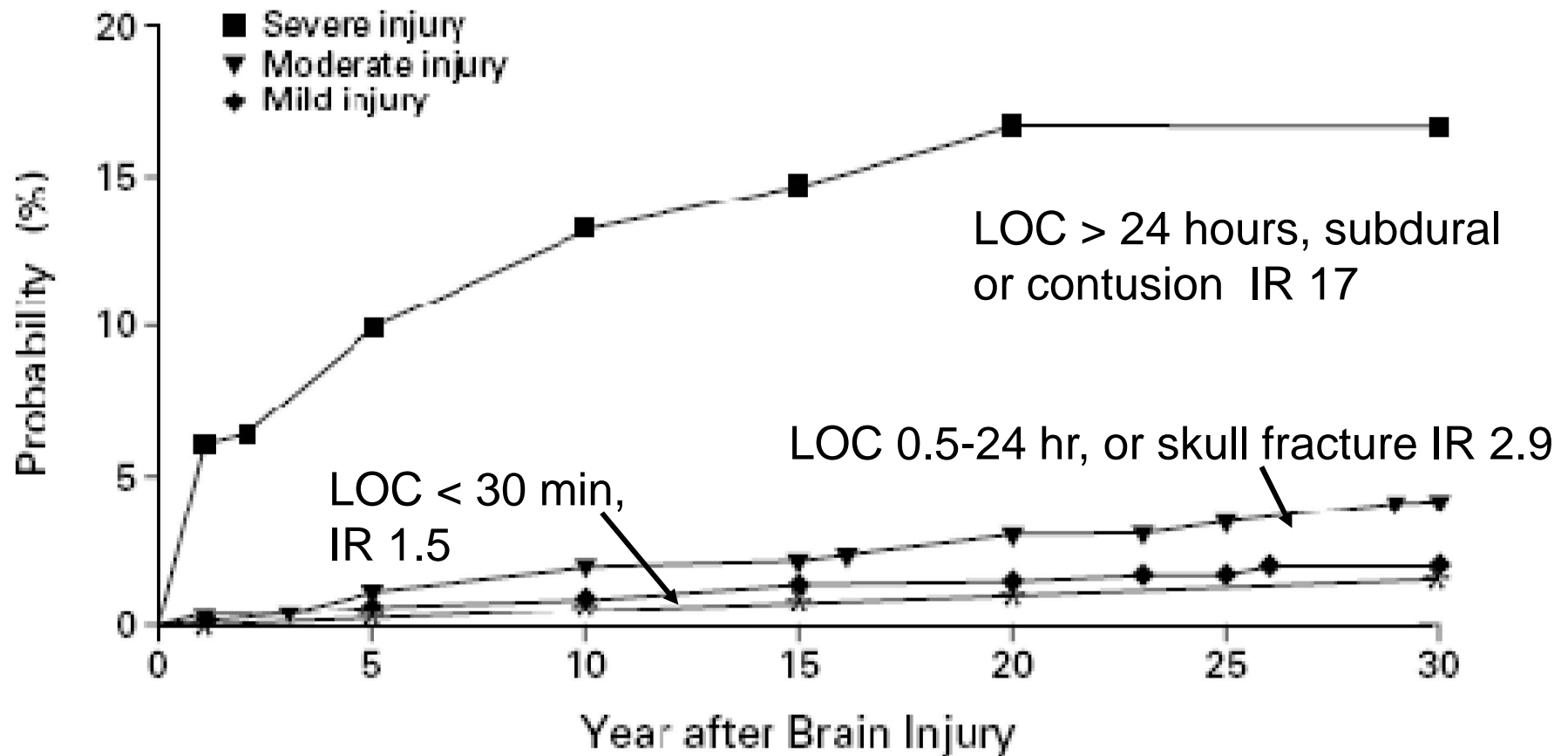




Further Patient Management

- Evaluated for obstructive sleep apnea, now on BIPAP
- Trail of lamotrigine
- If continues to be intractable, surgical evaluation
 - Invasive study
 - Neuropsychiatric evaluation
- Concern about SUDEP

Probability of Developing Injury After Head Trauma in a Civilian Population



Incidence of TBI & PTE in the Military

- **1.64 million** soldiers have served in OIF/OEF
- **320,000** or **19%** of these soldiers will screen positive for a traumatic brain injury.
- **15-34 %** of moderate to severe TBI cases also develop PTE and can be as high as **53%** with penetrating skull injury.
- Therefore a significant number of soldiers serving in OIF/OEF are expected to develop PTE.

