First Seizure: Diagnosis and Treatment

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Weill Cornell Medicine-Qatar

Information healthcare practitioners can't afford to miss!

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Basim Uthman

DOES NOT have a financial interest in commercial products or services

Three Take-Home Messages

- Not everything that shakes is seizure
- Not every seizure is epilepsy
- Great majority of patients with epilepsy become seizure free

Learning Objectives

- Outline the essentials of a first seizure workup and application of a decision tree in the initiation of treatment
- Distinguish major etiological categories of epileptic seizures, differentiating provoked seizures from unprovoked seizures
- Identify whether the episode is a seizure or another phenomenon presenting as mimickers of seizures

Nonepileptic Seizures

- Syncope
- Alcohol/drug withdrawal
- Movement disorders
- Drug toxicity
- Parasomnias
- Hypo-glycemia/-calcemia/-natremia
- Hyperglycemia
- Psychogenic

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GTC Sz vs Syncope (Harrison's 14th Ed., T 365-6, P 2319)

Feature	Seizure	Syncope
Precipitating Factor	Generally none	Pain, Emotion, Valsalva
Premonitory symptoms	None or vague	Tunneling/blurred vision, nausea, diaphoresis
Posture at onset	Any posture	Generally standing
Transition to unconsciousness	Immediate	Gradual over seconds
Duration of unconsciousness	Minutes	Seconds
Duration of tonic/clonic mvmnts	30-60 seconds	<15 seconds (if present at all)
Facial appearance	Cyanotic	Pallid
Post event confusion or lethargy	Minutes-hours	<5 minutes (if present)
Tongue biting	Occasionally	Rarely
Bladder Incontinence	Occasionally	Sometimes
Elevated CPK, myalgias	Frequent	Sometimes

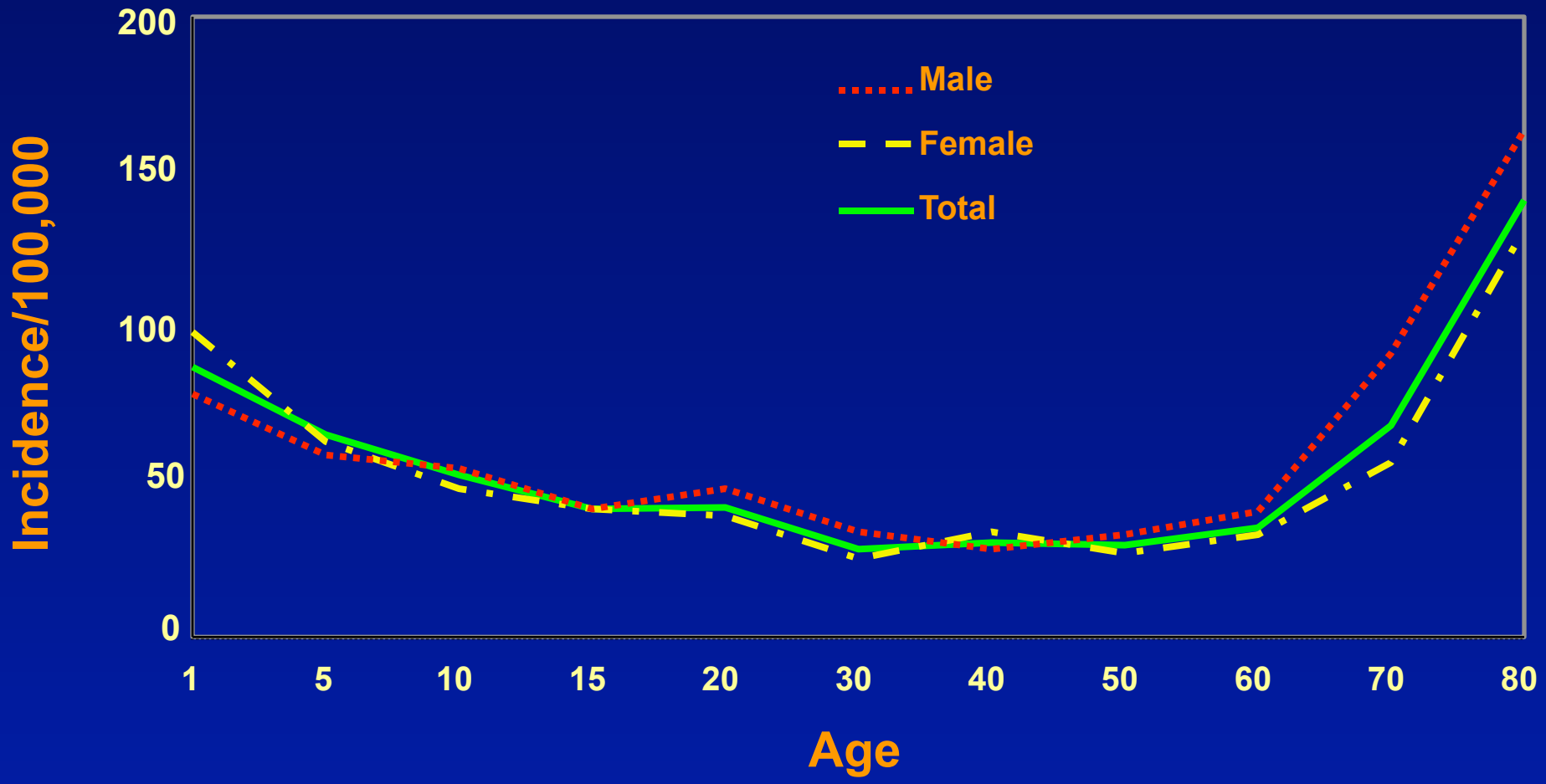

1% : Prevalence of
Epilepsy in Gen. Pop.
GATORS
85,000 +

Epilepsy Prevalence and Burden

- 10% of Americans will have a seizure in their lifetime
  - By age 75, 3% will have developed epilepsy
  - ~65% achieve seizure control, 25% or more have intractable epilepsy
- The costs of epilepsy are considerable
  - Total Annual cost in US: $12.5 Billion ($10.8 Billion indirect cost; mainly employment related)
  - Social, personal and intellectual disability can be devastating

Epilepsy Foundation of America; accessed 12/01

Incidence of Epilepsy
Rochester, Minn 1935-84



Hauser, *Epilepsia*, 33: 1992.

Most Important Step in Treating Epilepsy
Careful Diagnosis

- Careful history to identify:
  - seizure types
  - risk factors
  - provoking causes
  - Triggering factors
- Physical and neurological examination
  - Signs or symptoms of focality
  - Signs of toxicity
- Laboratory investigation
  - EEG
  - Neuroimaging
  - Blood tests
  - LP

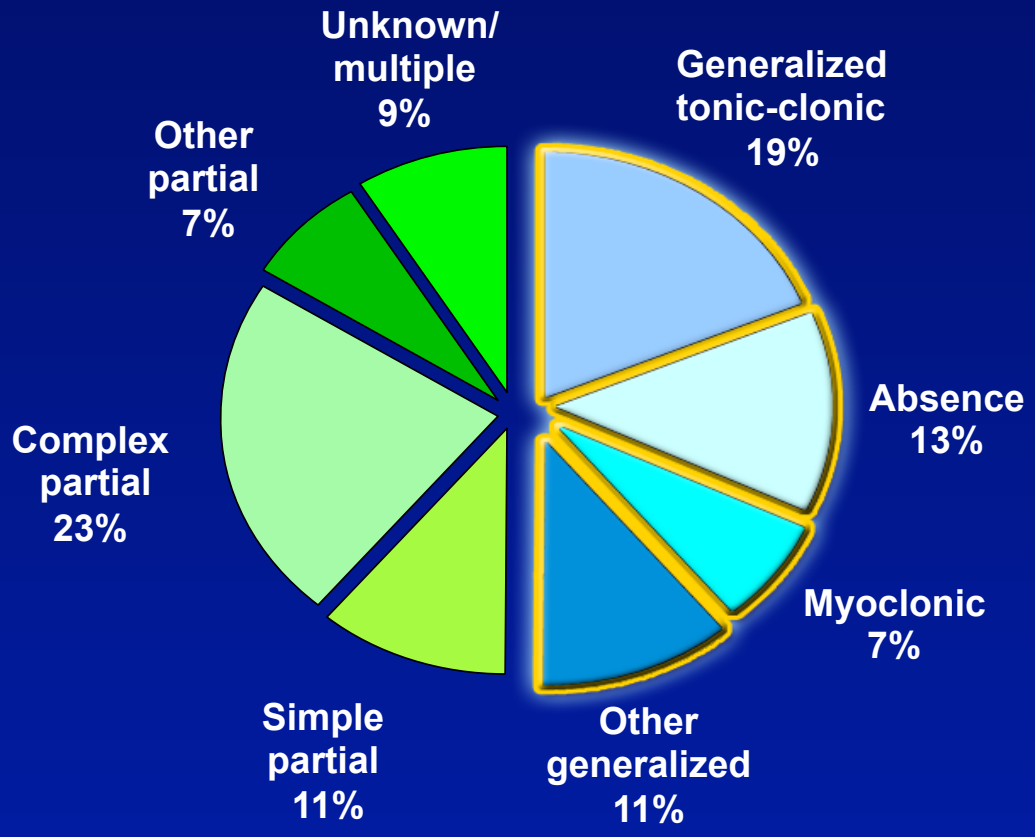
Classification of Seizure Types

- Partial Seizures
  - Simple partial (focal, local)
  - Complex partial
    - Impaired consciousness at outset
    - Simple partial evolving to impaired consciousness
  - Partial evolving to generalized seizures
- Generalized Seizures (loss of consciousness at outset)
  - Absence
  - Myoclonic
  - Tonic
  - Tonic-clonic
  - Clonic
  - Atonic

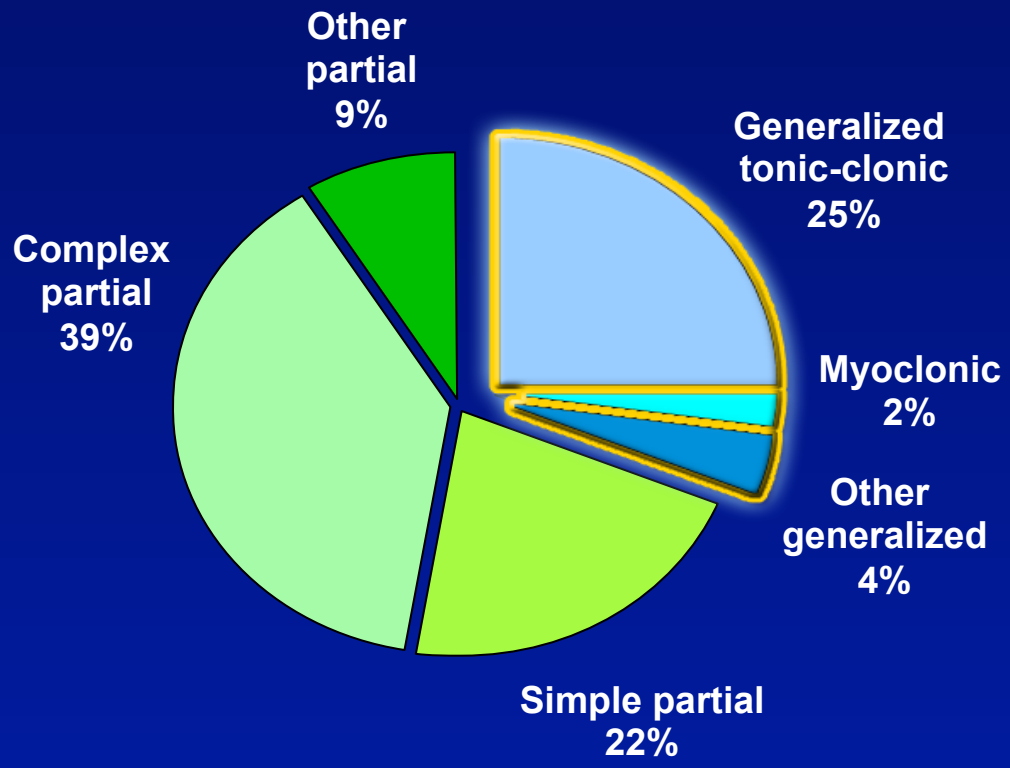
Commission on Classification and Terminology of the ILAE. *Epilepsia,* 1981; 22:489-501.

Prevalence of Generalized and Partial Seizures

Pediatric Patients <15 Years



Adults 35-64 Years



Hauser WA. 1992;33(suppl 4):S6-S14. Adapted with permission of Blackwell Publishing.

