2023 GW
Epilepsy Board Review
& Best Practices

Classification of Seizures and Epilepsy

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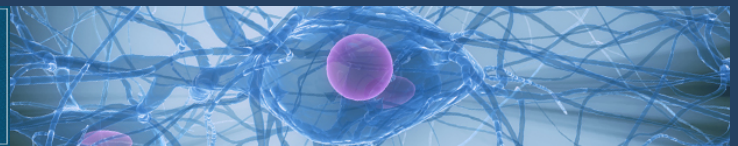
2023 GW Epilepsy Board Review & Best Practices

DISCLOSURES

- **Disclosure of Financial Relationships: None related to the current talk**

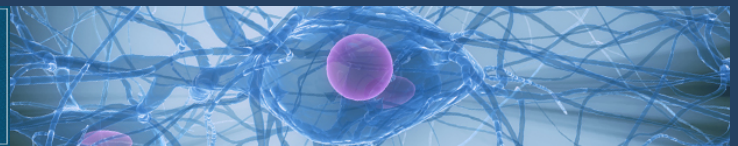
Definitions



Conceptual Definition of Seizure and Epilepsy – 2005 Report

- Seizure = a transient occurrence of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain
- Epilepsy = a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological, and social consequences of this condition.

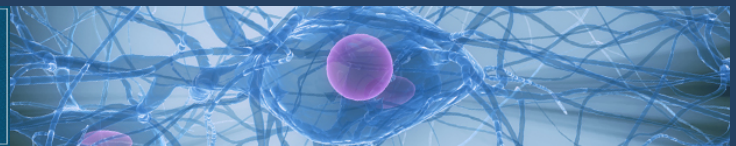
Fisher et al (2013). Epilepsia



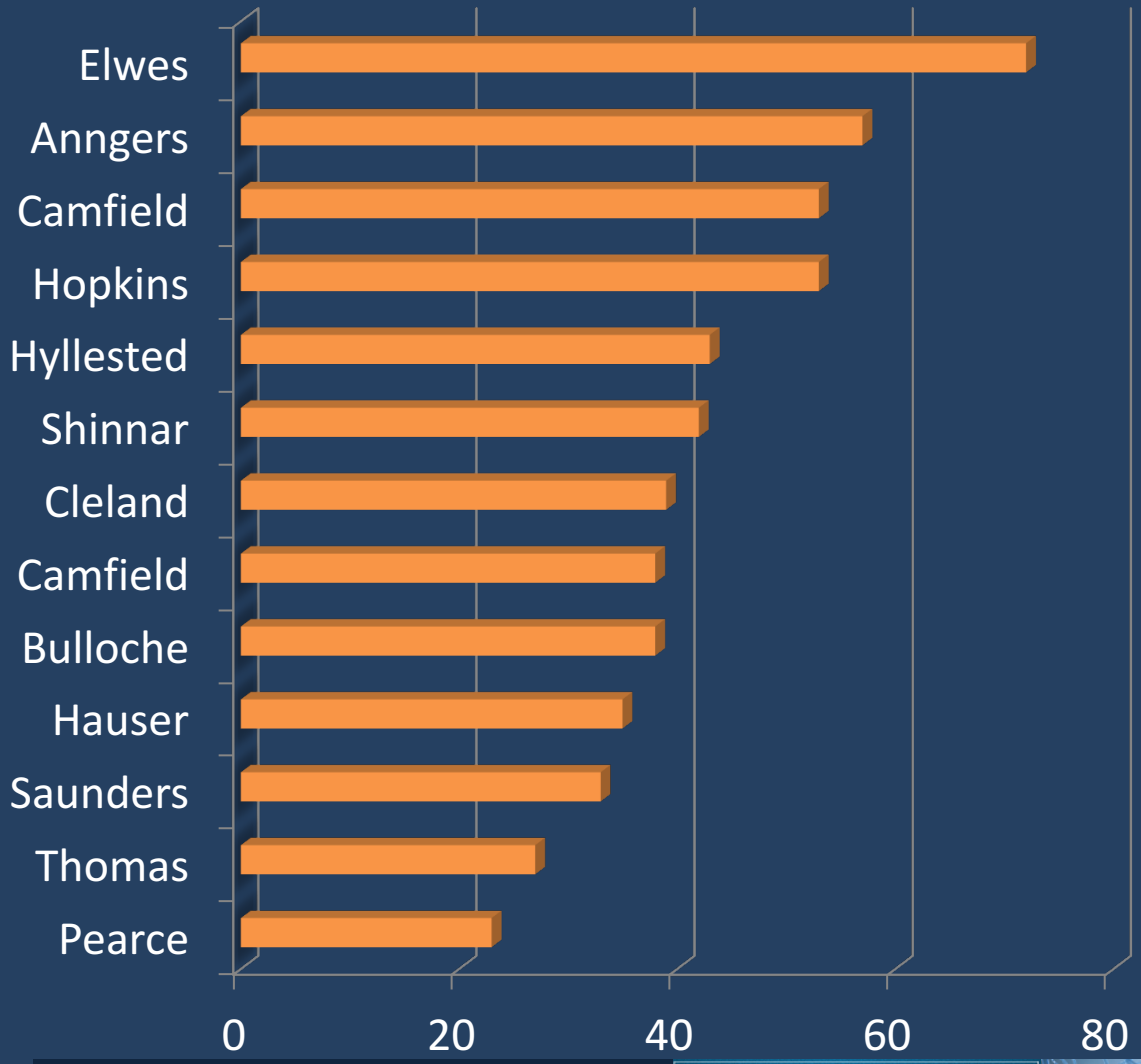
Operational Definition of Epilepsy

- Epilepsy = the occurrence of two unprovoked seizures occurring at least 24 hours apart (1).
- After two unprovoked non-febrile seizures, the chance of having another is 73% (1) at four years (95% CI is 59%-87%), versus 40-52% after a single unprovoked seizure (2).

1. Hauser WA et al (1998). N Engl J Med 338:429-434. (2) Berg AT, Shinnar S. (1991). Neurology 41:965-972.

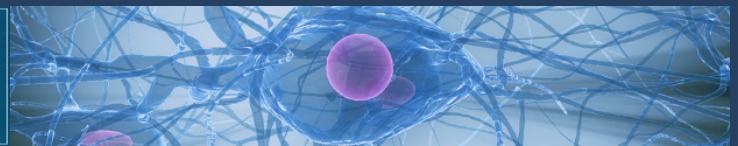


Percentage of Seizure Recurrence
2 Years After First Seizure in Untreated Patients



Pooled Recurrence Risk 42%

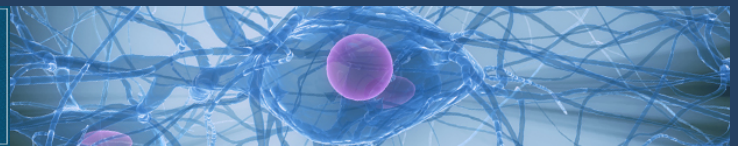
Percentage of Recurrence



Problems with that definition

- A patient with a single seizure and a structural brain lesion has a risk of a second unprovoked seizure that is comparable to the risk for further seizures after two unprovoked seizures (1)
- A patient with a single unprovoked seizure, but with an epilepsy syndrome with a high risk of seizure recurrence
- A patient with a single unprovoked seizure who has reflex (e.g. photosensitive) epilepsy

1. Hesdorffer DC et al (2009). Epilepsia 50:1102-1108.



2015 AAN/AES Evidence-based guideline

- Provoked seizures:

  Defined as seizures due to an acute symptomatic condition (e.g., a metabolic or toxic disturbance, cerebral trauma, stroke) and differ in prognosis from unprovoked seizures.

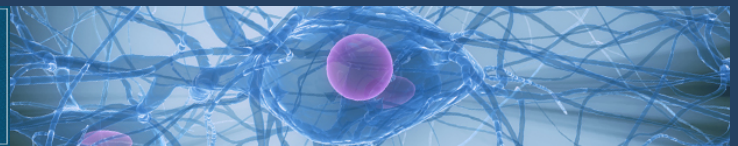
- Unprovoked seizures:

  (1) A seizure of unknown etiology, or

  (2) A seizure in relation to a demonstrated preexisting brain lesion or progressive CNS disorder (so-called “remote symptomatic” seizure).

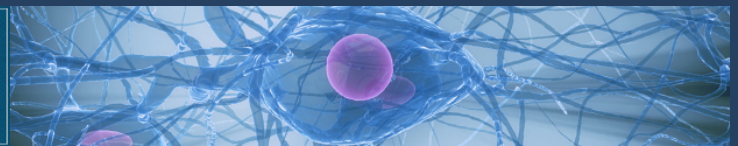
- Adults with an unprovoked first seizure have a seizure recurrence risk that is greatest early within the first 2 years (21%–45%) (Level A)

Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Krumholz A, Shinnar S, French J, Gronseth G, Wiebe S.