TBI Screening

- April 2007- August 31, 2010: 445,000 Veterans screened
- 90,000 (20%) screened positive
- 35,000 given a ICD9 TBI code
- Most common cause is Improvised Explosive Device (IED), blast injury, a new type of injury

Defense and Veterans Brain Injury Center (DVBIC)

- Defense and Veterans Brain Injury Consortium (<http://www.dvbic.org/>)
- From 2000-Feb 2011 202,281 TBI cases identified

TBI Severity

Concussion/mild TBI (mTBI) is characterized by the following: A confused or disoriented state which lasts less than 24 hours; loss of consciousness for up to 30 minutes; memory loss lasting less than 24 hours; and structural brain imaging (MRI or CT scan) yielding normal results.

Moderate TBI is characterized by the following: A confused or disoriented state which lasts more than 24 hours; loss of consciousness for more than 30 minutes, but less than 24 hours; memory loss lasting greater than 24 hours but less than seven days; and structural brain imaging yielding normal or abnormal results.

Severe TBI is characterized by the following: A confused or disoriented state which lasts more than 24 hours; loss of consciousness for more than 24 hours; memory loss for more than seven days; and structural brain imaging yielding normal or abnormal results.

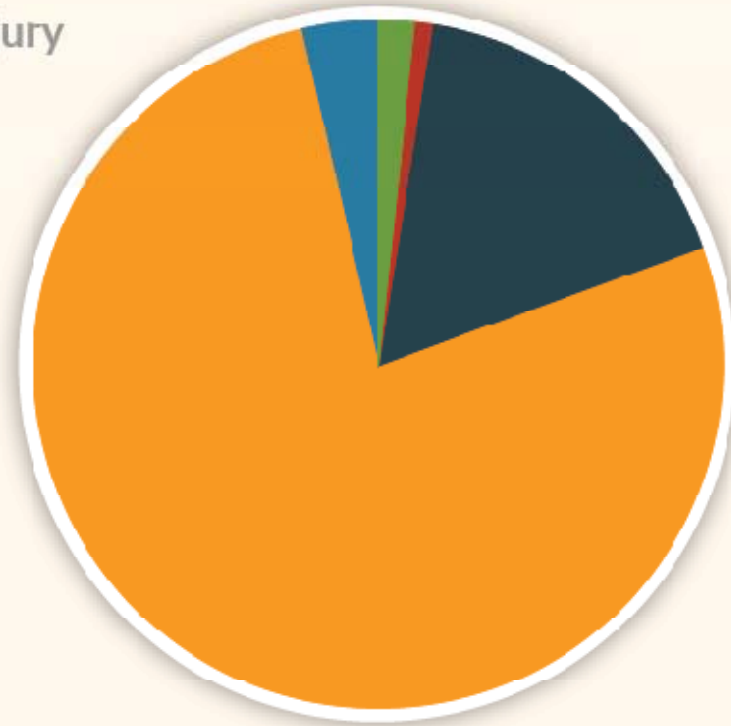
Penetrating TBI, or open head injury, is a head injury in which the dura mater, the outer layer of the meninges, is penetrated. Penetrating injuries can be caused by high-velocity projectiles or objects of lower velocity such as knives, or bone fragments from a skull fracture that are driven into the brain.



TBI Numbers By Severity – All Armed Forces

DoD Numbers for Traumatic Brain Injury
'00-'10 Q4 Totals

Penetrating	3,451
Severe	2,124
Moderate	34,001
Mild	155,623
Not Classifiable	7,082
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Total - All Severities	202,281