Classification of Seizures by Etiology

- Idiopathic
  - Age related onset
  - Clinical and electroencephalographic characteristics
  - Presumed genetic etiology
- Symptomatic
  - CNS disorder or lesion
- Cryptogenic
  - Presumed symptomatic
  - Etiology unknown

Wolf P. In: Engel J Jr. et al, eds. *Epilepsy: A Comprehensive Textbook. 1997:773-777.*

Seizure v/s Epilepsy

- A seizure can be a one time event that can be caused/provoked by one of many transient disorders
- Epilepsy is a disorder characterized by 2 or more unprovoked seizures and a high likelihood of seizure recurrence

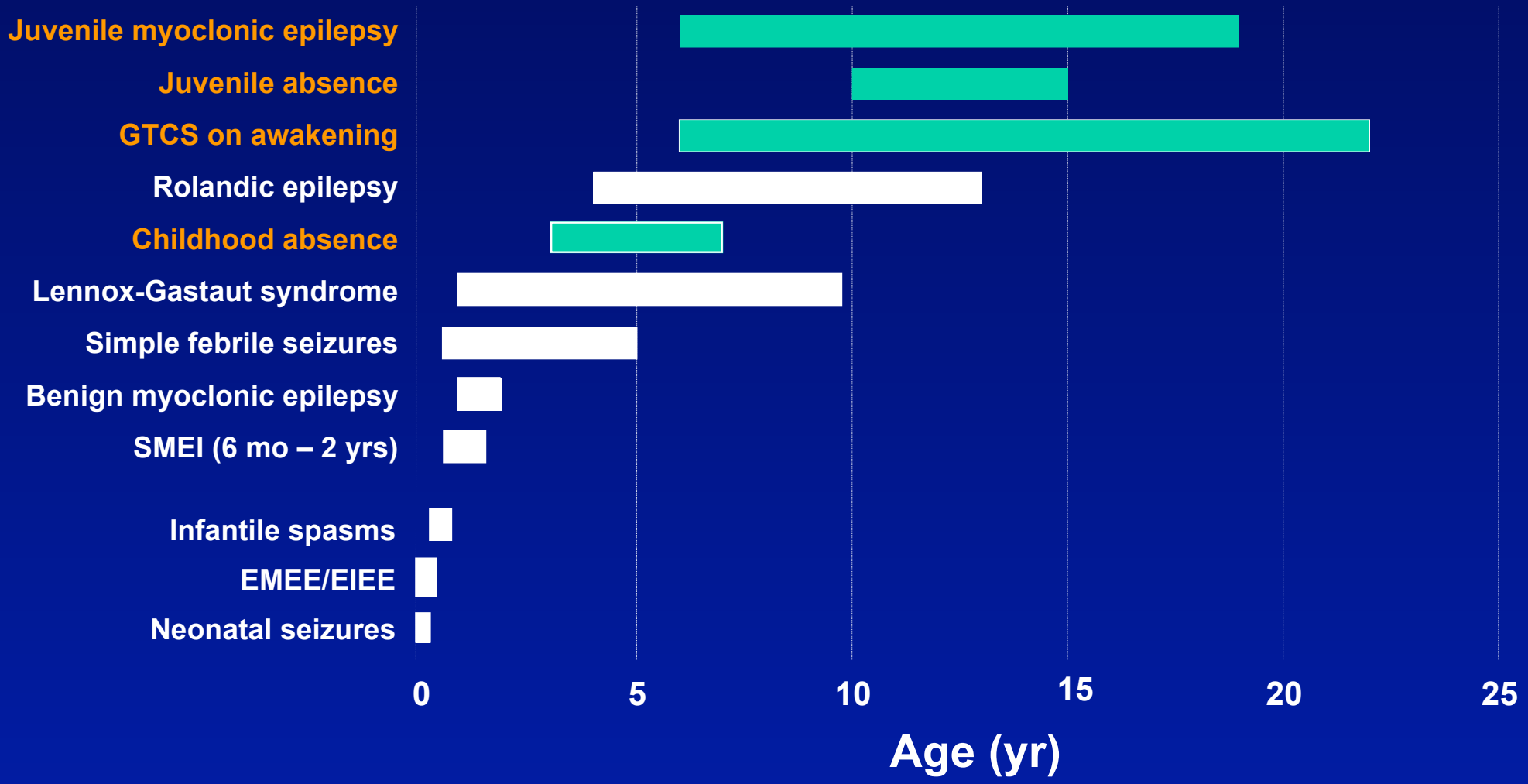
Seizure Type vs Epileptic Syndrome

A seizure type is determined by the patient's behavior and the EEG pattern during the ictal event

An epileptic syndrome is determined by:

- seizure type(s)
- natural history
- EEG (ictal and interictal)
- response to AEDs
- etiology
- age at onset

Seizures and Syndromes: Age of Onset



Courtesy of John M. Pellock, MD

Seizure Types in IGE Syndromes

Epilepsy Type	Frequency (%)		
	Tonic-clonic or clonic-tonic-clonic	Absence	Myoclonic
CAE	30 – 60	100	-
JME	80 – 95	7 – 38	100
JAE	Common	100	14-20

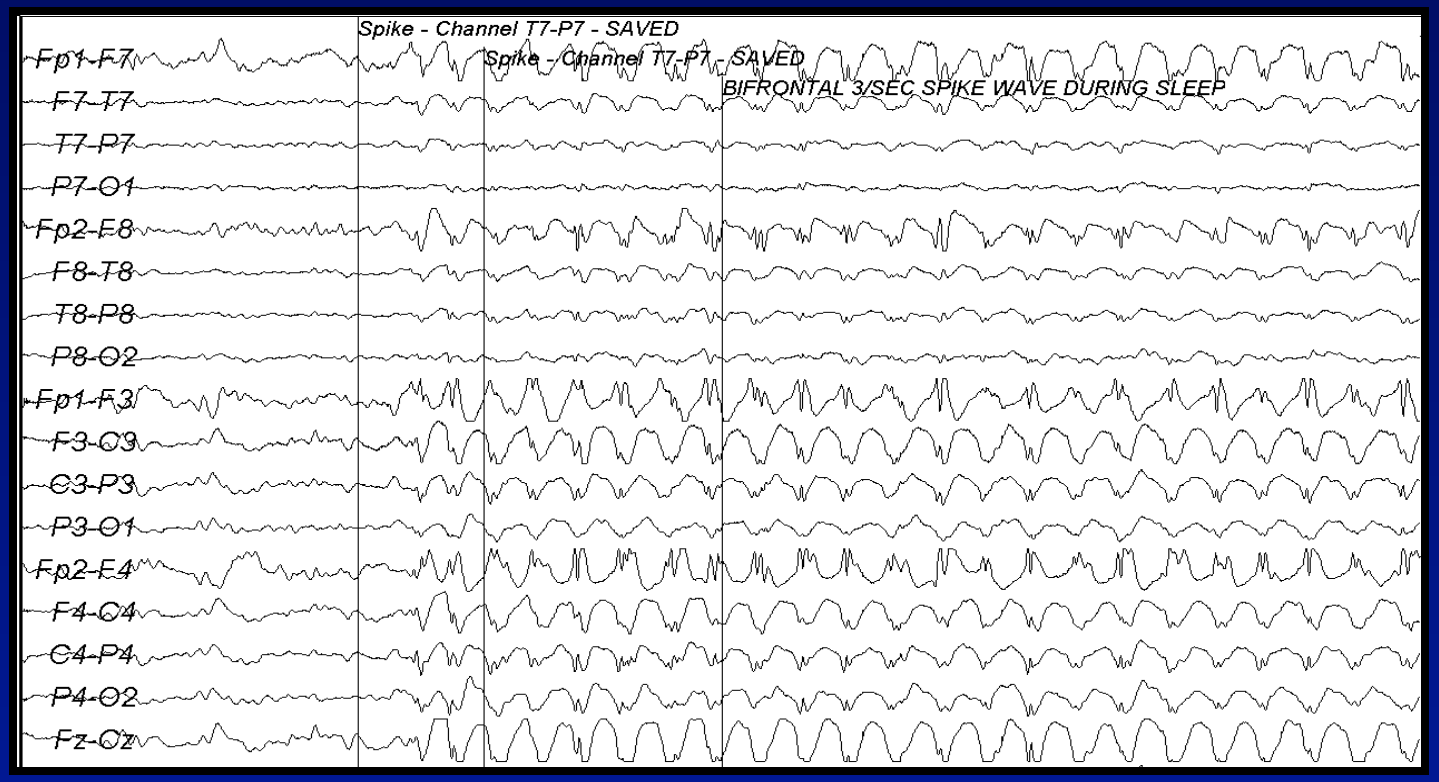
CAE = Childhood absence epilepsy; JME = juvenile myoclonic epilepsy;
JAE = juvenile absence epilepsy

Adapted from Duron RM, et al. Epilepsia. 2005;46:34-47.

Primary Generalized Epilepsy: Childhood Absence Epilepsy

- Onset between ages 4 – 8; peak 6 – 7 yrs
- Frequent, brief absence seizures
- Normal intelligence
- No imaging abnormalities
- EEG – well-organized spike wave pattern; typically 3 – 4 Hz

Childhood Absence Epilepsy

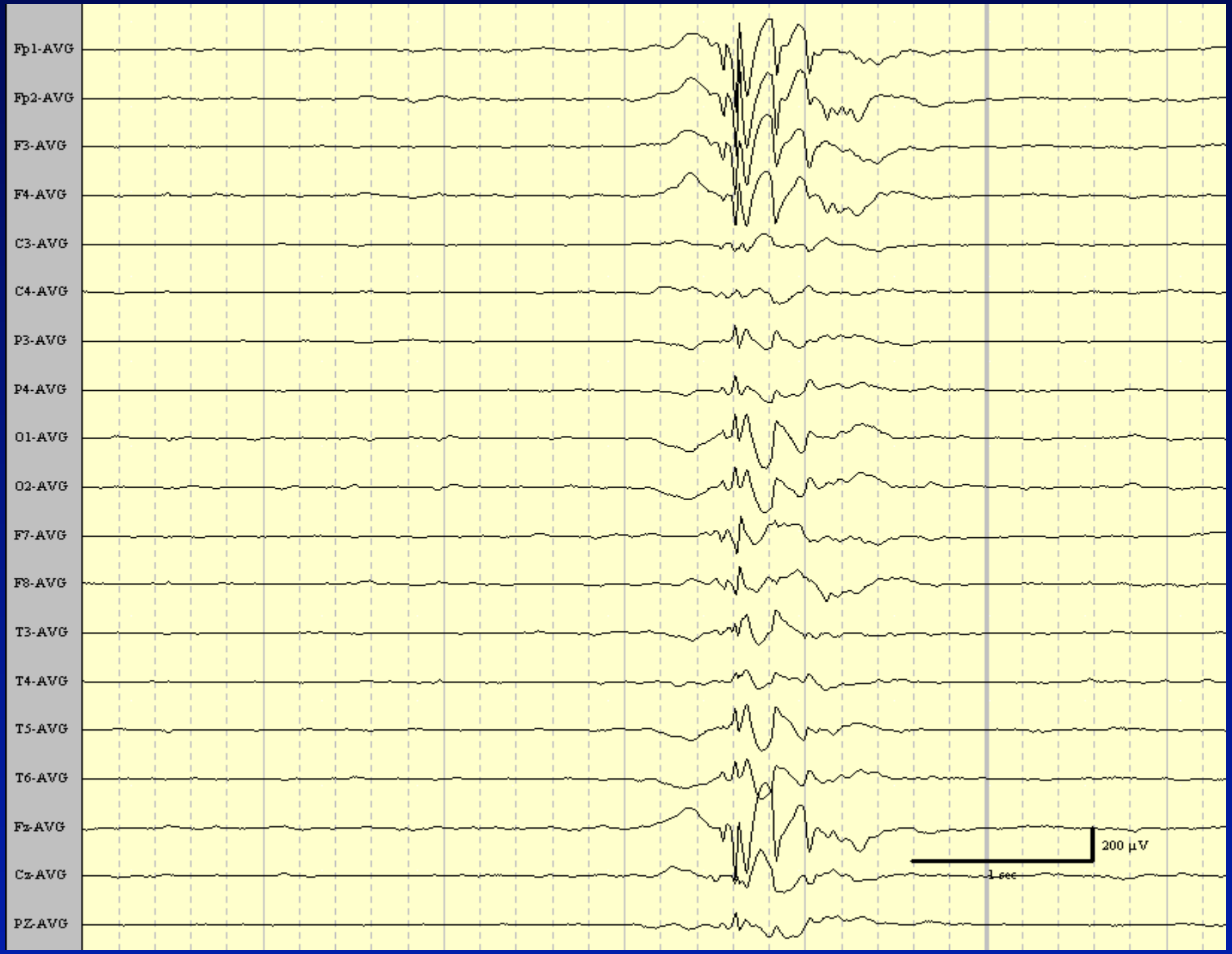


3 cps bilateral spike-wave discharges during sleep

D. H. Primary Generalized Discharge 01/02

Primary Generalized Epilepsy: Juvenile Myoclonic Epilepsy (JME)