MCQ 1

- Which of the following is an unprovoked seizure?
  - A. Alcohol withdrawal seizure
  - B. Seizure in the setting of high dose wellbutrin
  - C. Seizure in the setting of hyponatremia due to beer potomania
  - D. Seizure in the setting of flickering lights
  - E. Convulsive movements following fainting due to dehydration



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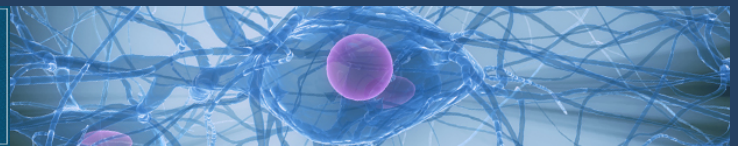
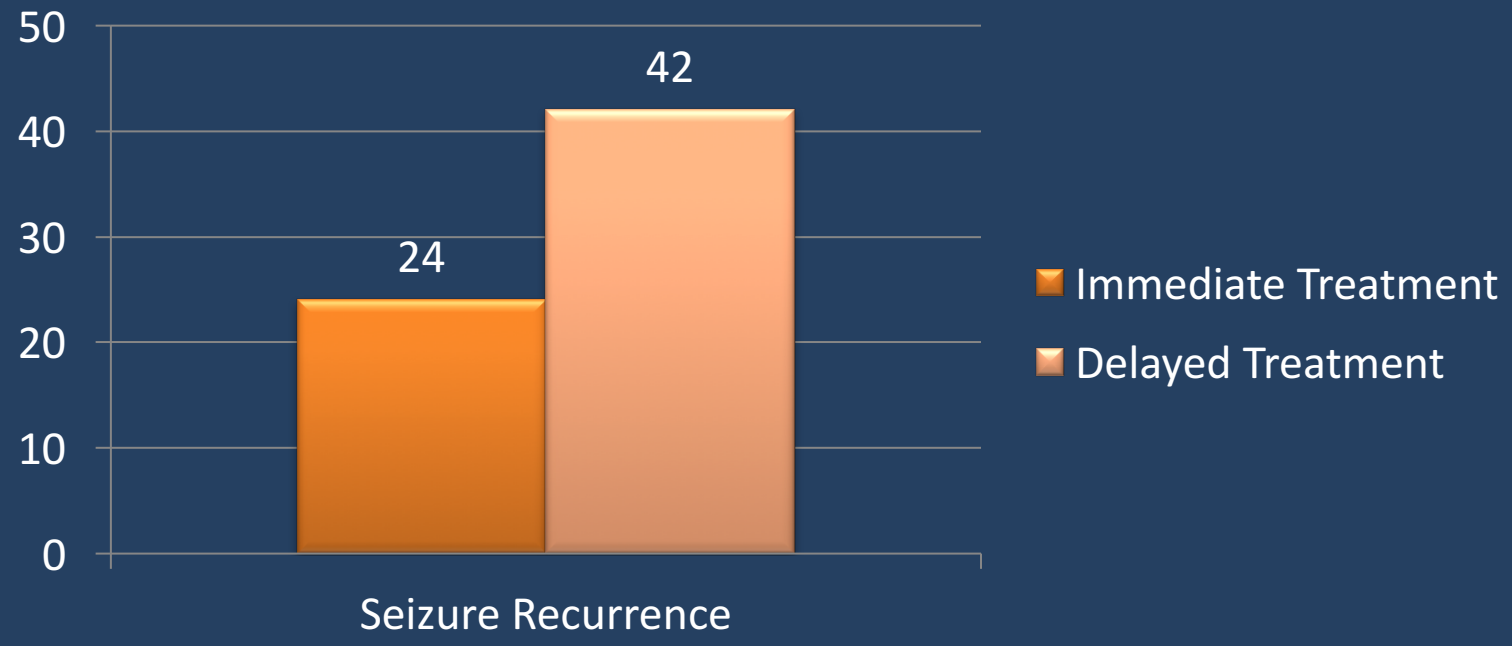


FIRST Trial

- Multicenter, randomized, open trial
- First GTC seizure - randomized to immediate treatment or to treatment only after another seizure.

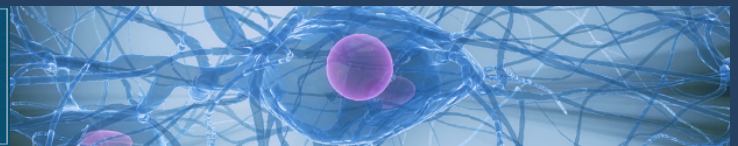


FIRST trial: (*Neurology. 1997 Oct;49(4):991-8. Treatment of first tonic-clonic seizure does not improve the prognosis of epilepsy. First Seizure Trial Group (FIRST Group). Musicco M, Beghi E, Solari A, Viani F.)*

FIRST Trial - Conclusions

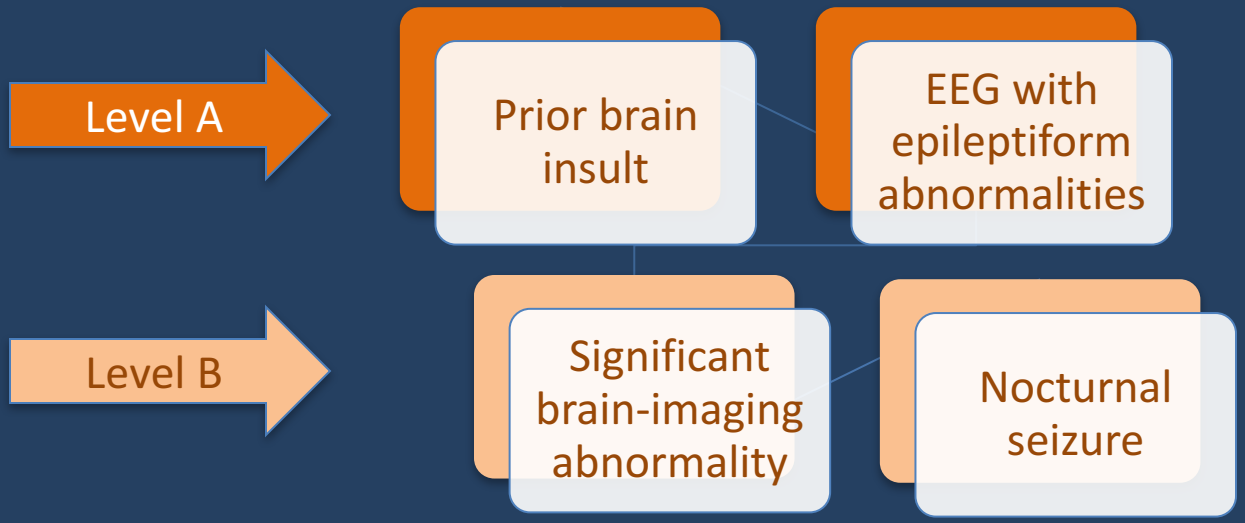
- Both groups had the same time-dependent probability of achieving 1 and 2 seizure-free years
- None of the prognostic predictors of relapse was significantly associated with the probability of having 1 or 2 years of seizure control
- ASMs in patients presenting a first GTC seizure reduce the risk of relapse
- Half of the untreated patients will never experience a second seizure
- The probability of long-term remission is not influenced by treatment of the first seizure

FIRST trial: (*Neurology. 1997 Oct;49(4):991-8. Treatment of first tonic-clonic seizure does not improve the prognosis of epilepsy. First Seizure Trial Group (FIRST Group). Musicco M, Beghi E, Solari A, Viani F.)*



2015 AAN/AES Evidence-based guideline

- Clinical variables associated with increased risk may include:

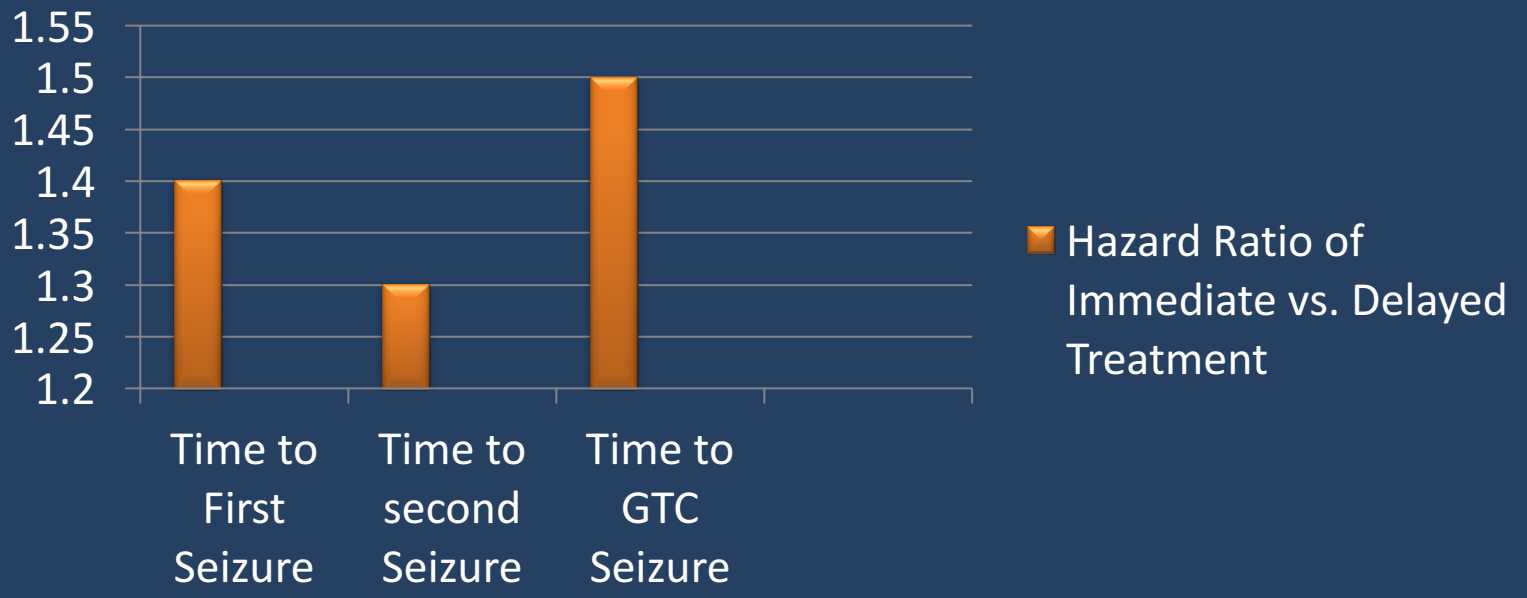


- Immediate medical therapy, as compared with delay of treatment pending a second seizure, is likely to reduce recurrence risk within the first 2 years (Level B) but may not improve quality of life (Level C)

Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Krumholz A, Shinnar S, French J, Gronseth G, Wiebe S.