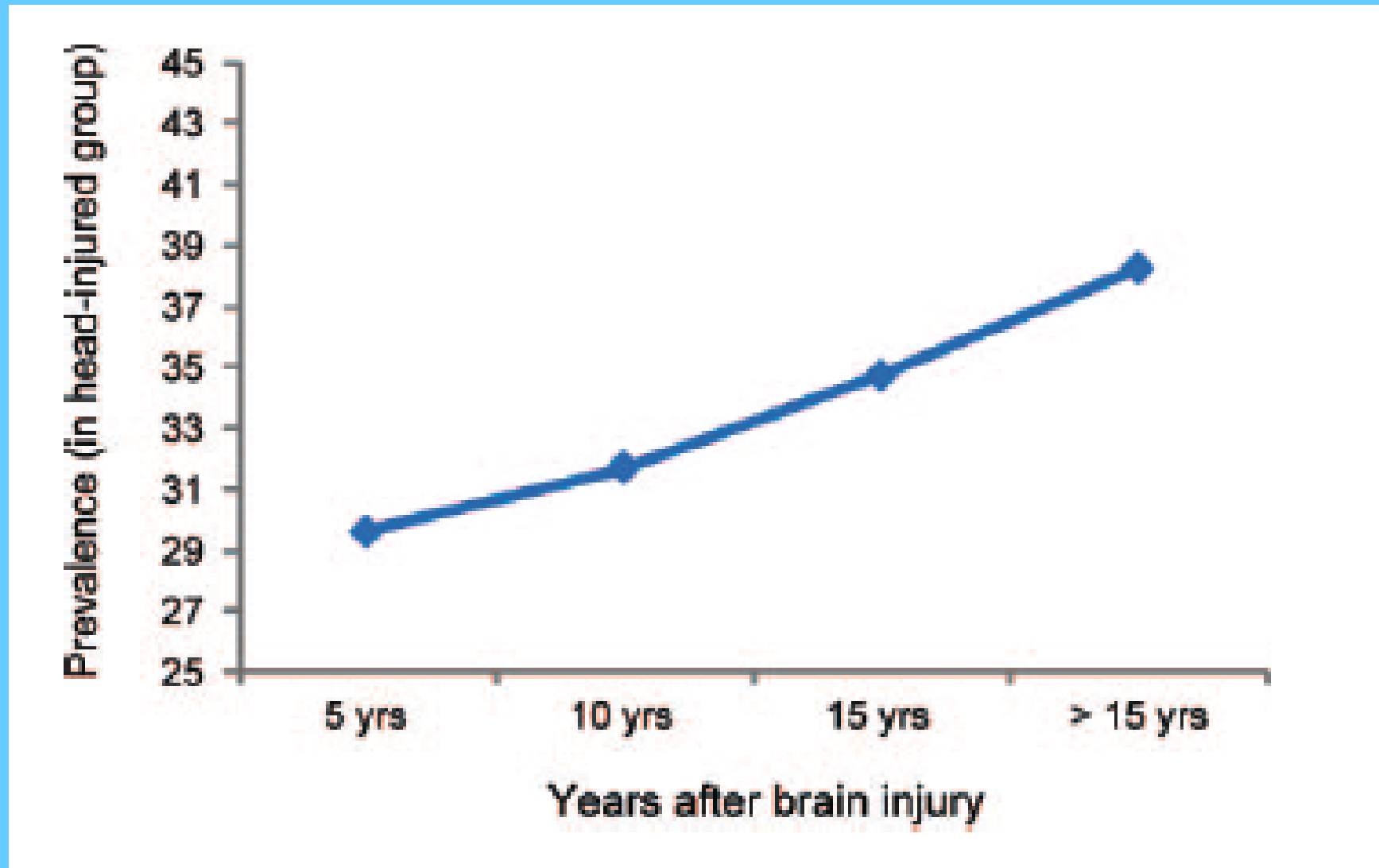


Source: Armed Forces Health Surveillance Center

Numbers for 2000 - 2010 Q4, as of 17 Feb 2011

<http://dvbic.org/images/pdfs/TBI-Numbers/2009-2010Q4-updated-as-of-17-FEB-2011/dod-tbi-2000-2010Q4-as-of-110217.aspx>

Probability of Developing Injury After Penetrating Head Trauma in Viet Nam Veterans