- Most common primary generalized epilepsy
  - 7% of all epilepsy
- Onset typically in teens
- Myoclonic seizures in all
  - Often after awakening
- Most patients have GTCS at some time
- 30% have absence
- Seizures exacerbated by sleep deprivation, alcohol, photic stimulation
- Exam and MRI normal
- EEG may show 4-6 Hz polyspike in generalized pattern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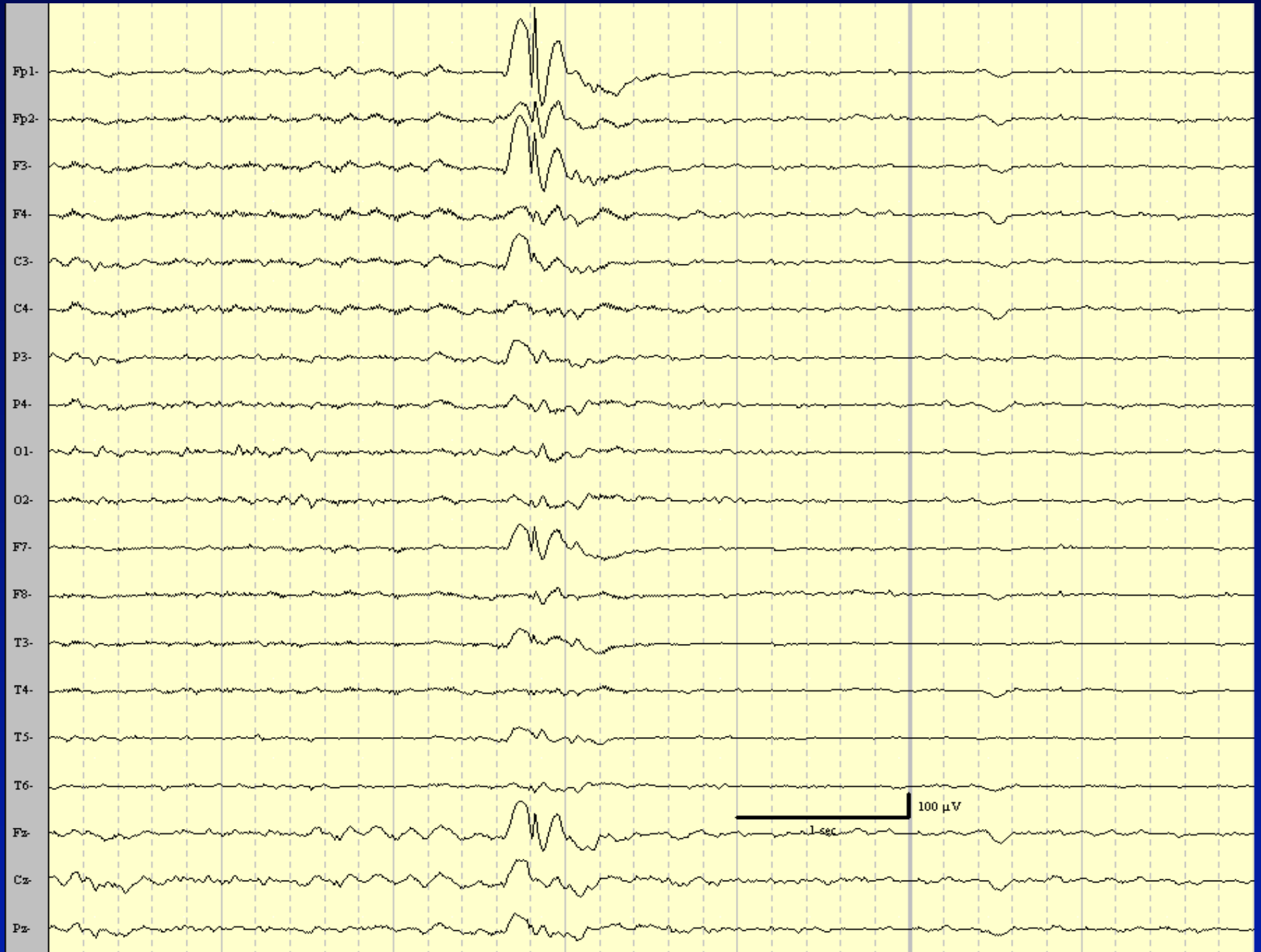
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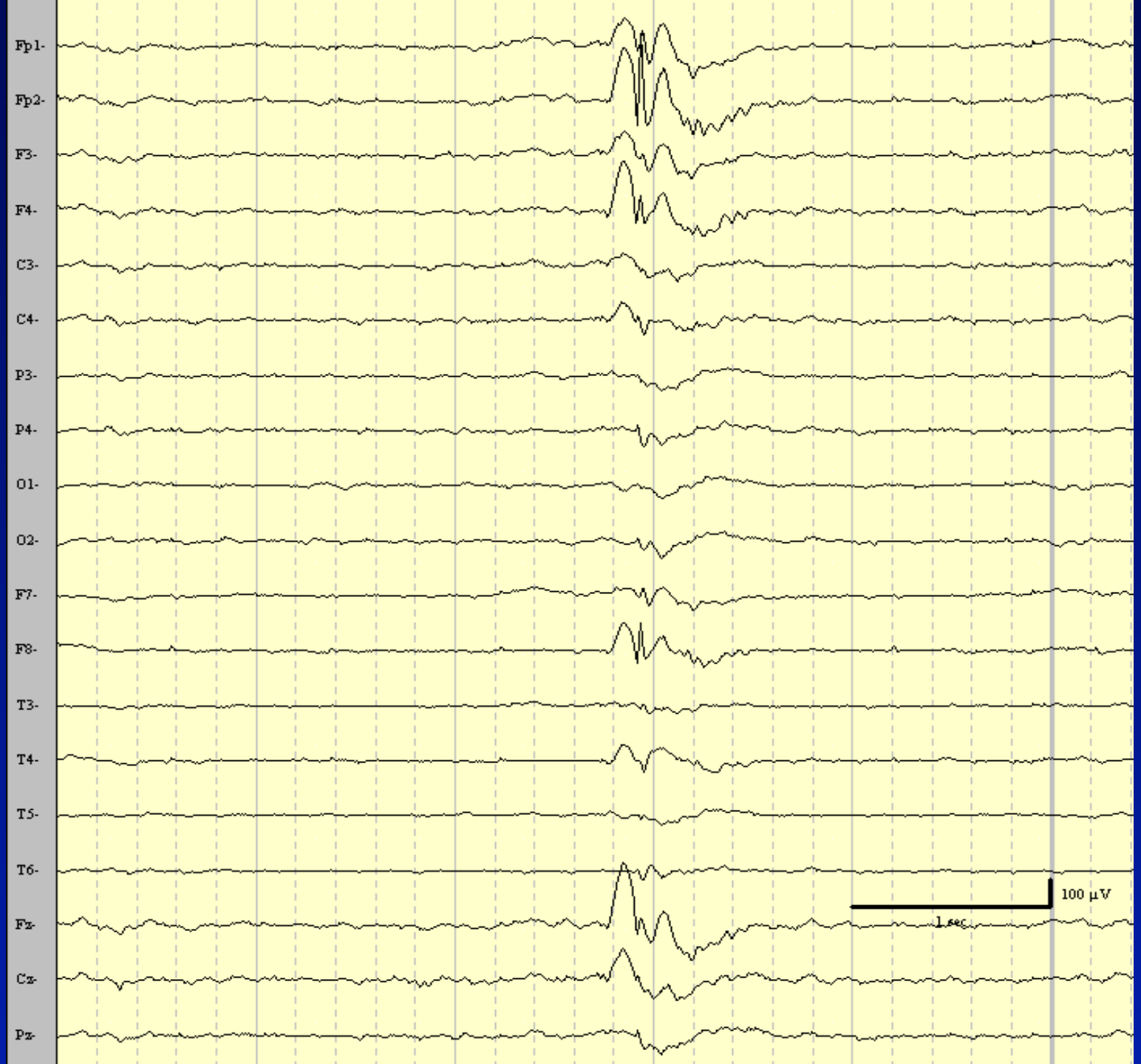
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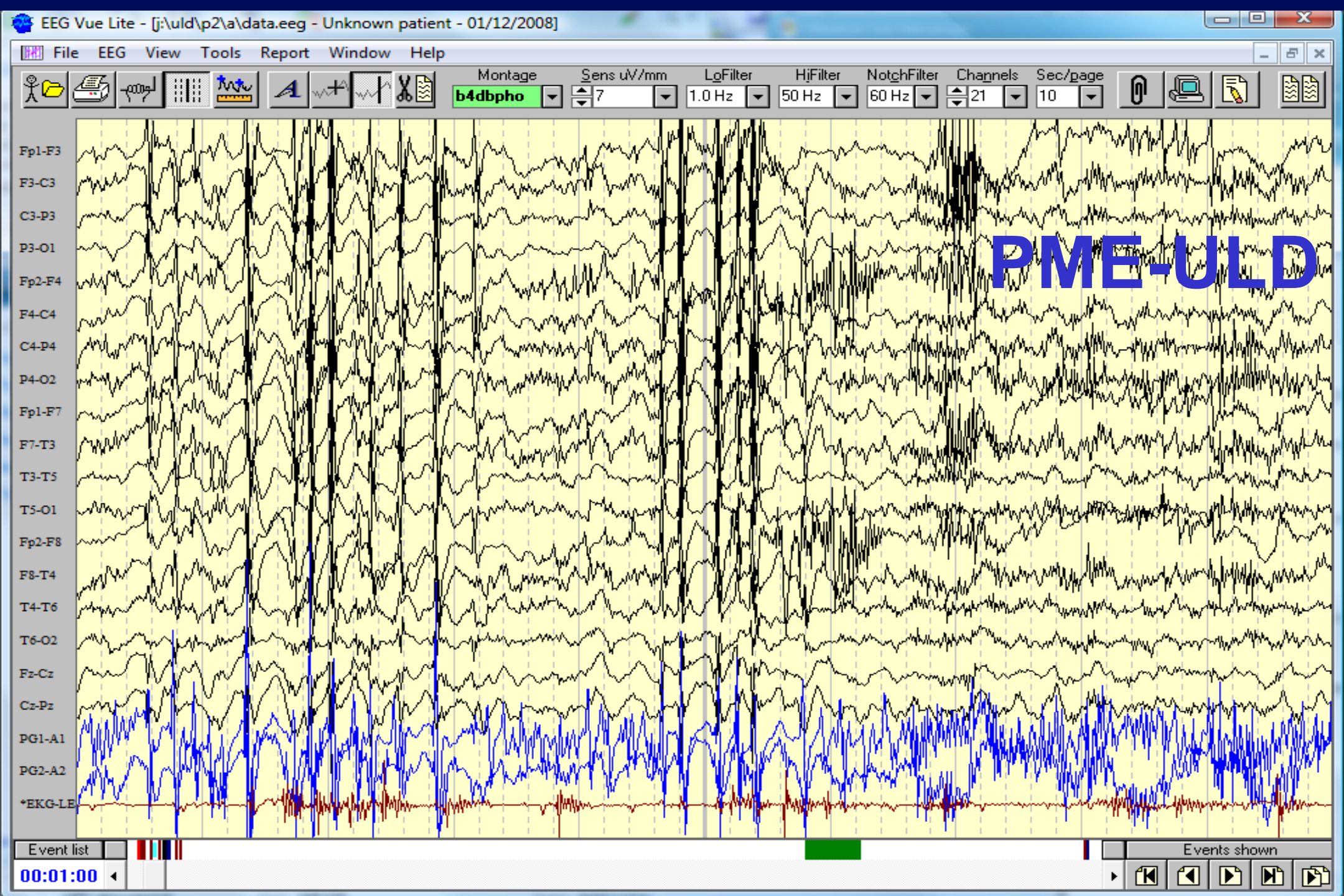
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Case Presentation

- A 7 years old boy was referred to ER because of facial twitching associated with speech arrest
- The spells are brief, lasting no more than 1 min

Case Presentation
Witness Account of the Event

On awakening at 5 AM he come into his parents' room c/o « a slobber »

Not able to speak initially

Then he told his parents « I had a funny feeling in my tongue and mouth, there was a lot of saliva, and then my cheek twitched»

Case Presentation

- The boy reports one similar episode
  - 6 months prior to presentation
  - With a brief clonic activity of the left hand & arm

Case Presentation

- Normal physical exam
- No developmental delay
  - He is in 2nd grade and doing well
- Family History
  - Epilepsy: 0
  - Tics: +