MESS Study

- Unmasked, multicenter, randomized study of immediate (n=722) and deferred (n=721) ASM treatment in individuals with single seizures and early epilepsy

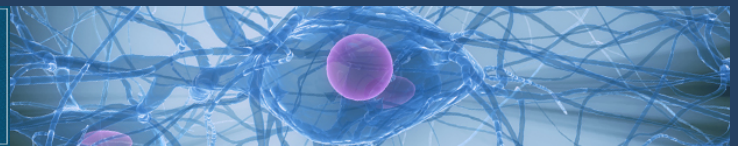


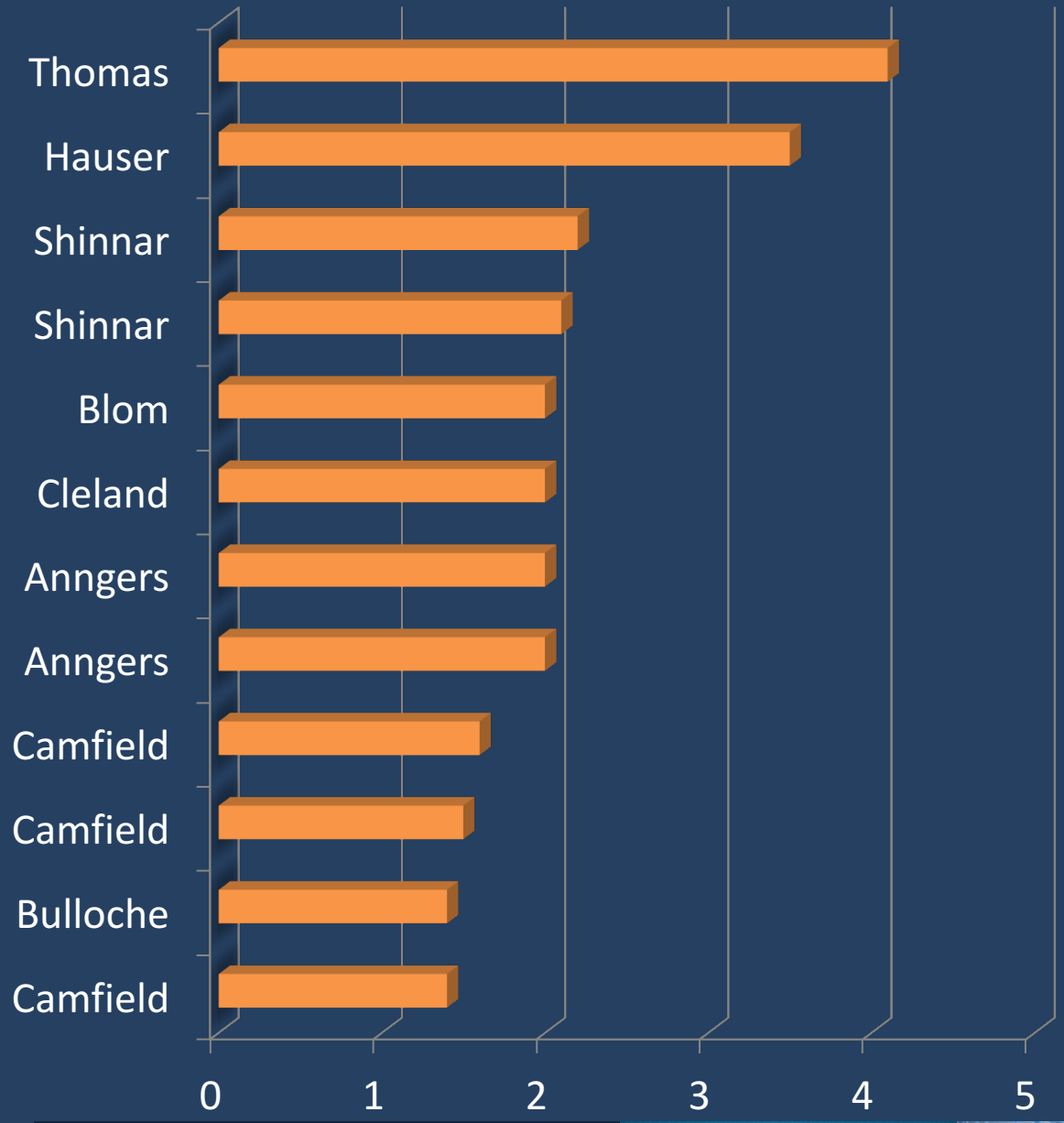
MESS study (Lancet. 2005 Jun 11-17;365(9476):2007-13. Immediate versus deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial. Marson A, Jacoby A, Johnson A, Kim L, Gamble C, Chadwick D; Medical Research Council MESS Study Group.)

MESS Study

- Immediate treatment reduced the time to achieve 2-year remission of seizures (p=0.023)
- The two groups did not differ with respect to quality of life outcomes or serious complications
- Immediate ASM treatment reduces the occurrence of seizures in the next 1-2 years, but does not affect long-term remission in individuals with single or infrequent seizures

MESS study (Lancet. 2005 Jun 11-17;365(9476):2007-13. Immediate versus deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial. Marson A, Jacoby A, Johnson A, Kim L, Gamble C, Chadwick D; Medical Research Council MESS Study Group.)

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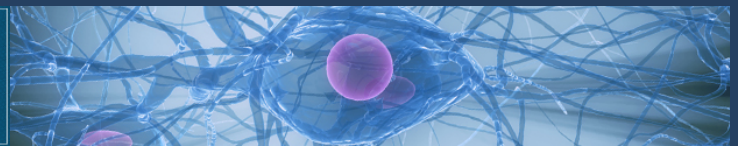
Recurrence Risk with EEG Abnormality

2015 AAN/AES Evidence-based guideline

- In the long term, immediate treatment is unlikely to improve prognosis as measured by sustained seizure remission (Level B).

- Patients should be advised that risk of ASM adverse events (AEs) may range from 7% to 31% (Level B) and that these AEs are likely predominantly mild and reversible

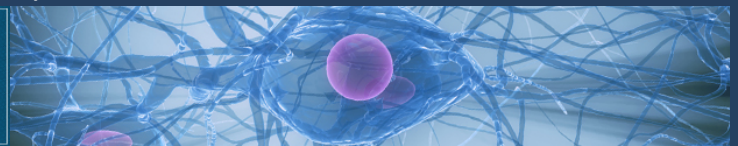
Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Krumholz A, Shinnar S, French J, Gronseth G, Wiebe S.



Broadened Definition by the ILAE Task Force: 2013

- Epilepsy is defined by any of the following conditions:
  - 1. At least two unprovoked seizures more than 24 hrs apart
  - 2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (approximately 75% or more)
  - 3. At least two seizures in a setting of reflex epilepsy
- Epilepsy is considered to be no longer present for
  - individuals who had an age-dependent epilepsy syndrome but are now past the applicable age
  - If seizure-free for at least 10 years off anti-seizure medicines, provided that there are no known risk factors associated with a high probability (>75%) of future seizures

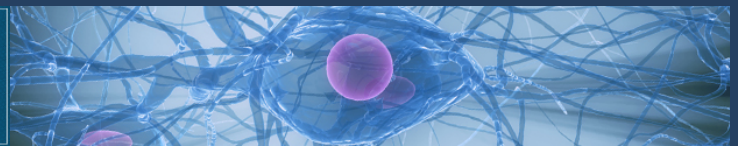
Fisher, R. et al. 2013. Epilepsia



Which of the following is epilepsy?

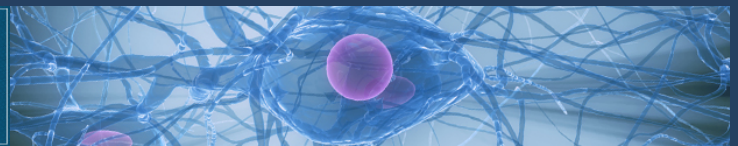
- Febrile seizures in children age 0.5 – 6 years old
- Alcohol-withdrawal seizures
- Metabolic seizures (sodium, calcium, magnesium, glucose, oxygen)
- Toxic seizures (drug reactions or withdrawal, renal failure)
- Convulsive syncope
- Acute concussive convulsion
- Seizures within first week after brain trauma, infection or stroke

None of the Above

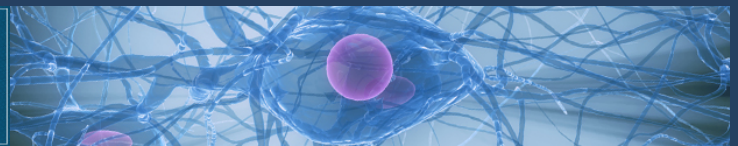


Examples

Case	Old Definition	New Definition
A 30 year-old man with two unprovoked seizures one year apart		
A 70 year-old man with first unprovoked seizure one year after L MCA stroke		
A 6 year-old boy has had 2 seizures 2 days apart while playing a videogame with flashing lights. EEG shows an abnormal photoparoxysmal response.		
A 25 year-old man had seizures with face twitching when falling asleep at age 9-11; none since. Past EEG showed centro-temporal spikes.		
A 40 year-old man had a left focal motor seizure with secondary generalization. MRI shows right frontal periventricular heterotopia and EEG shows right frontal spikes.		