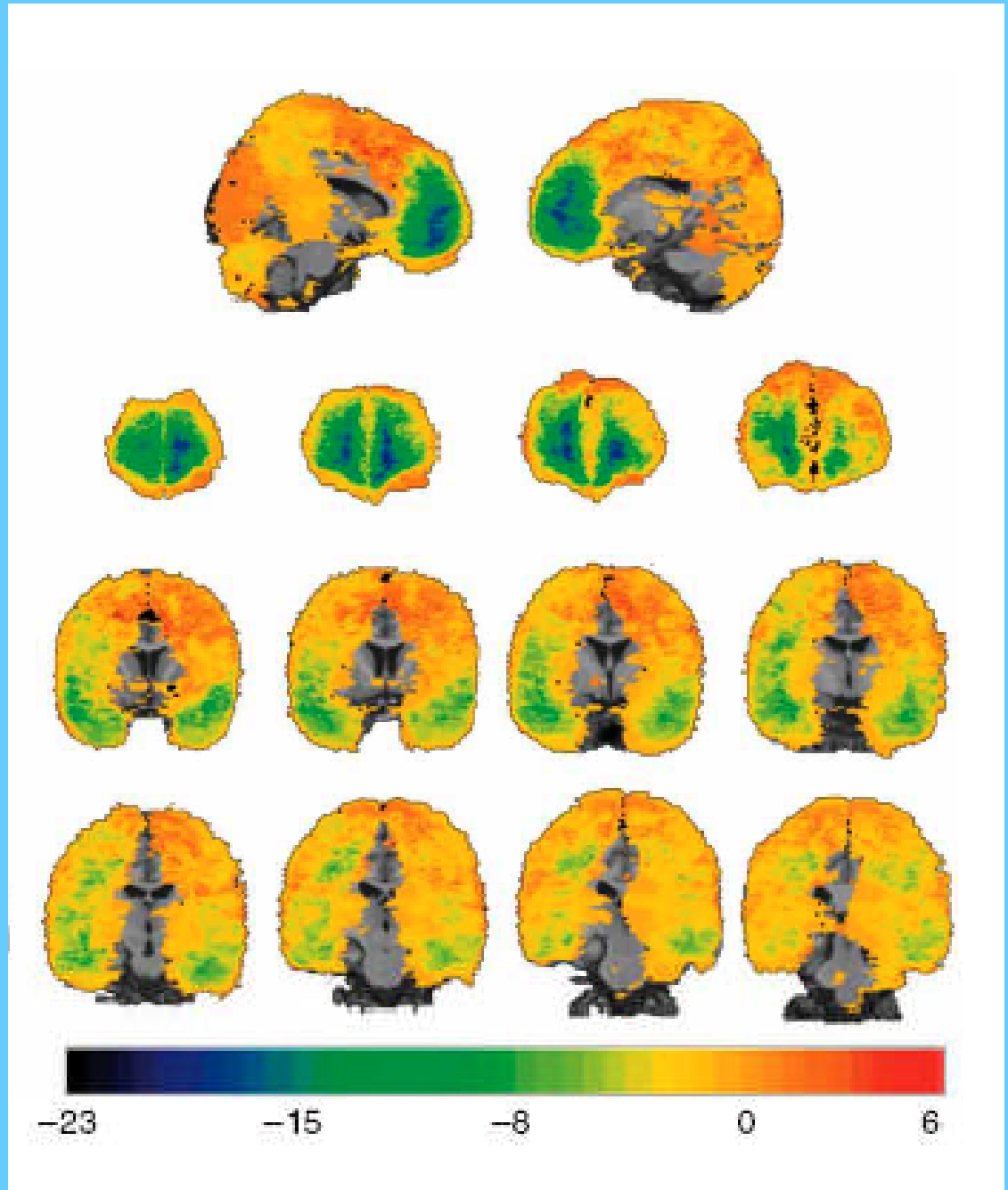


Diagnosing PTE

- Easy when clear convulsive seizures
- More difficult when subtle symptoms that may be confused with TBI co-morbidities
 - Attention problems
 - Sleep problems
 - PTSD
 - Generalized anxiety disorder

Traumatic lesions of ventromedial prefrontal cortex and anterior temporal lobe/amygdala (blue/green) were associated with a reduced risk for PTSD in Viet Nam Veterans

Koenigs et al, Nature Neuroscience, 2008



PTE and Video-EEG monitoring

Diaz-Arrasita, et al., Epilepsia 2009

Table 1. Results of CVEEG evaluations

Diagnostic conclusion		% (n)
Total evaluations		100 (125)
Nondiagnostic		18 (23)
NES		33 (34)
Epileptic		65 (68)
	Generalized onset	9 (6)
	Focal onset	91 (62)
	Temporal	54 (36)
	Frontal	33 (21)
	Occipital	3 (2)
	Parietal	5 (3)