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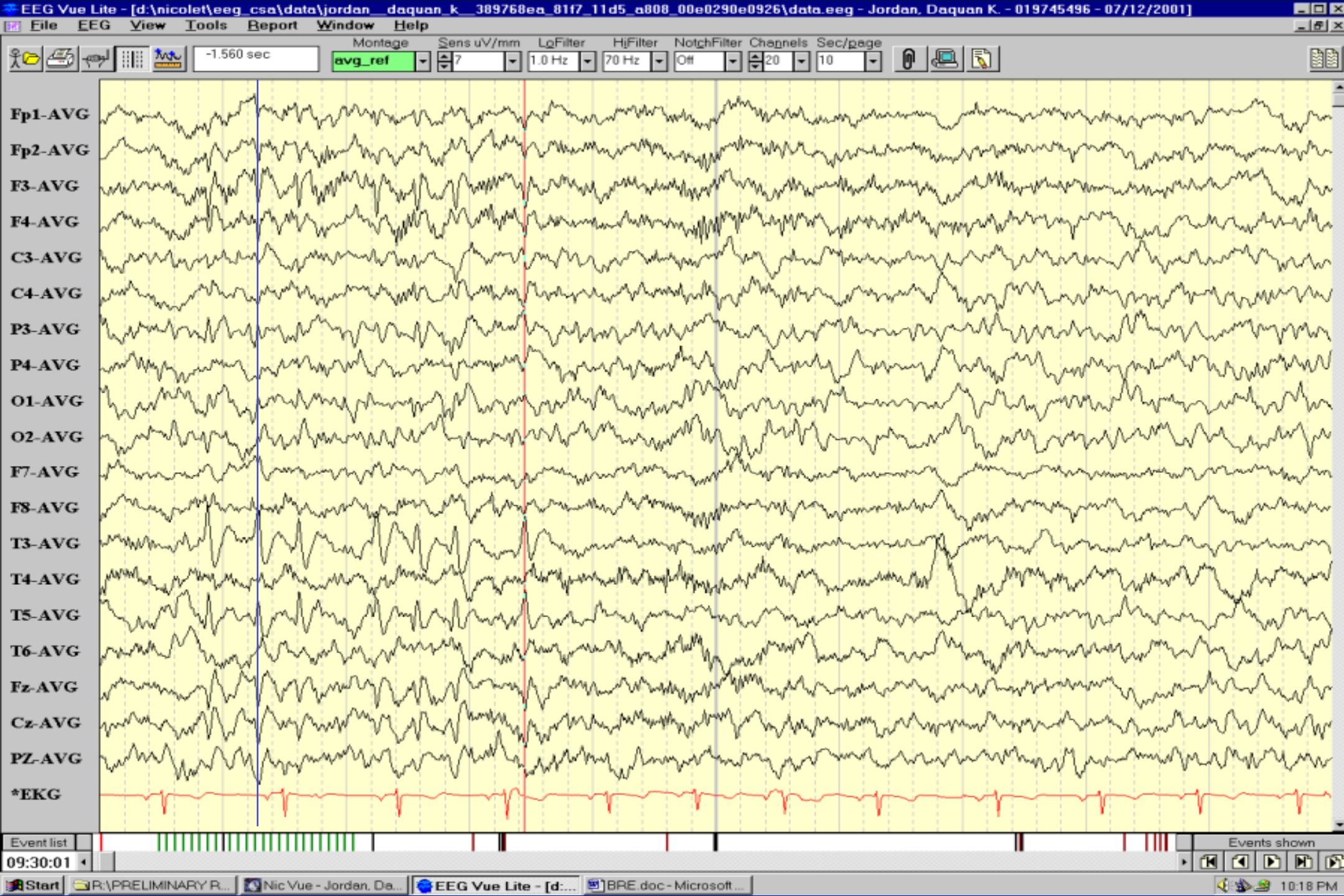
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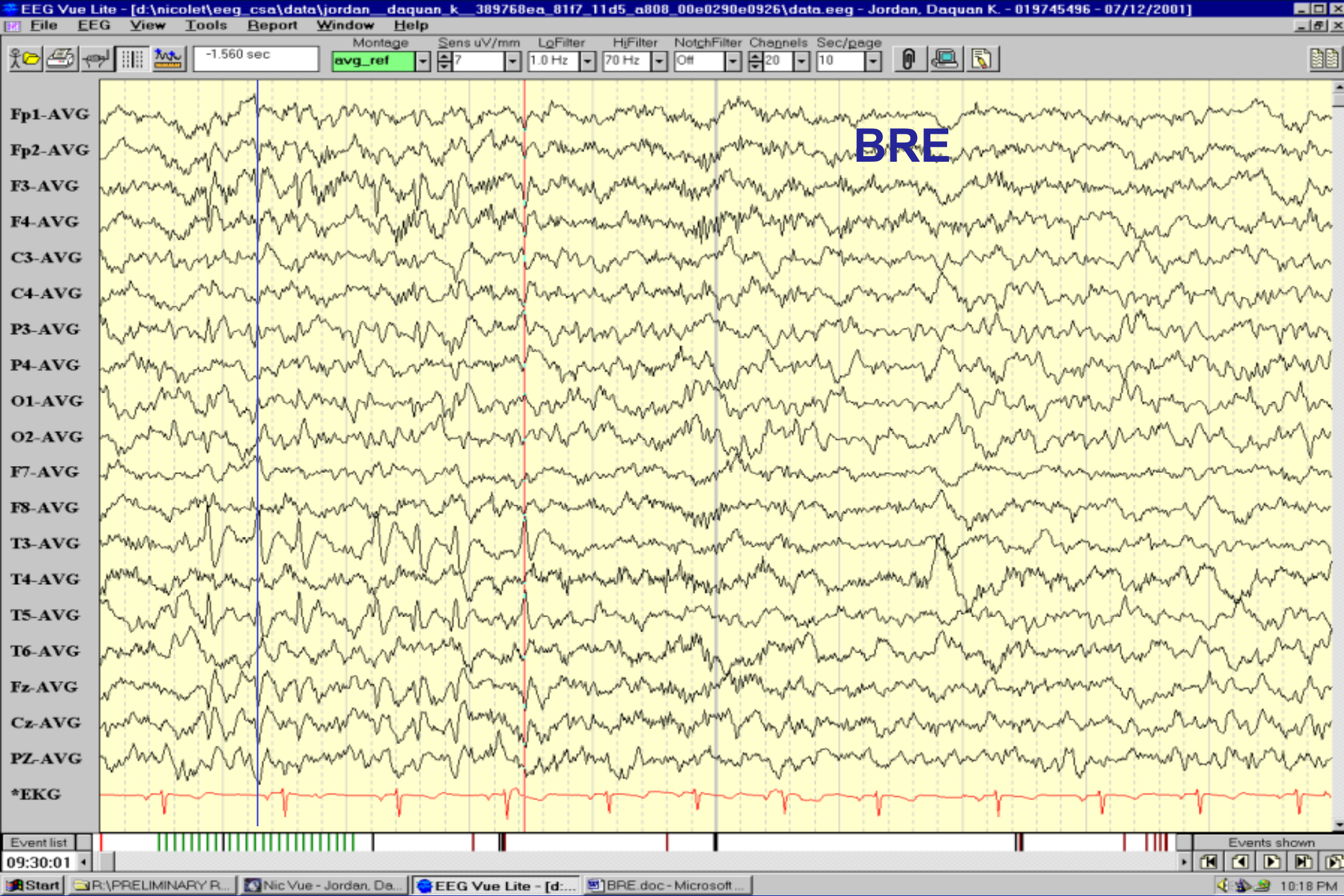
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Evaluation of the Patient with New Onset Seizures

- Careful history to identify:
  - seizure types
  - risk factors (head trauma, febrile seizures, family hx)
  - provoking causes (hypo-glycemia/natremia/calemia, hyperglycemia, uremia, alcohol, alcohol withdrawal, iatrogenic, etc.)
  - Triggering factors (sleep deprivation, stress)
- Physical and neurological examination
  - Signs of head trauma, congenital anomalies
  - Signs of focality (asymmetries) or mental retardation
  - Signs of toxicity
- EEG with sleep, HV, and IPS
  - Best yield for epileptiform activity is in the first 24 hours post-ictally
- Neuroimaging (depends on seizure types/epilepsy syndrome)
- Laboratory (CBC, CMP, toxic screen)
- LP?

Treatment of Epilepsy

- Medications
- Resective surgey
- Neurostimulation
- Diet

Antiepileptic Drugs - 2005

AED	Brand	Year
bromides		1857
phenobarbital	Luminal	1912
phenytoin	Dilantin	1937
primidone	Mysoline	1954
ethosuximde	Zarontin	1960
diazepam	Valium	1968
carbamazepine	Tegretol	1974
clonazepam	Klonopin	1975
Valpr/oic acid/ate	Depakene/Depakote	1978
clorazepate	Tranxene	1981
felbamate	Felbatol	1993
gabapentin	Neurontin	1993
lamotrigine	Lamictal	1994
topiramate	Topamax	1996
tiagabine	Gabitril	1997
levetiracetam	Keppra	1999
oxcarbazepine	Trileptal	2000
zonisamide	Zonegran	2000
Pregabalin	Lyrica	2005

Antiepileptic Drugs > 2005

AED	Brand	Year
Rufinamide	Banzel	2007/8
Lacosamide	Vimpat	2008
Vigabatrin	Sabril	1989/2009
Ezogabine	Potiga	2011
Perampanel	Fycompa	2012
Eslicarbazepine	Aptiom	2013

AED Adverse Events

- AEDs are mostly well tolerated
- Some patients experience AEs
  - Dose related
  - Chronic use
  - Idiosyncratic

Epilepsy Is a Serious Disorder

- Seizures cause injuries
- Seizures cause social problems
- Epilepsy causes death
- The most desirable treatment outcome is 100% seizure control

Early Identification of Refractory Epilepsy

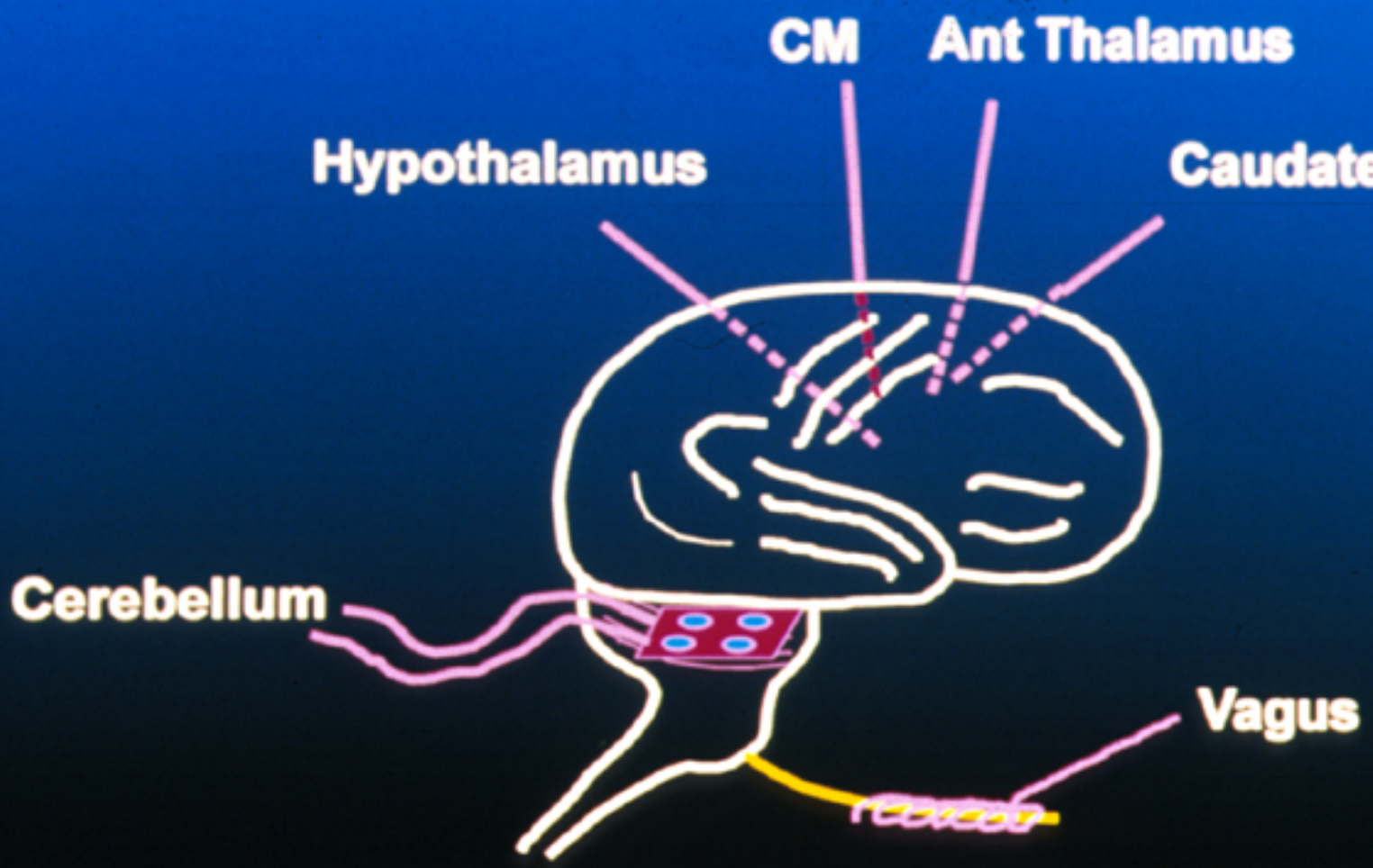
	Probability of Control
Before any drug tried	64%
After the first drug failed*	32%
After the second drug failed	9.6%
After the third drug or a combination failed	0