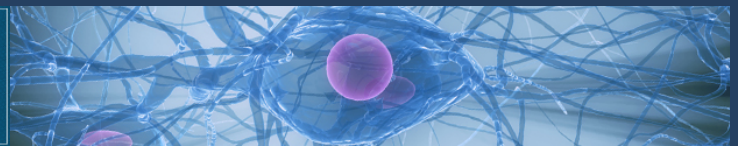


Classifications



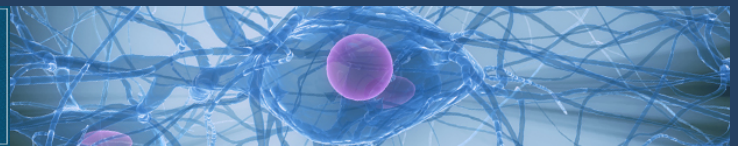
Background/History

- Purpose of classification: to provide a framework for diagnosis, management, and prognosis.
- 1964: Henri Gastaut: first endeavor to systematically classify seizures and epilepsies
- 1969: Gastaut published classification on behalf of the International League against Epilepsy (ILAE)
  - Focused on distinguishing between partial onset from generalized onset
  - Multidimensional classification: ictal semiology and EEG, interictal EEG, age of onset, neuropsychiatric phenomena, treatment responses, cause, and the known or hypothesized pathophysiology



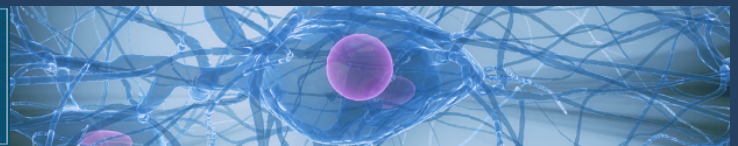
Background/History

- 1981: The ILAE modified the seizure classification
  - Partial seizures were subdivided into complex partial, simple partial, and secondarily generalized
- 1985: ILAE proposed a classification of epilepsies and epileptic syndromes
  - The seizure semiology in some epilepsies was described; many of the well defined syndromes were included



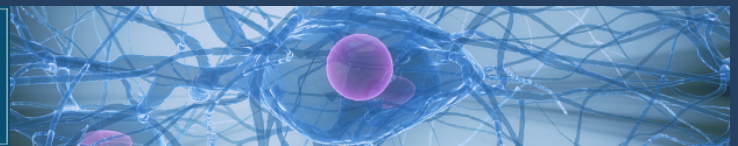
Background/History

- 1989: The concept of an epilepsy syndrome was refined and has been essential for diagnosis of epilepsy to this day
  - Epilepsy syndrome: defined by a cluster of coexisting signs and symptoms, including specific seizure type(s), EEG features, age of onset, and often a shared cause and prognosis
  - Causes were divided into idiopathic, symptomatic or cryptogenic ('presumed symptomatic')



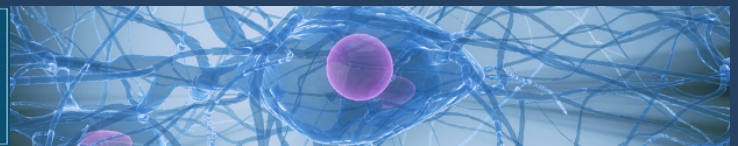
The 2010 ILAE Classification

- Generalized seizures do not involve the entire cortex as shown by imaging and neurophysiological studies
- ‘complex partial’ and ‘simple partial’ terminologies are not endorsed
- Focal versus generalized dichotomy is not applied – may coexist
- Retained versus altered awareness during seizures in infants?
- The terms idiopathic, symptomatic, and cryptogenic can be misleading.



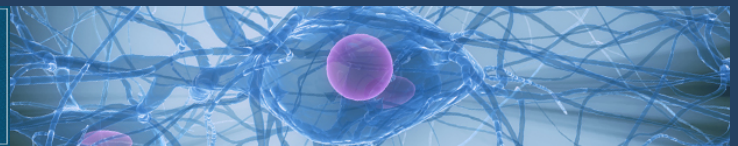
The 2010 ILAE Classification: Generalized Seizures

- Definition: Seizures originating at some point within, and rapidly engaging, bilaterally distributed networks. These networks can include cortical and subcortical structures, but do not necessarily involve the entire cortex
- Generalized seizures can be asymmetric



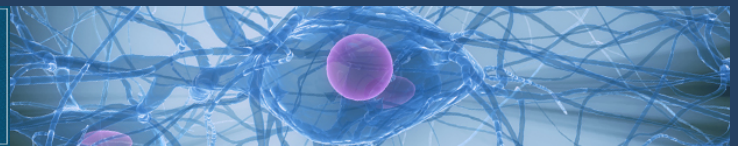
The 2010 ILAE Classification: Generalized Seizures

- Absence Seizures
  - Typical
  - Atypical
  - With Special Features
    - Myoclonic Absences
    - Absences with Eyelid myoclonia
- Myoclonic Seizures
  - Myoclonic
  - Myoclonic-Atonic
  - Myoclonic-Tonic



The 2010 ILAE Classification: Generalized Seizures

- Absence seizures
- Myoclonic seizures
- Tonic–clonic seizures (in any combination)
- Tonic
- Atonic
- Clonic



The 2010 ILAE Classification: Focal Seizures

Definition: Seizures originating within networks limited to one hemisphere, discretely localized or more widely distributed. For each seizure type, ictal onset is consistent from one seizure to another, with preferential propagation patterns that can involve the contralateral hemisphere

"Complex Partial"	Focal dyscognitive /with impaired awareness
"Simple Partial"	Focal without impairment of consciousness or awareness

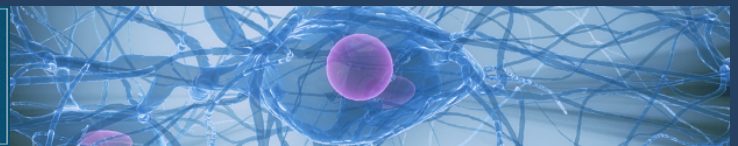


Table 1. Classification of seizures[a]

- Generalized seizures
  - Tonic–clonic (in any combination)
  - Absence
    - Typical
    - Atypical
    - Absence with special features
      - Myoclonic absence
      - Eyelid myoclonia
  - Myoclonic
    - Myoclonic
    - Myoclonic atonic
    - Myoclonic tonic
  - Clonic
  - Tonic
  - Atonic
- Focal seizures
- Unknown
  - Epileptic spasms

[a]Seizure that cannot be clearly diagnosed into one of the preceding categories should be considered unclassified until further information allows their accurate diagnosis. This is not considered a classification category, however.

Berg, A. et al. 2010. Epilepsia

Table 2. Descriptors of focal seizures according to degree of impairment during seizure[a]

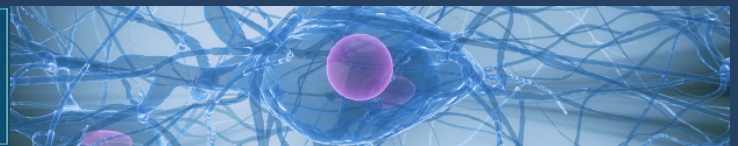
Without impairment of consciousness or awareness

- With observable motor or autonomic components. This roughly corresponds to the concept of "simple partial seizure. "Focal motor" and "autonomic" are terms that may adequately convey this concept depending on the seizure manifestations).
- Involving subjective sensory or psychic phenomena only. This corresponds to the concept of an aura, a term endorsed in the 2001 Glossary.
- With impairment of consciousness or awareness. This roughly corresponds to the concept of complex partial seizure. "Dyscognitive" is a term that has been proposed for this concept (Blume et al., 2001).
- Evolving to a bilateral, convulsive[b] seizure (involving tonic, clonic, or tonic and clonic components). This expression replaces the term "secondarily generalized seizure."

[a]For more descriptors that have been clearly defined and recommended for use, please see Blume et al., 2001.

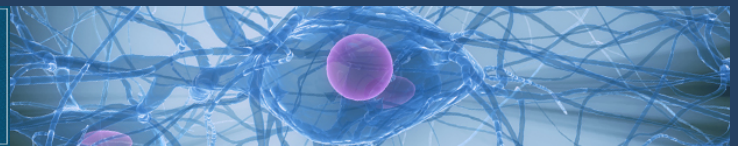
[b]The term "convulsive" was considered a lay term in the Glossary; however, we note that it is used throughout medicine in various forms and translates well across many languages. Its use is, therefore, endorsed.

Berg, A. et al. 2010. Epilepsia



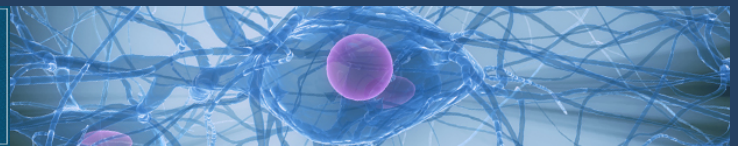
The 2010 ILAE Classification: Notable changes

- Neonatal seizures are no longer a separate entity
- "idiopathic, symptomatic, and cryptogenic" → genetic, structural, metabolic, and unknown. These categories are not mutually exclusive.
- Diagnosis of electroclinical syndromes remains unchanged.
- 'Constellations' define clinically distinctive entities with specific associations, such as hypothalamic hamartoma and gelastic seizures, or mesial temporal lobe epilepsy and hippocampal sclerosis



The 2010 ILAE Classification: Notable changes

- Removal of the emotionally laden words ‘catastrophic’ and ‘benign’ to describe different epilepsies
- Epileptic encephalopathies have been redefined as diseases in which ‘the epileptic activity itself may contribute to severe cognitive and behavioral impairments above and beyond what might be expected from the underlying pathology alone, and that these can worsen over time



2017 Classification

- 2010 Classification engendered debate within the epilepsy community
- 7 years of an iterative process with worldwide public engagement
- The 2017 classification changed as a result

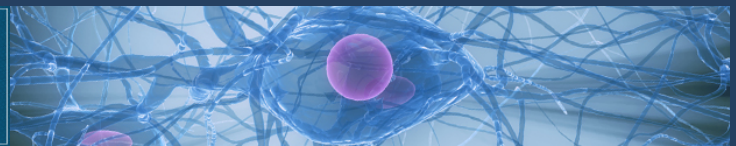
ILAE 2017 Classification[1]

Focal Onset		Generalized Onset		Unknown Onset	
Aware	Impaired Awareness				
Motor	Non-motor	Motor - GTC - Other motor	Non-motor - Absence	Motor - GTC - Other motor	Non-motor
Focal to bilateral tonic-clonic					
				Unclassified[2]	

1 Definitions, other seizure types and descriptors are listed in the accompanying paper & glossary of terms

2 Due to inadequate information or inability to place in other categories

From Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia doi: 10.1111/epi.13671