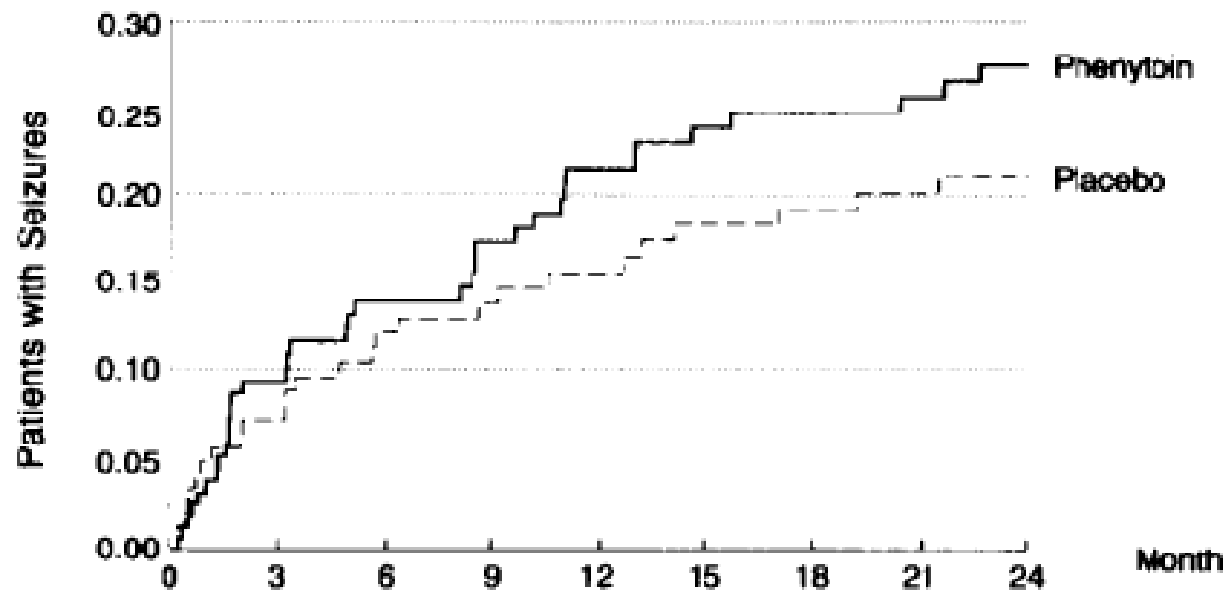
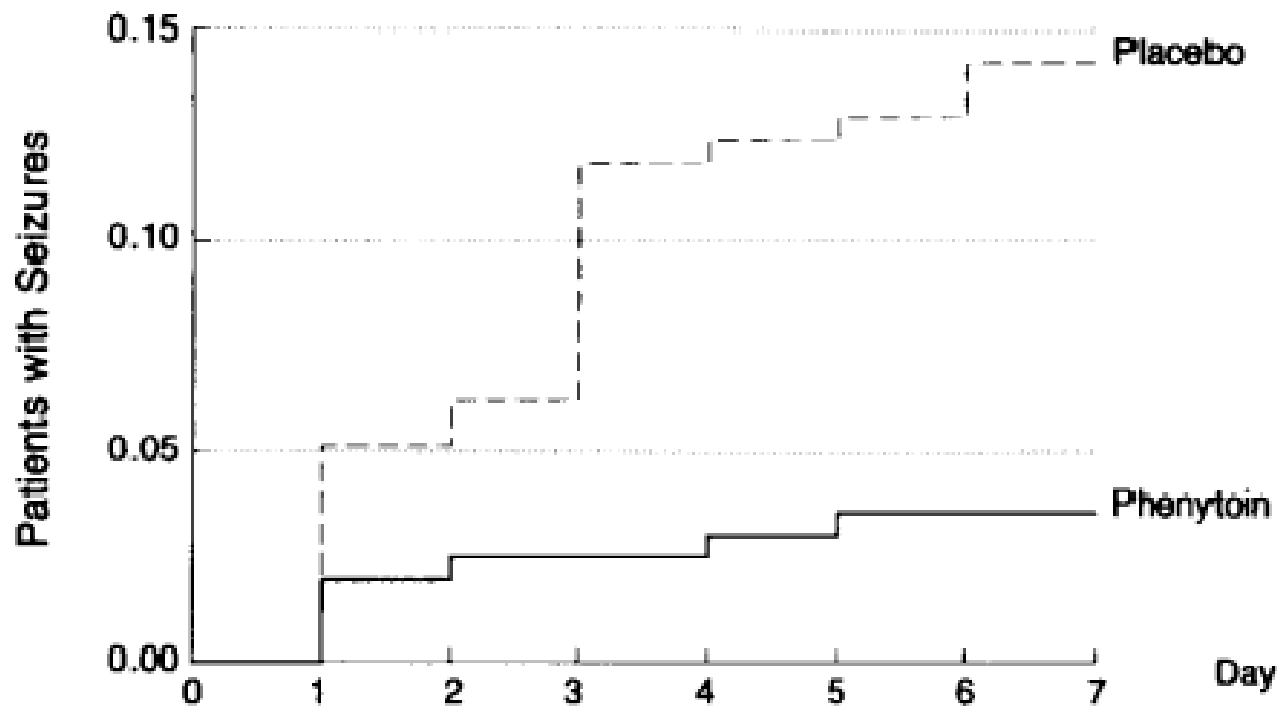
NES, nonepileptic seizures.