*If failure of drug 1 due to lack of efficacy: 11% probability; If failure of drug 1 due to idiosyncratic reaction: 55% probability; Kwan P, Brodie MJ. N Engl J Med. 2000(Feb 3);342(5):314-319

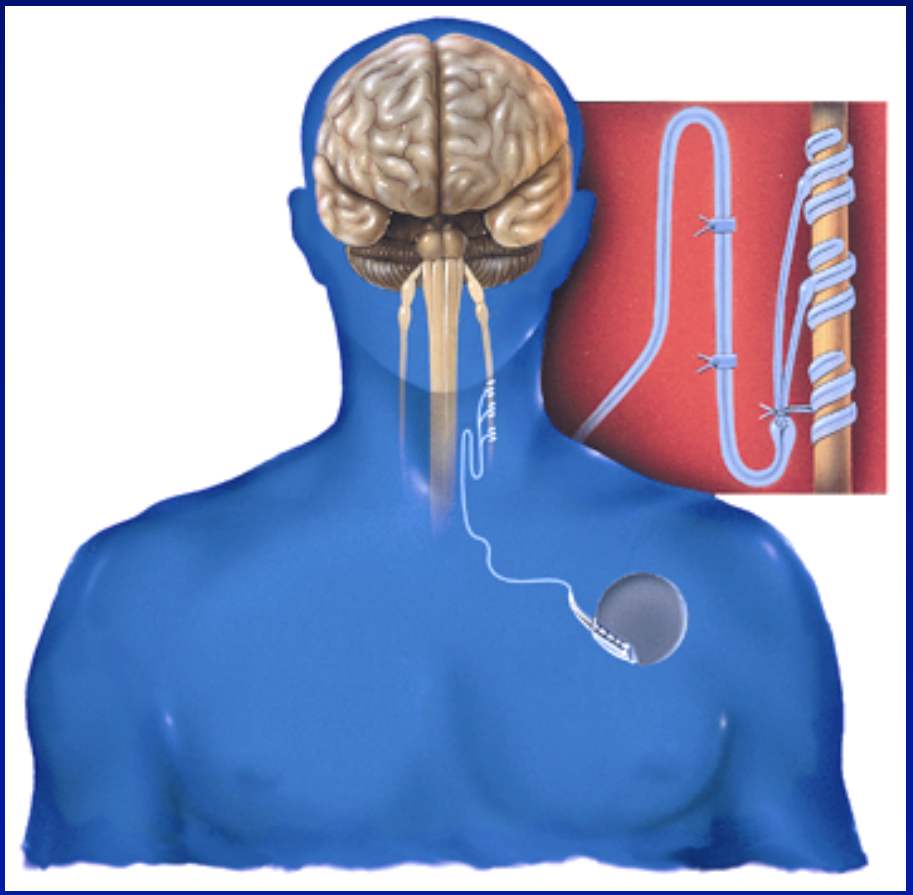
Medically Intractable Epilepsy

- When 2-3 AEDs fail to control seizures refer to a Comprehensive Epilepsy Center and consider other options
  - Epilepsy surgery
  - Ketogenic diet
  - Neurostimulation

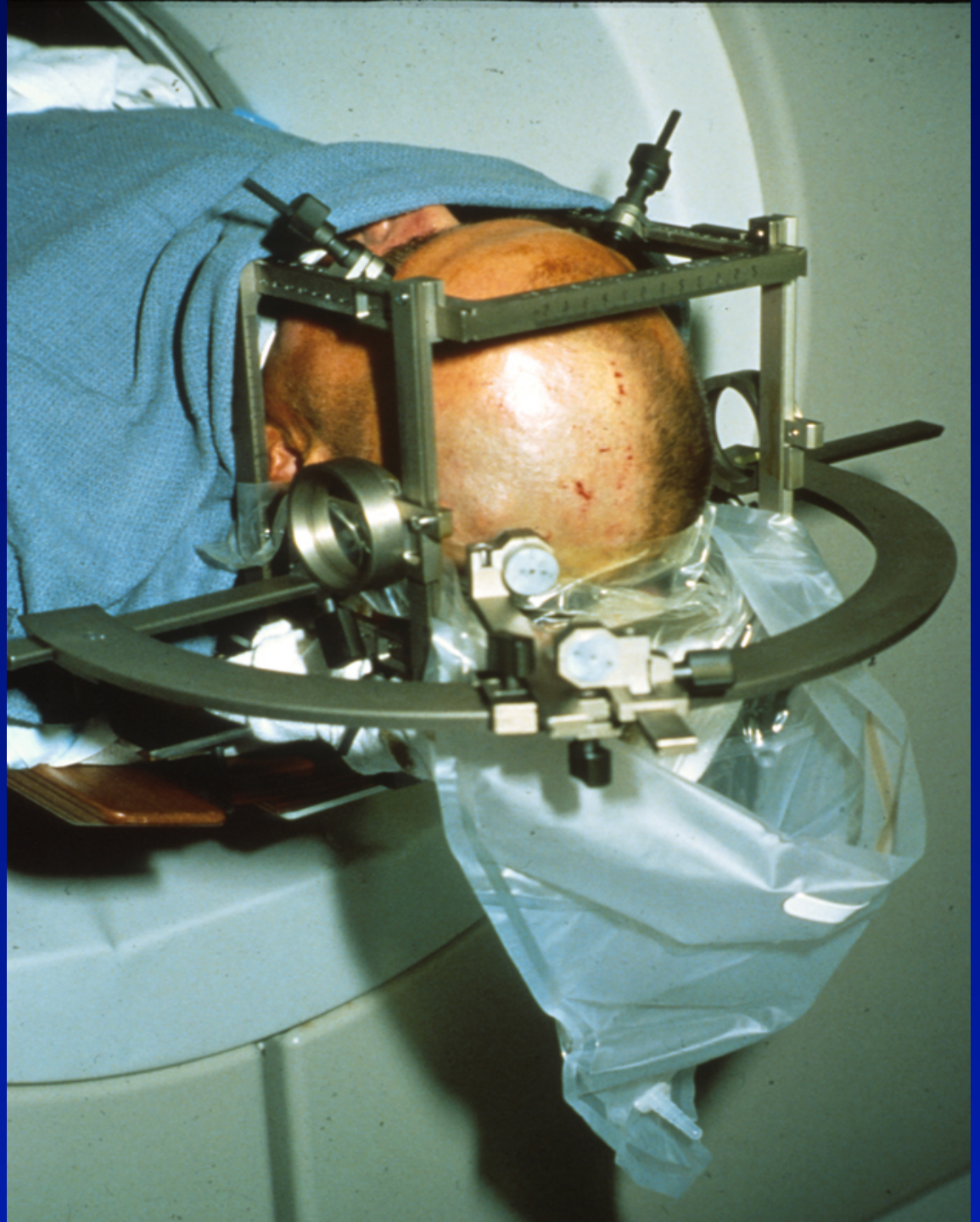
Electrical Stimulation Therapy for Epilepsy



The NCP System:
An Implantable Vagus Nerve Stimulator



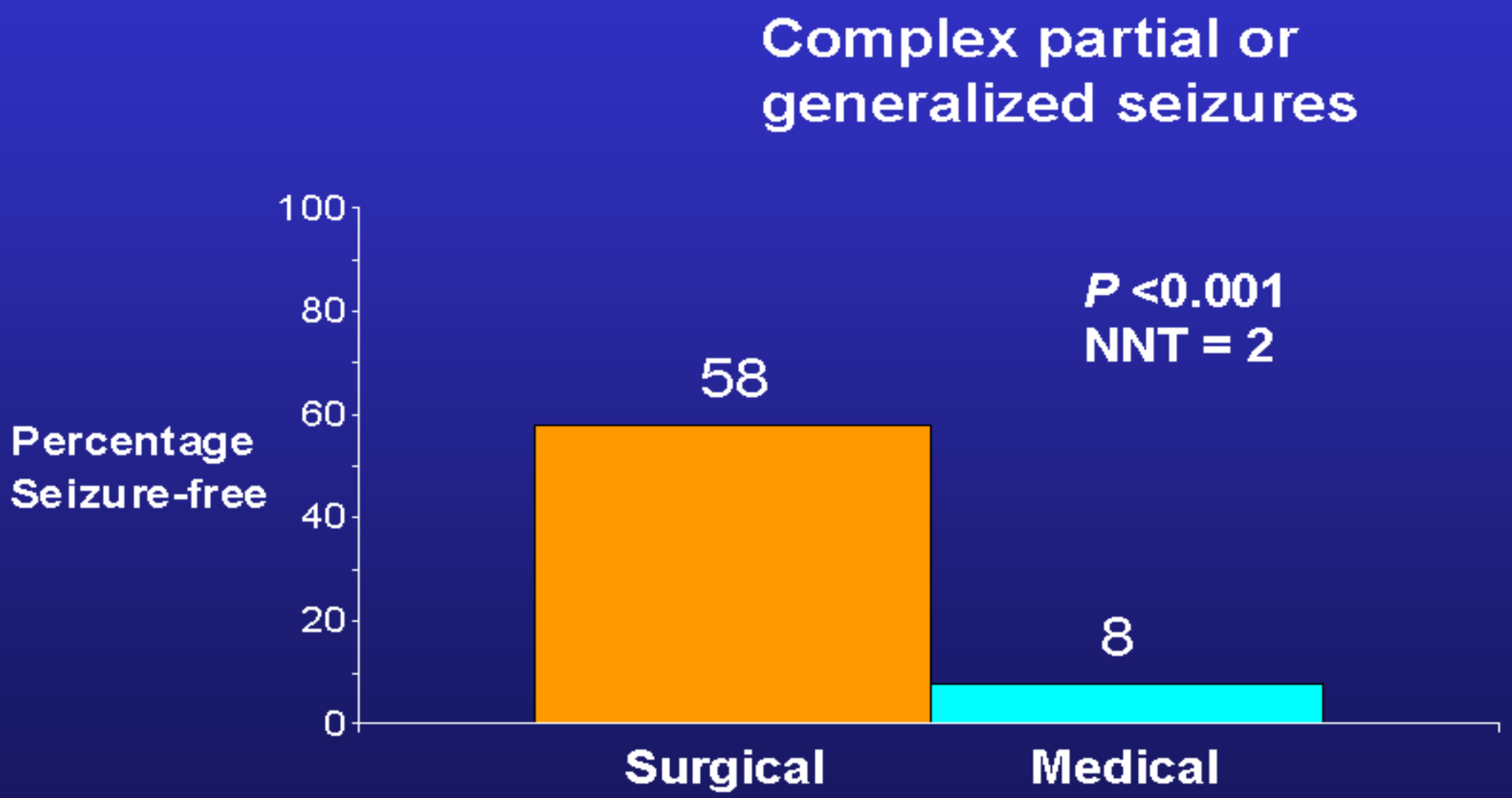
Stereotaxic Technique



Epilepsy Surgery

- Consider when 2-3 drugs fail
- Age is no barrier: consider children and consider older patients if healthy
- Not a last resort
- Safer than poor seizure control

Seizure Freedom at 12 Months



Wiebe S, et al. *N Engl J Med*. 2001;345(5):311-318.