ILAE 2017 Classification - Expanded

Focal Onset

Motor Onset

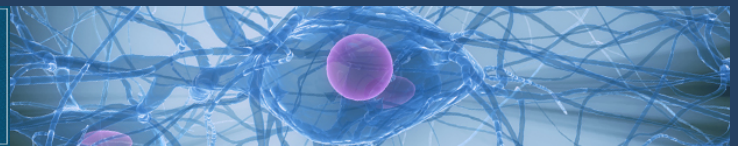
- automatisms
- atonic*
- clonic
- epileptic spasms*
- hyperkinetic
- myoclonic
- tonic

Non-Motor Onset

- autonomic
- behavior arrest
- cognitive
- emotional
- sensory

Focal to bilateral tonic-clonic

From Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia doi: 10.1111/epi.13671



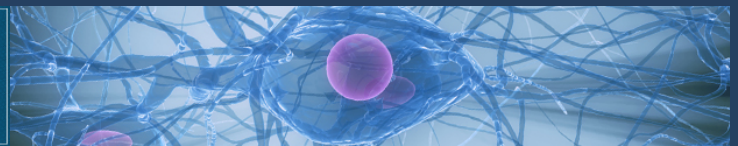
ILAE 2017 Classification - Expanded

Generalized Onset

Motor
- tonic-clonic
- clonic
- tonic
- myoclonic
- myoclonic-tonic-clonic
- myoclonic-atonic
- atonic*
- epileptic spasms*

Non-Motor (absence)
- typical
- atypical
- myoclonic
- eyelid myoclonia

From Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia doi: 10.1111/epi.13671



ILAE 2017 Classification - Expanded

Unknown Onset

Motor

tonic-clonic

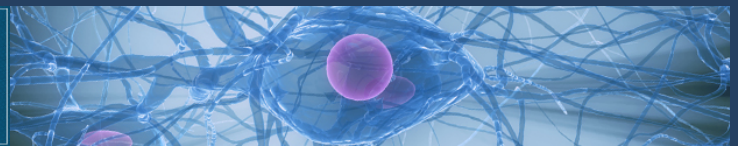
epileptic spasms

Non-Motor

behavior arrest

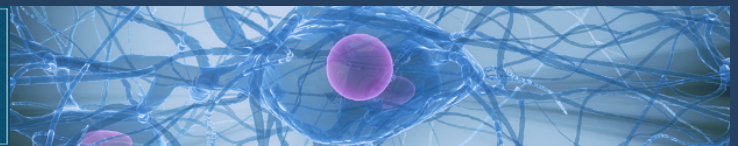
Unclassified

From Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia doi: 10.1111/epi.13671



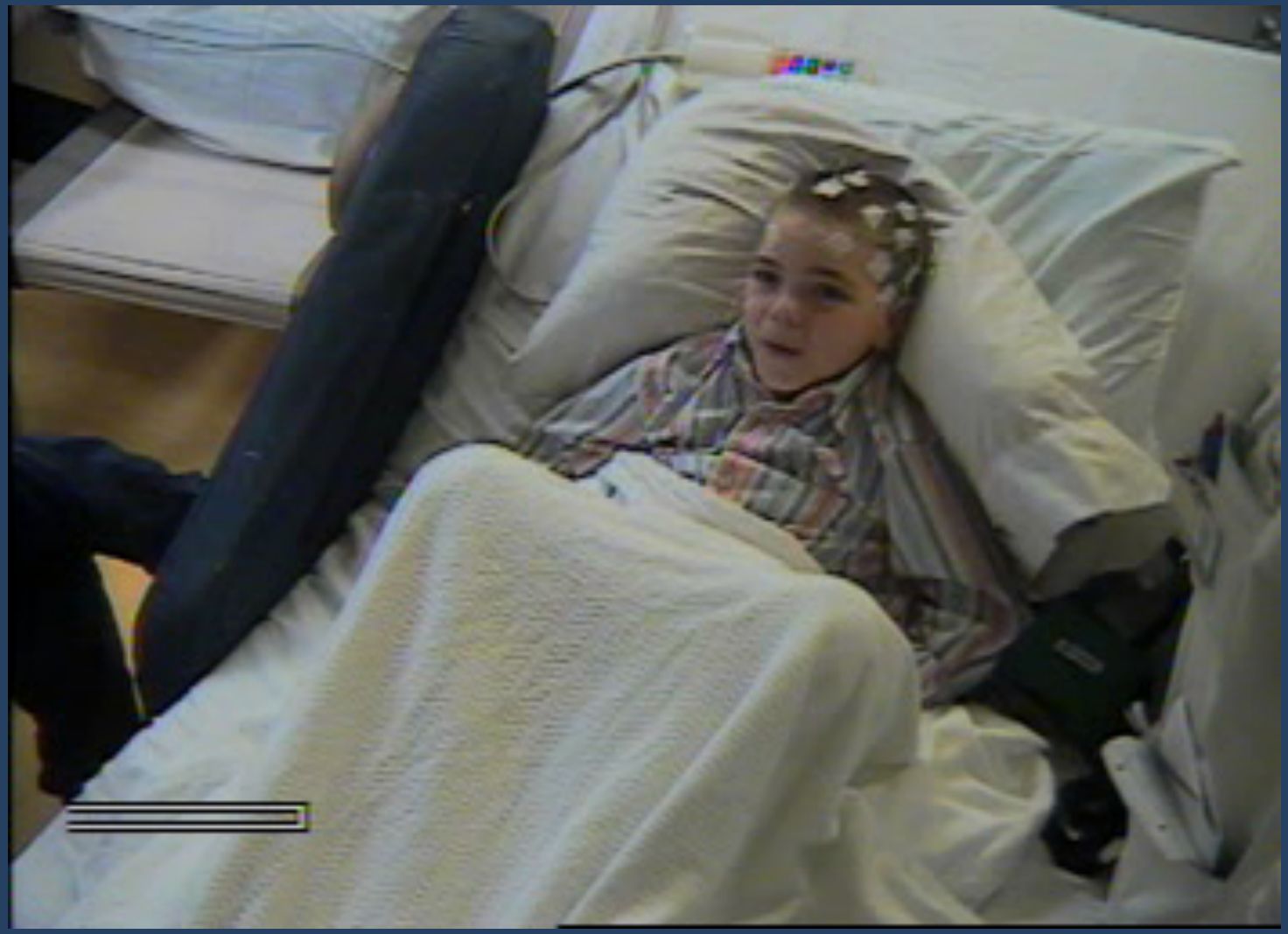
2017 ILAE Classification

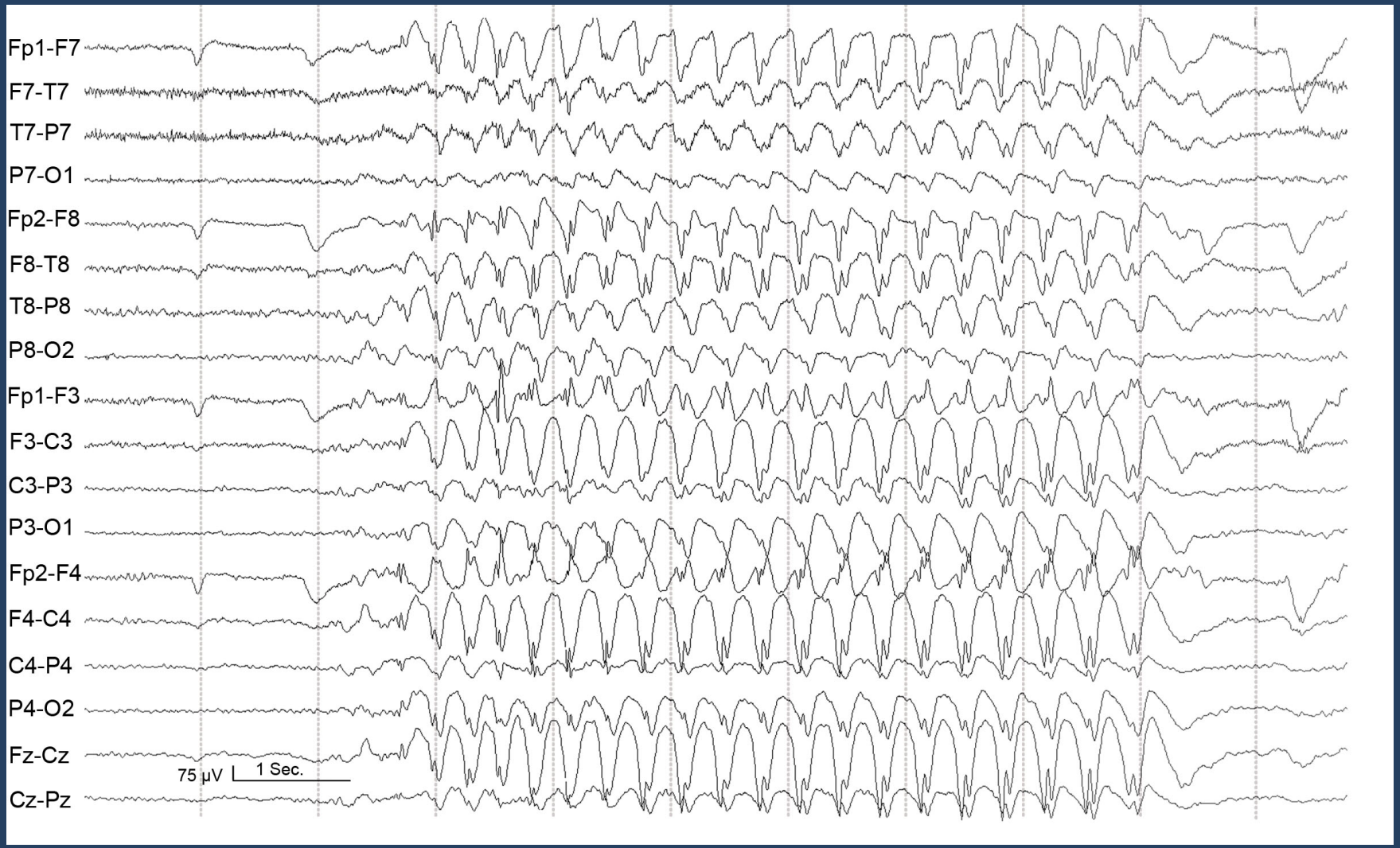
- First diagnose the seizure type
- Then diagnose epilepsy type
  - focal, generalized, combined generalized/focal, and unknown
- Then diagnose the epilepsy syndrome
- Etiology is incorporated along each stage
  - 6 subgroups, selected because of potential therapeutic consequences: structural, genetic, infectious, metabolic, immune, and unknown
- New terminology: developmental and epileptic encephalopathy
- The term benign is replaced by the terms self-limited and pharmacoresponsive



Absence Seizures

- Childhood or teenage onset
- Sudden onset, without aura, prompt offset
- Momentary loss of consciousness
- Eyelid flutter/minor automatisms
- 3-15 seconds duration
- Family History
- EEG: 3 Hz Spike-Wave / HV sensitive




Fp1-F7
F7-T7
T7-P7
P7-O1
Fp2-F8
F8-T8
T8-P8
P8-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fz-Cz
Cz-Pz
75 µV
1 Sec.