PTE Treatment

- No evidence based guidelines
- No clinical trials comparing AEDs
- Role of resective surgery unclear
- No treatment to prevent PTE
- TBI may be associated with progressive changes, worsening of epilepsy, progressive atrophy

PTE Surgery

- May be associated with hippocampal sclerosis
- Yale study (Marks, et al, Neurology, 1995)
 - 25 patients, 17 mesial temporal onset, 8 neocortical
 - 21 treated surgically, 9 seizure free
 - Those with good outcome had hippocampal sclerosis and early (< 5 yo) head trauma or focal cortical abnormality with hemosiderin



Phenytoin prevents early symptomatic seizures but not the development of epilepsy

(Tempkin et al, NEJM, 1990)

Major Gap in Prevention of Posttraumatic Epilepsy

- We have no proven preventative treatment for the development of epilepsy
- Phenytoin (Dilantin) protects against seizures the first week after trauma
- Valproate (Depakote) did not prevent the development of epilepsy in TBI
- Anti-epileptic drugs \neq Anti-epileptogenic drugs

TBI and PTE in OIF/OEF Veterans

Development of data base
research strategies

Specific Aims

- 1. To plan the content of a database that allows research to identify risk factors for PTE among veterans with Severe, Moderate, and Mild TBI.**
 - Understand the existing TBI screening database developed by the VHA Rehabilitation service and determine how the epilepsy centers can tap into these data to conduct prospective PTE research.**
 - Understand the data available from the Joint Theater Trauma Registry**

Specific Aims

- 2. To plan the content of a registry for Veterans with post traumatic epilepsy.**
- 3. Arrive at consensus regarding tools/ measures that will be used throughout the VA healthcare system to prospectively identify the onset of post-traumatic epilepsy in Veterans with TBI.**

Specific Aim 1: Understand the Existing Data Bases

- All patients who screen positive for TBI
 - About 20% of OIF/OEF Veterans
 - As of October 10/2010, 93,108 positive screens since 4/2007
 - 35,169 confirmed TBI diagnosis
- Need DOD numbers to determine the denominator, ie those seeking care outside of the VA, DOD positive TBI diagnosis was over 45,000 for 2003-07
- DVBIC 2000-2011, > 202,000 with TBI, 75% mild TBI, over 3,000 penetrating

Specific Aim 2: To begin a registry of Veterans with post traumatic epilepsy

- Determine what to include
 - Clinical, seizure diagnosis
 - Medications
 - MRI, EEG
 - Co-morbidities
- Can begin with focus on those Veterans referred to an ECoE, false positives of patients with non-epileptic seizures

Specific Aim 3: Identify information in the data base that predict developing of PTE.

- Use data to earmark Veterans with higher risk of epilepsy
 - MRI
 - Cognitive data
 - EEG
- Early identification and treatment (identify false negatives)
- Could allow for prophylaxis studies

Develop tools to identify the onset of post-traumatic epilepsy in Veterans with TBI.

- Target TBI positives and repeat screening for epilepsy longitudinally
 - Vietnam study, about 12% developed epilepsy 15 years or more after the trauma

Take Home Messages

- The more severe the TBI, the more likely to develop epilepsy
- We have no prophylactic treatment for PTE
- PTSD and PTE may co-exist and diagnosis may not be clear
- Need to evaluate patients with intractable epilepsy with video-EEG monitoring which can be obtained through ECoE