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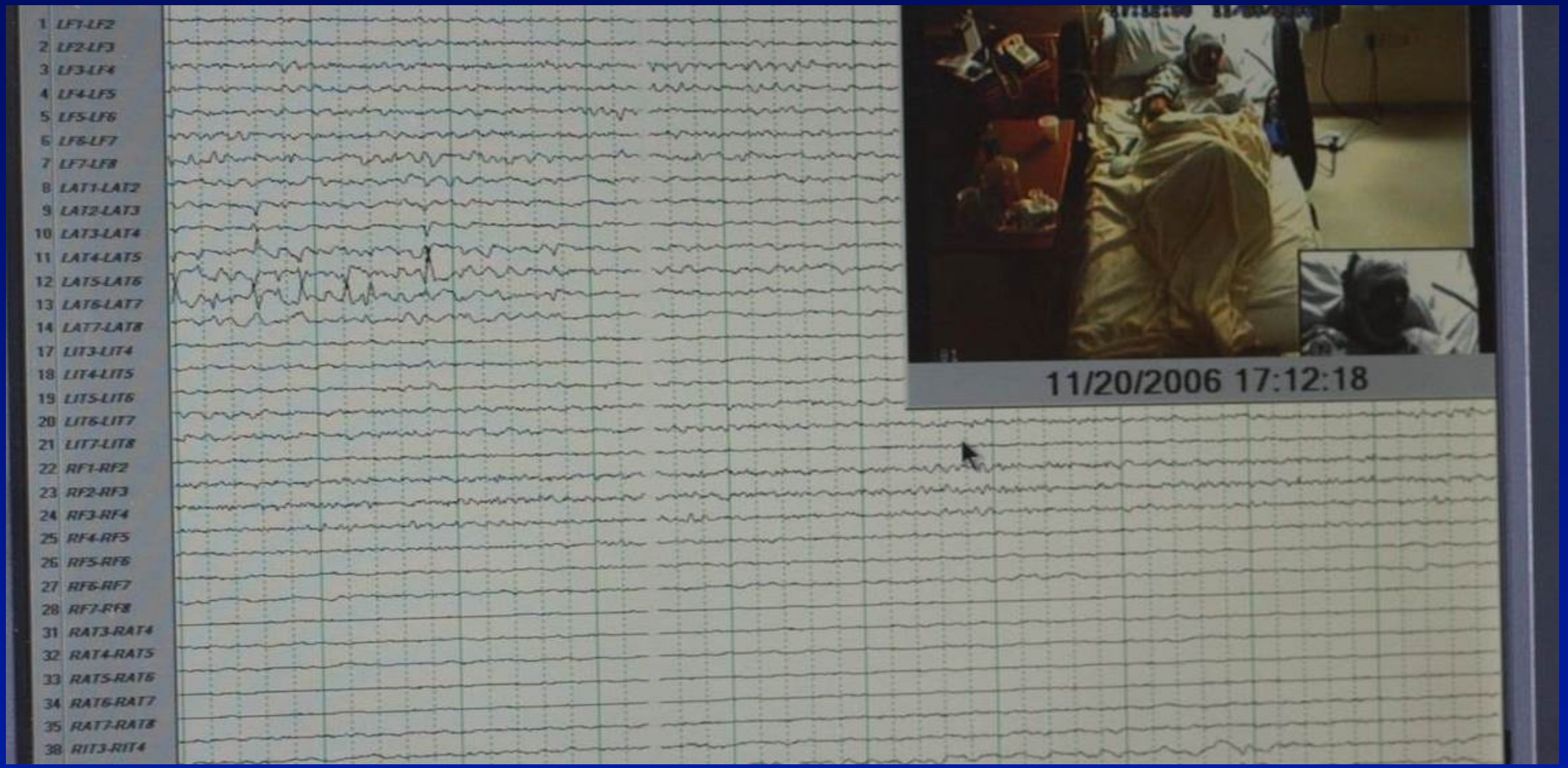
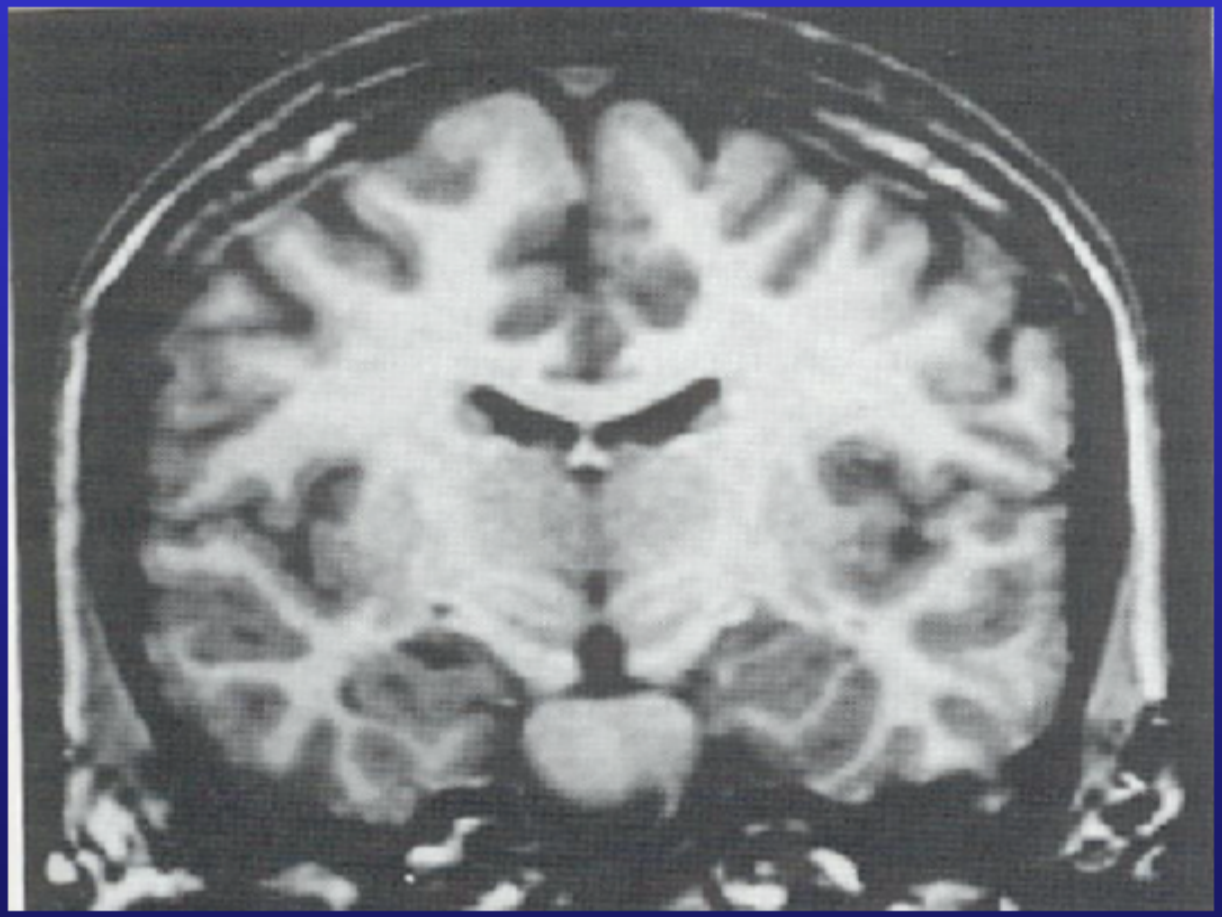
EMU Monitoring



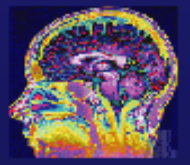
Johns Hopkins Medicine

Magnetic Resonance Images



Right hippocampal atrophy in a 34-year-old man with uncontrolled complex partial seizures

Courtesy of Basim M. Uthman, MD

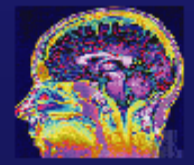


Johns Hopkins Medicine

Magnetic Resonance Images

Vascular malformation with hemorrhage in a 74-year-old woman with 40-year history of complex partial seizures – axial view