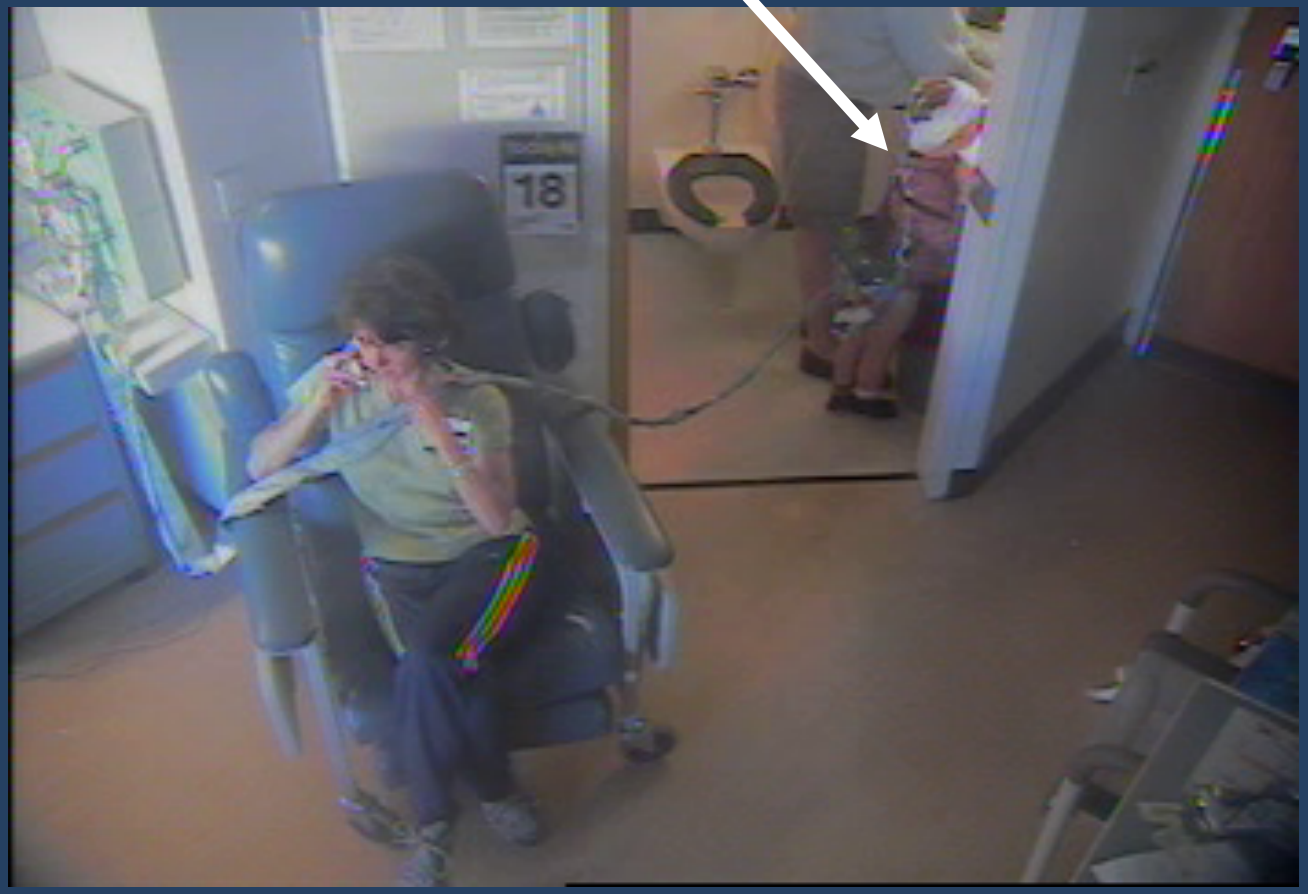
Tonic Seizures

- Sudden stiffening
- Extension maximal in arms
- A few seconds in duration
- Associated with falls and injury
- Extra-temporal origin
- Refractory to therapy
- EEG: Flattening/high frequency discharge

Atonic Seizures

- Abrupt onset
- Sudden loss in tone
- Head drop/falls/injuries
- A second or two in duration
- Poor response to AEDs
- Poor overall prognosis
- EEG: Slow spike-wave/flattening

LOOK AT THE PATIENT HERE



Myoclonic Seizures

- Sudden jerks
- Usually bilateral, maximal in arms
- One second in duration
- Often multiple
- May be photic or sensory triggered
- Often maximal on awakening
- EEG: generalized polyspike-wave burst

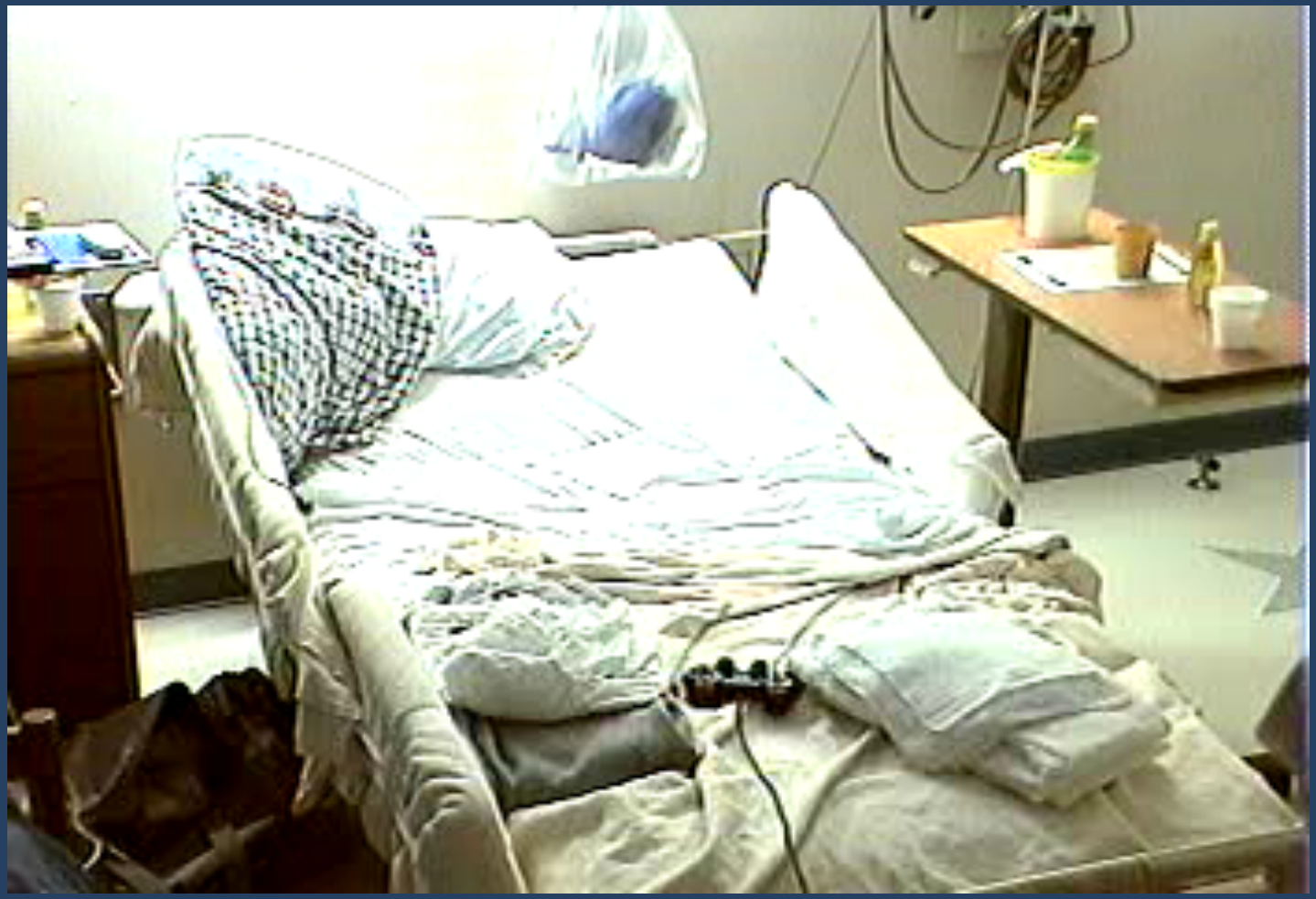
Tonic-Clonic Seizures

- Loss of Consciousness
- May have a focal or generalized onset
- Tonic Extension of limbs (about 20-40 sec)
- Evolves to rhythmic clonic jerking of extremities (about 30-50 secs)
- Cessation of breathing, tongue biting, incontinence
- Post-ictal sleep
- EEG: Variable, often obscured.