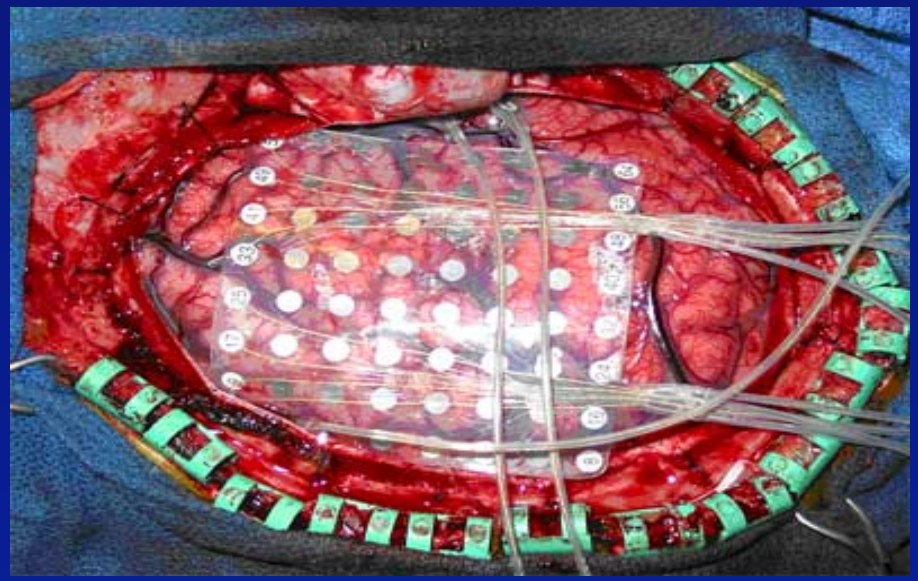
Courtesy of Basim M. Uthman, MD



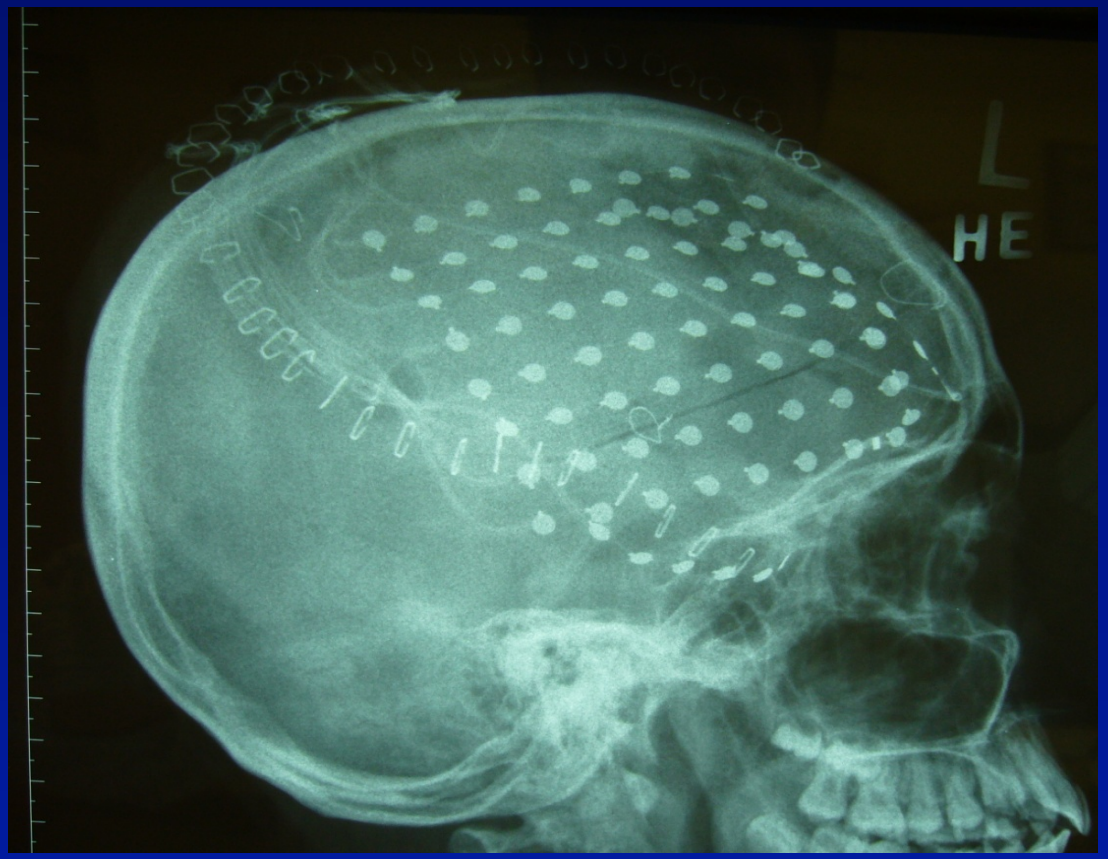
Invasive Procedures For evaluation

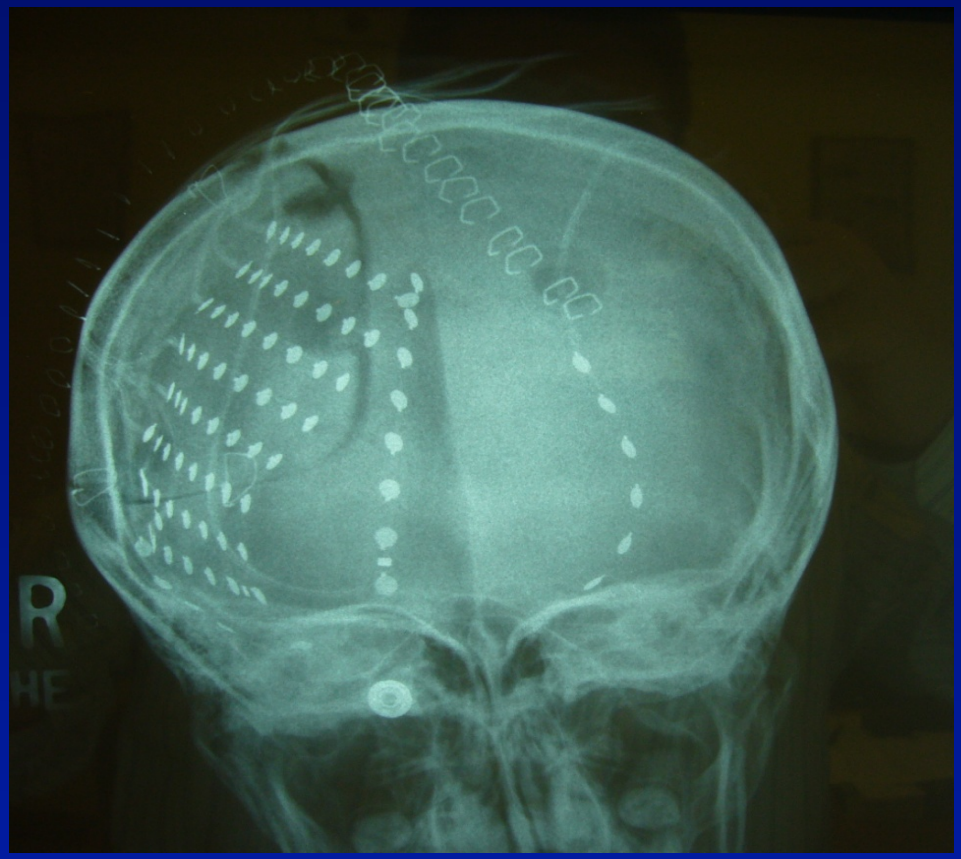
Stereotactic
Depth Electrodes

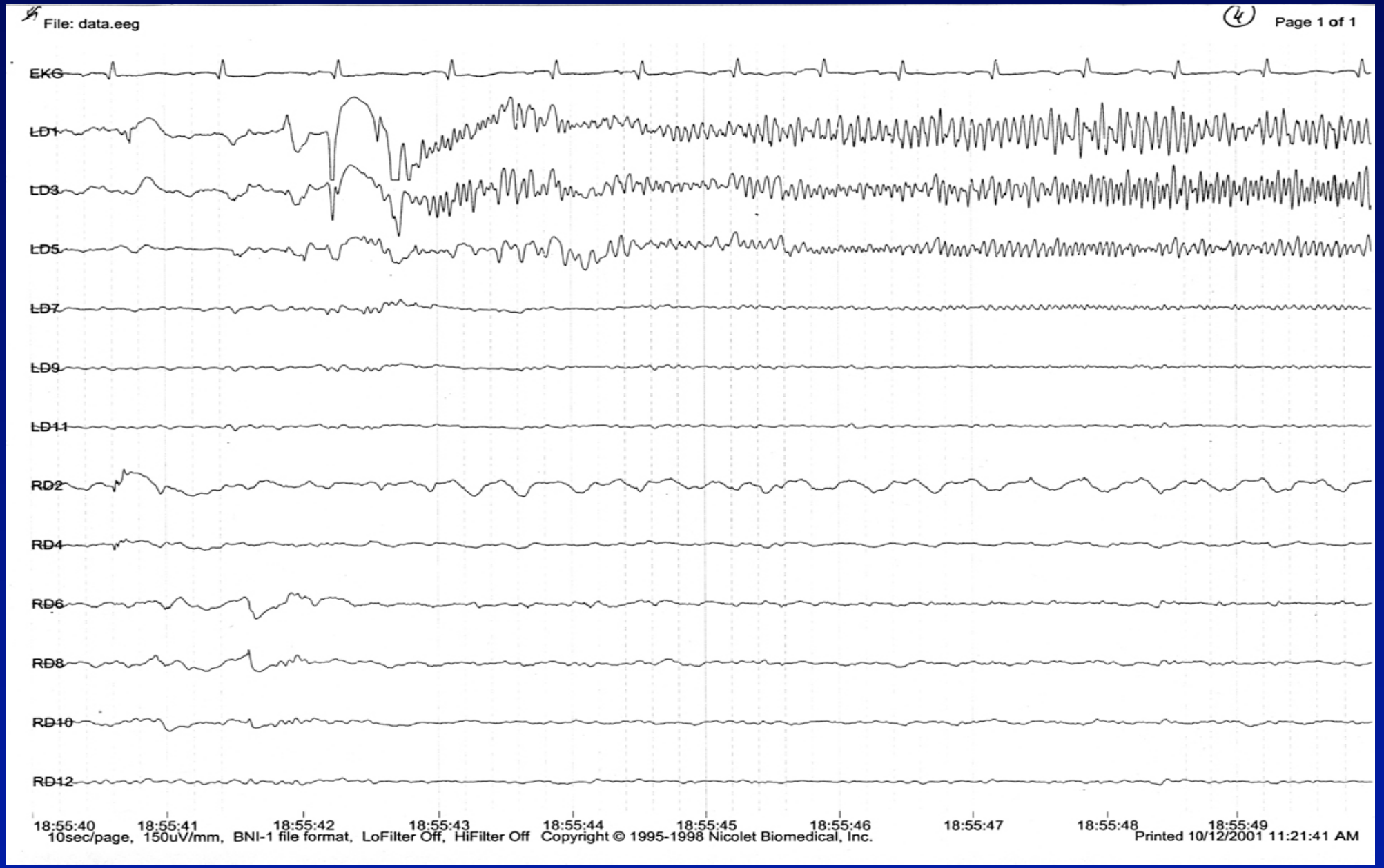
Craniotomy/Insertion
Of Subdural grids



Subdural Electrodes



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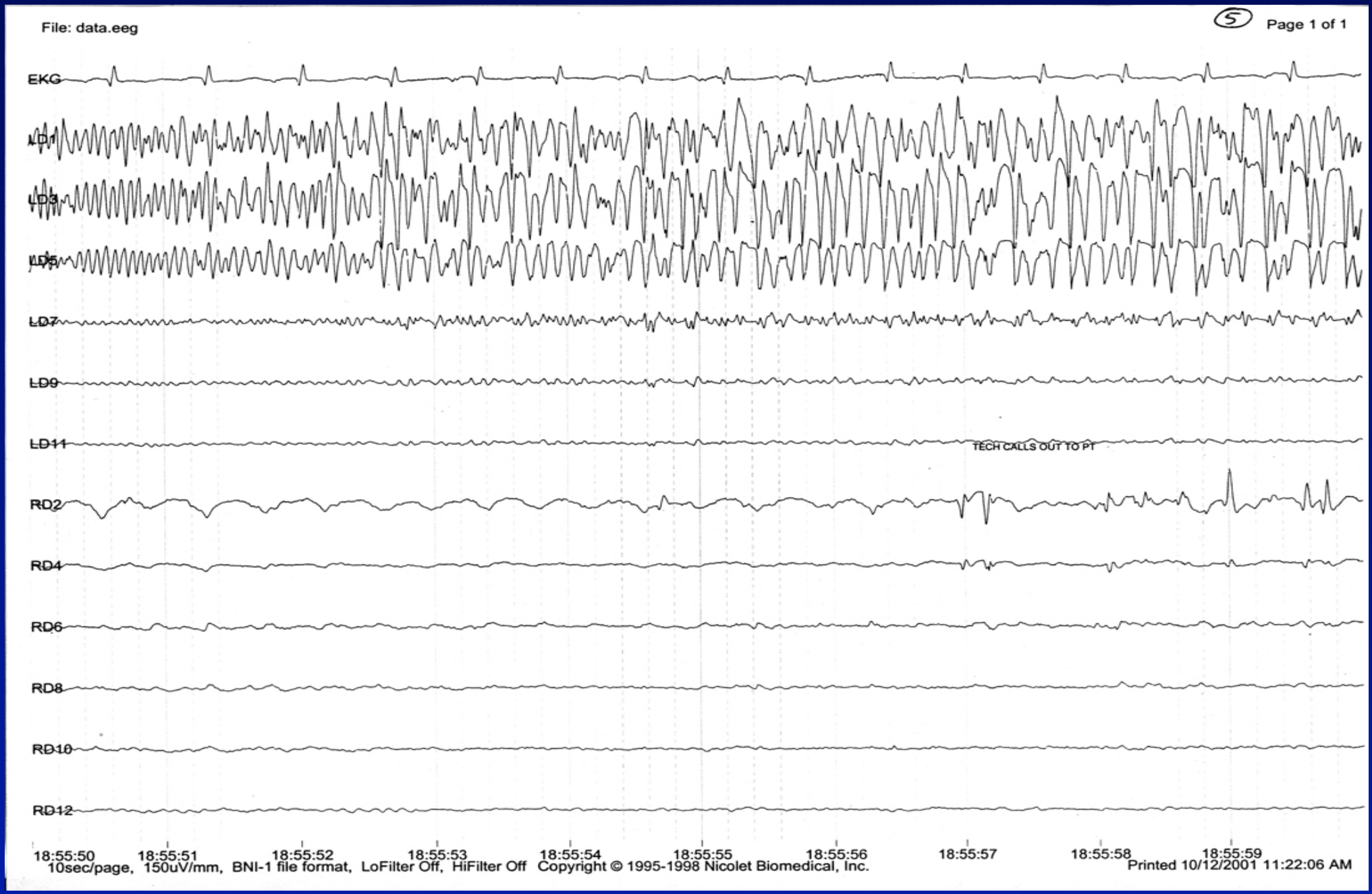
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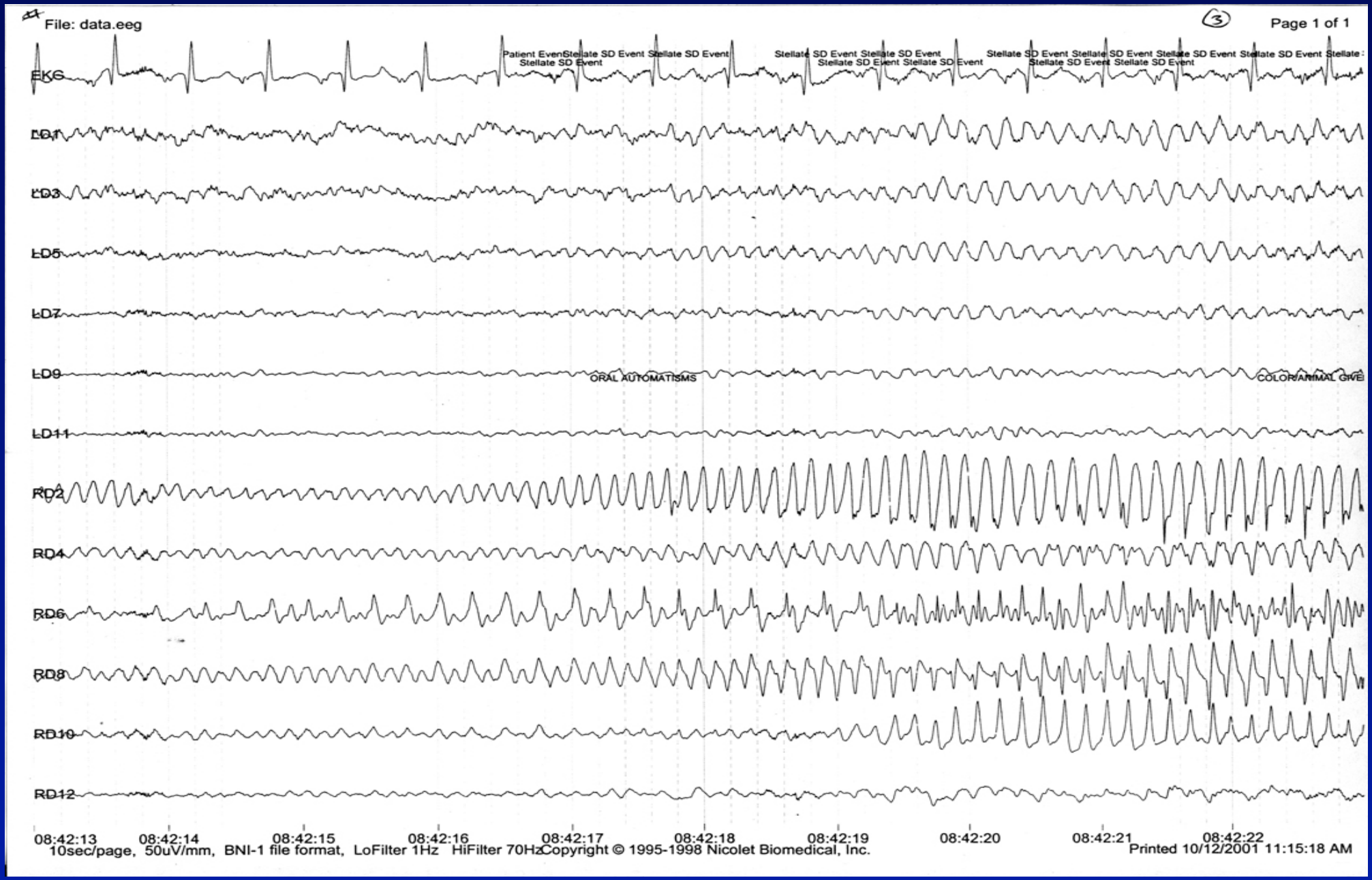
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LD1
LD3
LD5
LD7
LD9
LD11
RD2
RD4
RD6
RD8
RD10
RD12
Patient Event
Stellate SD Event
ORAL AUTOMATISMS
COLOR/ANIMAL GIVE
08:42:13
08:42:14
08:42:15
08:42:16
08:42:17
08:42:18
08:42:19
08:42:20
08:42:21
08:42:22
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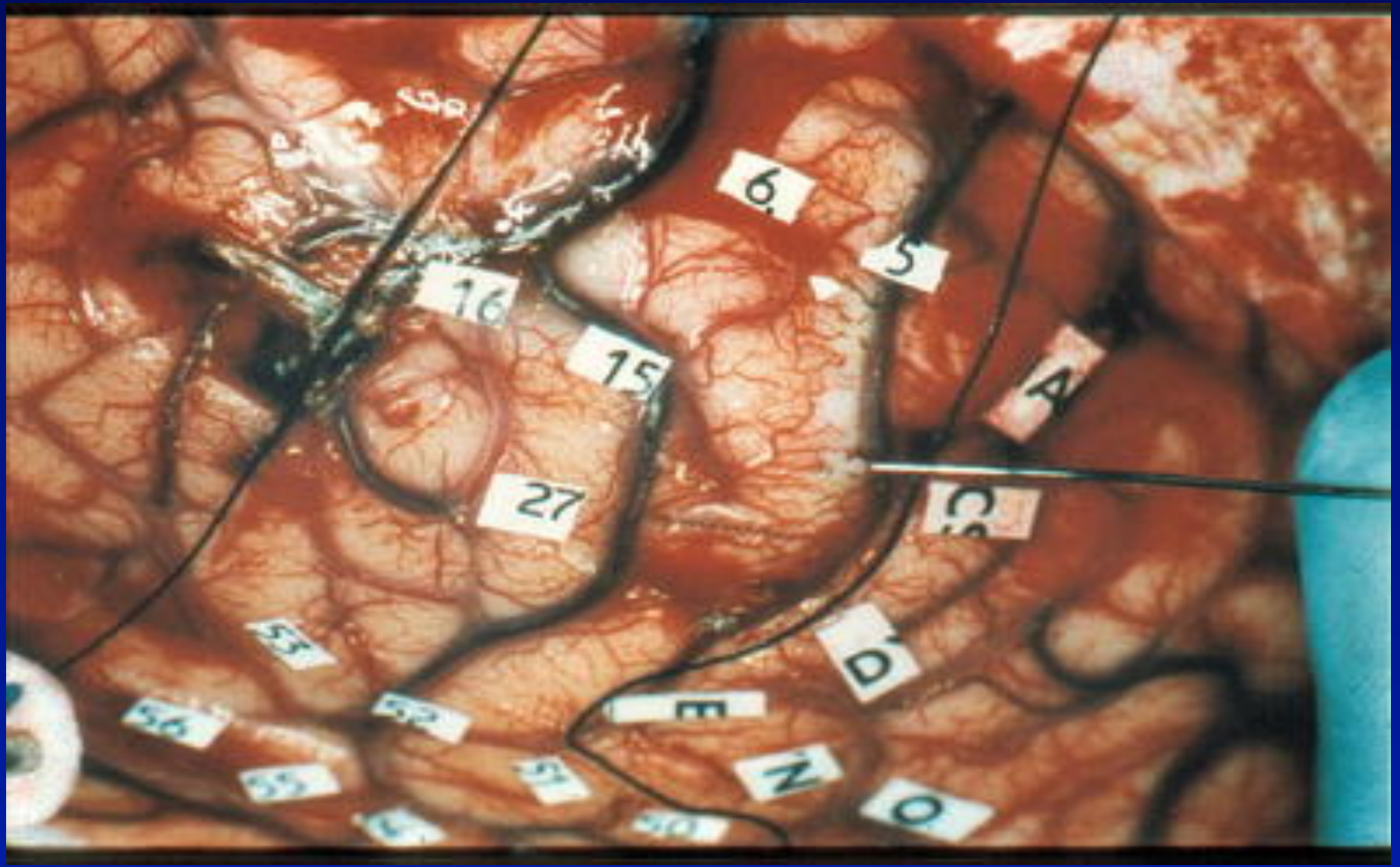
6
5
16
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A