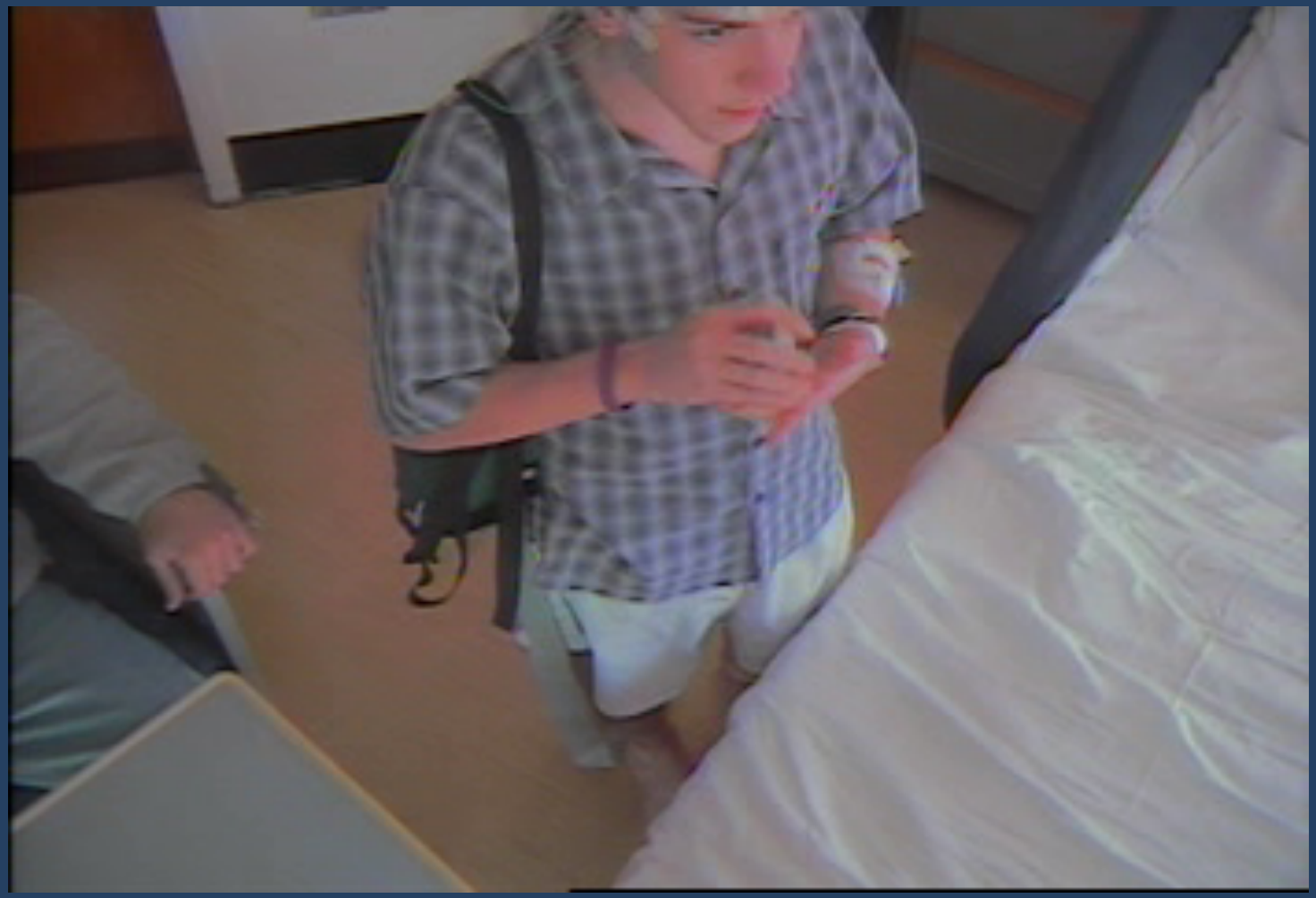
Focal Seizures

Focal Aware Seizures

- Motor, sensory, psychic or autonomic signs or symptoms
- Preservation of consciousness & awareness
- May progress to focal impaired awareness or tonic-clonic seizures
- EEG: Interictal-focal sharp or slow; ictal-rhythmic discharge or often normal!

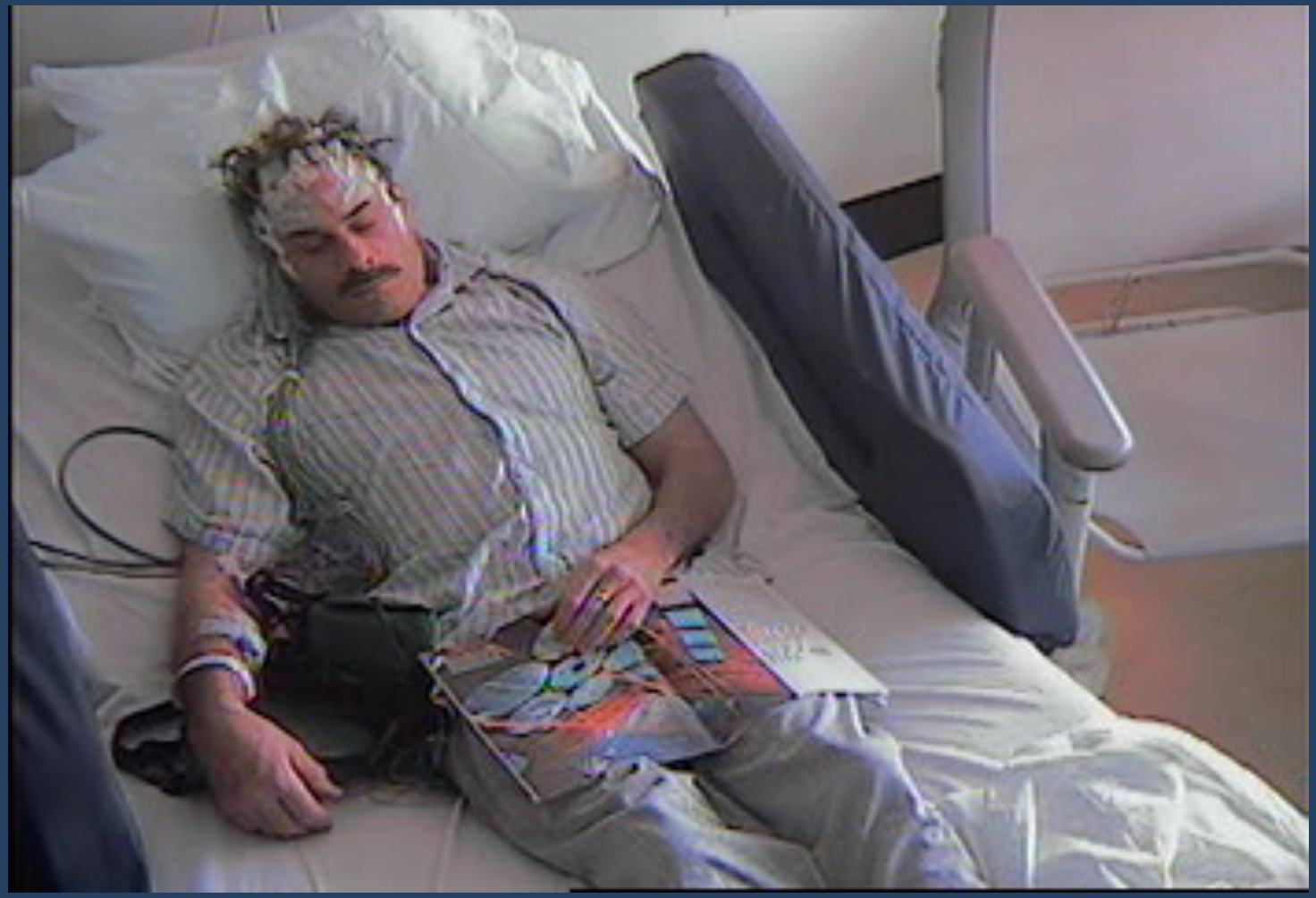


Abou Khalil & Misulis. Atlas of EEG and Seizure Semiology. Elsevier 2006.