27
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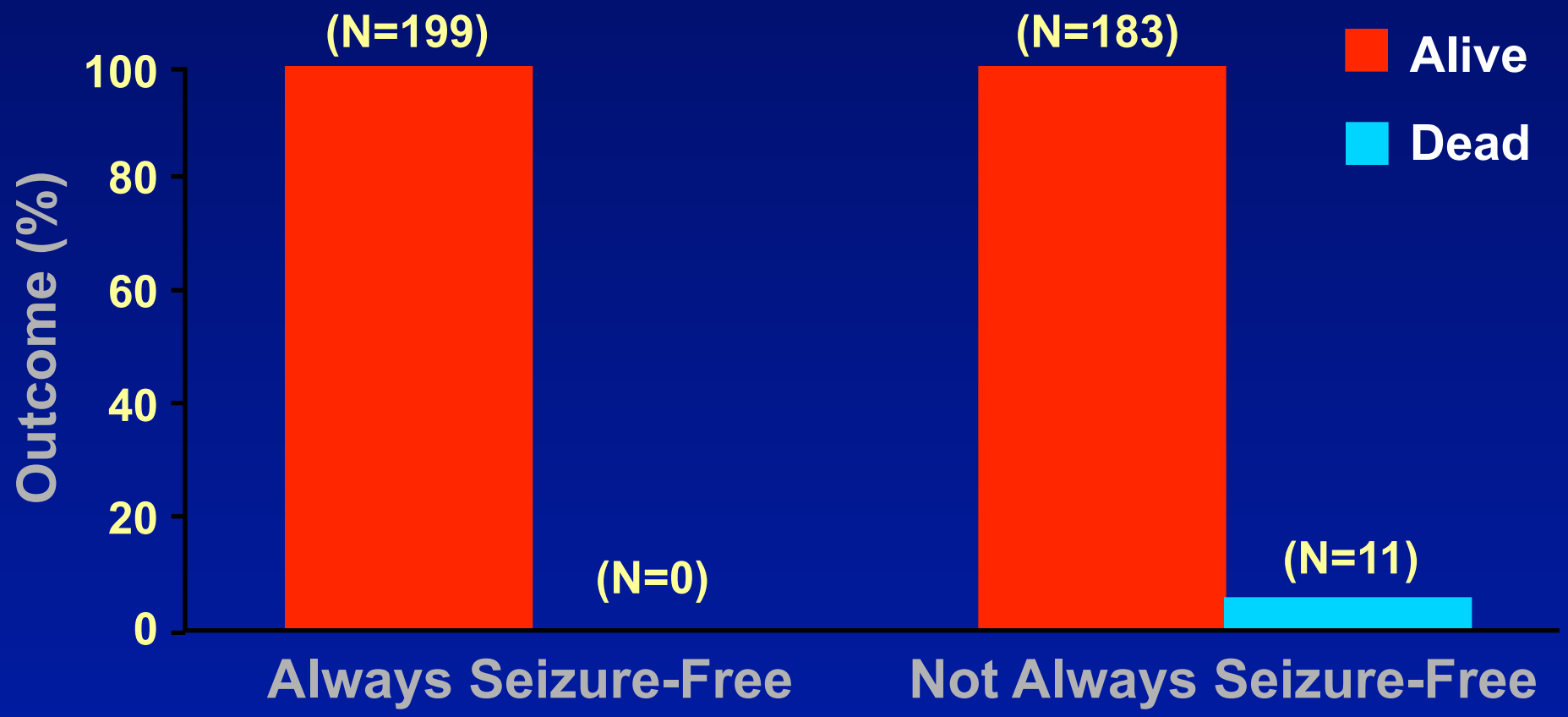
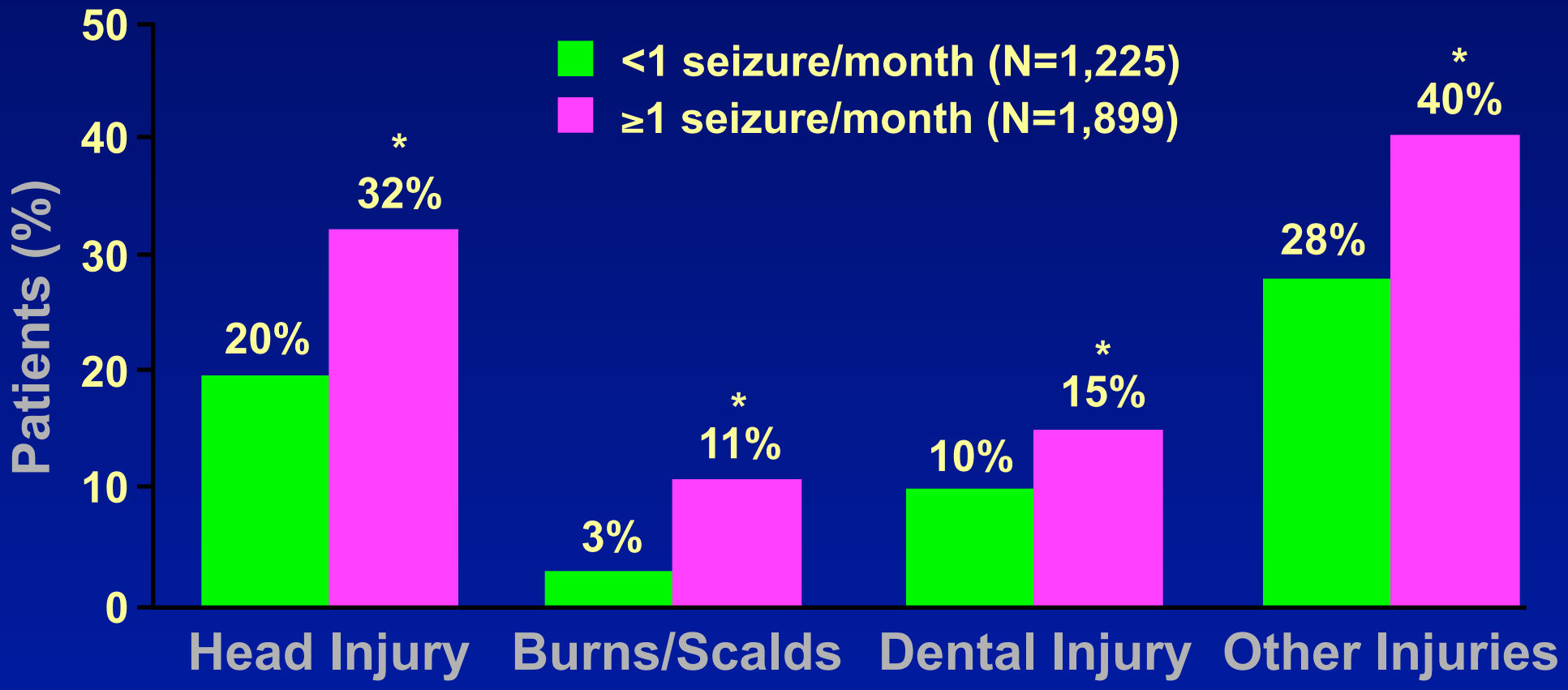
N
O

Successful Surgery for Seizures Reduces Mortality



Sperling MR, Feldman H, Kinman J, Liporace JD, O'Connor MJ. Ann Neurol. 1999(July);46(1):45-50

Seizure-Related Injuries vs. Seizure Frequency (N=3,124)



*p<0.001; Baker GA, Jacoby A, Buck D, Stalgis C, Monnet D. Epilepsia. 1997(March);38(3):353-362

Great Achievers

Julius Caesar (100BC-44BC)
Joan of Arc (1412-1431)
Leonardo da Vinci (1452-1519)
Michelangelo (1475-1564)
Napoleon Bonaparte (1769-1821)
Ludwig van Beethoven (1770-1827)
Lord George Gordon Byron (1788-1824)
Charles Dickens (1812-1870)
Gustave Flaubert (1821-1880)
Fyodor Dostoyevsky (1821-1881)
Alfred Nobel (1833-1896)
Peter Ilich Tchaikovsky (1840-1893)
Thomas Alva Edison (1847-1931)
Vincent Van Gogh (1853-1890)
Dame Agatha Christie (1890-1976)