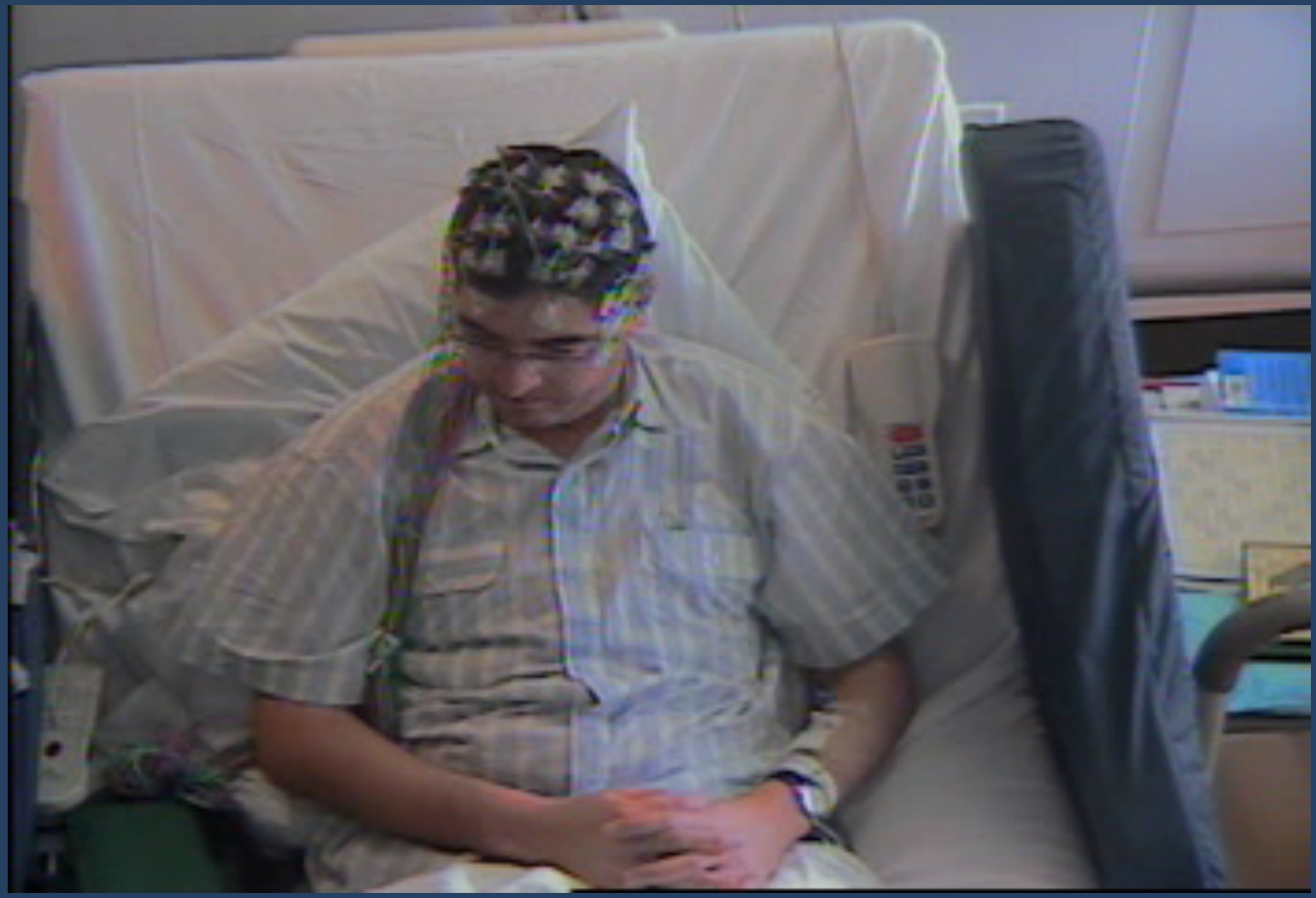
Focal Impaired Awareness Seizures

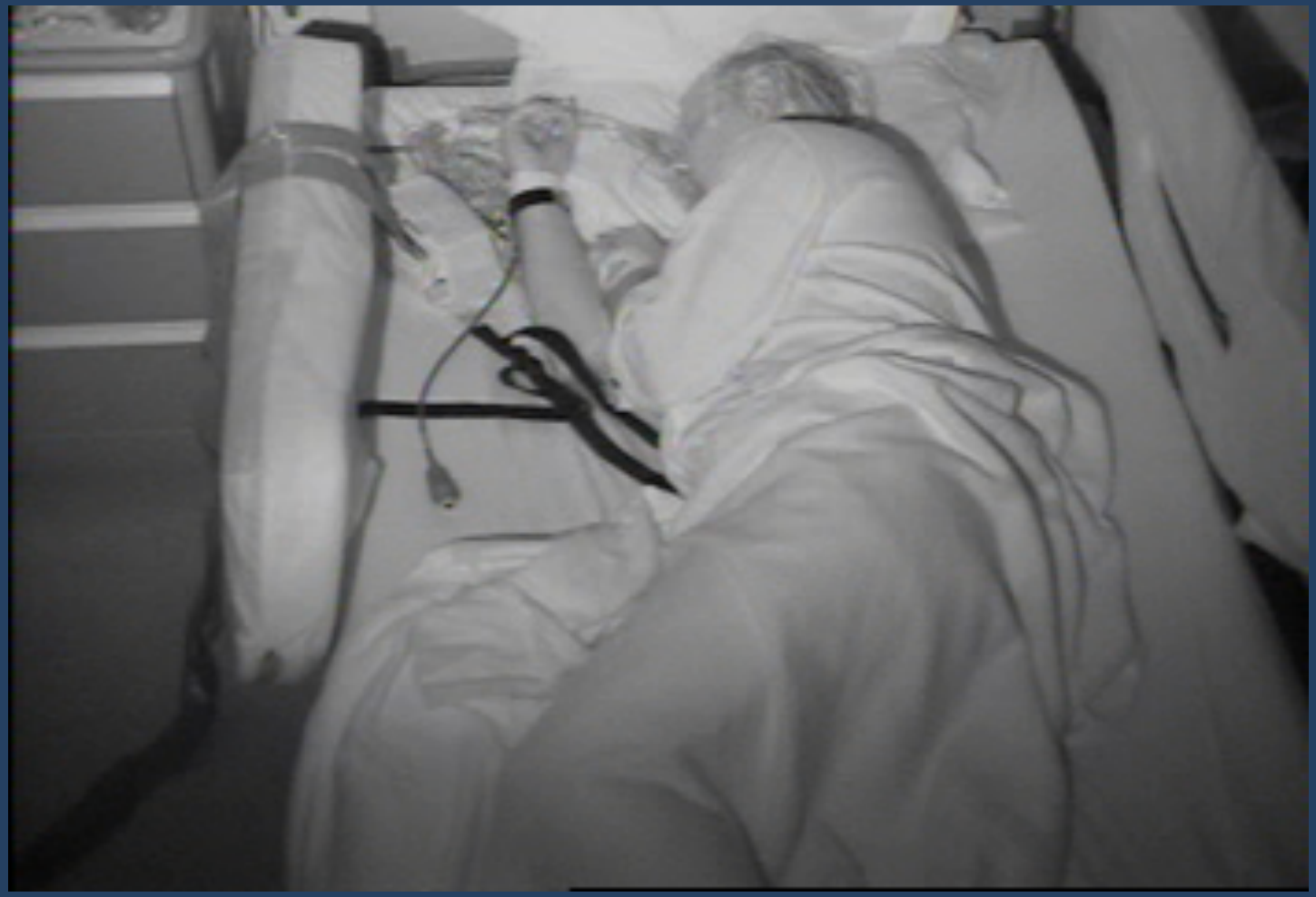
- Altered consciousness/awareness
- Duration 30 sec to 3 min
- Purposeless automatisms
  - Arms
  - Oral
- Amnesia
- Semiology varies with site of origin
- EEG: Interictal- sharp waves or spikes; Ictal- focal or bilateral rhythmic sharp

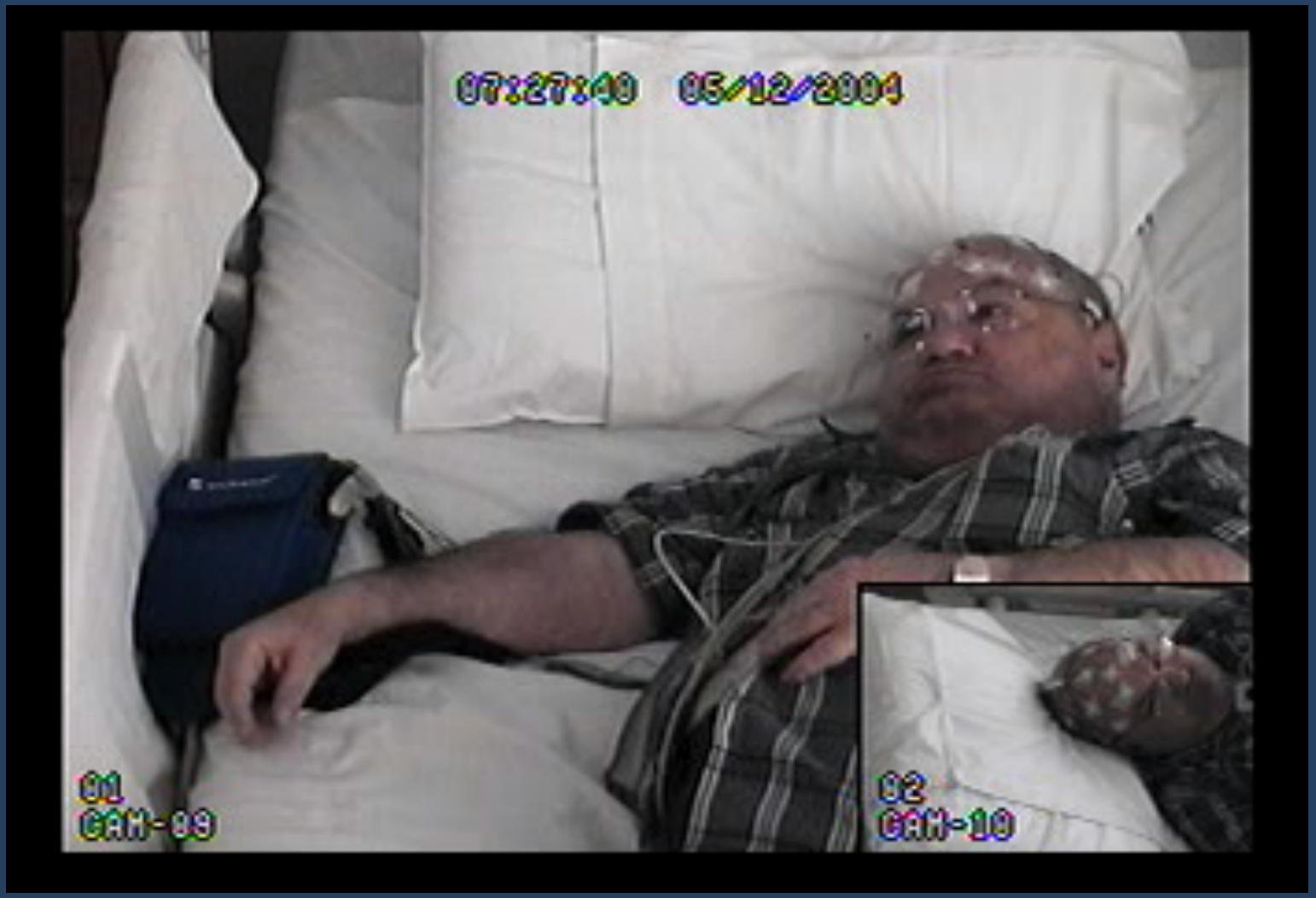


Abou Khalil & Misulis. Atlas of EEG and Seizure Semiology. Elsevier 2006.

Guess the seizure type







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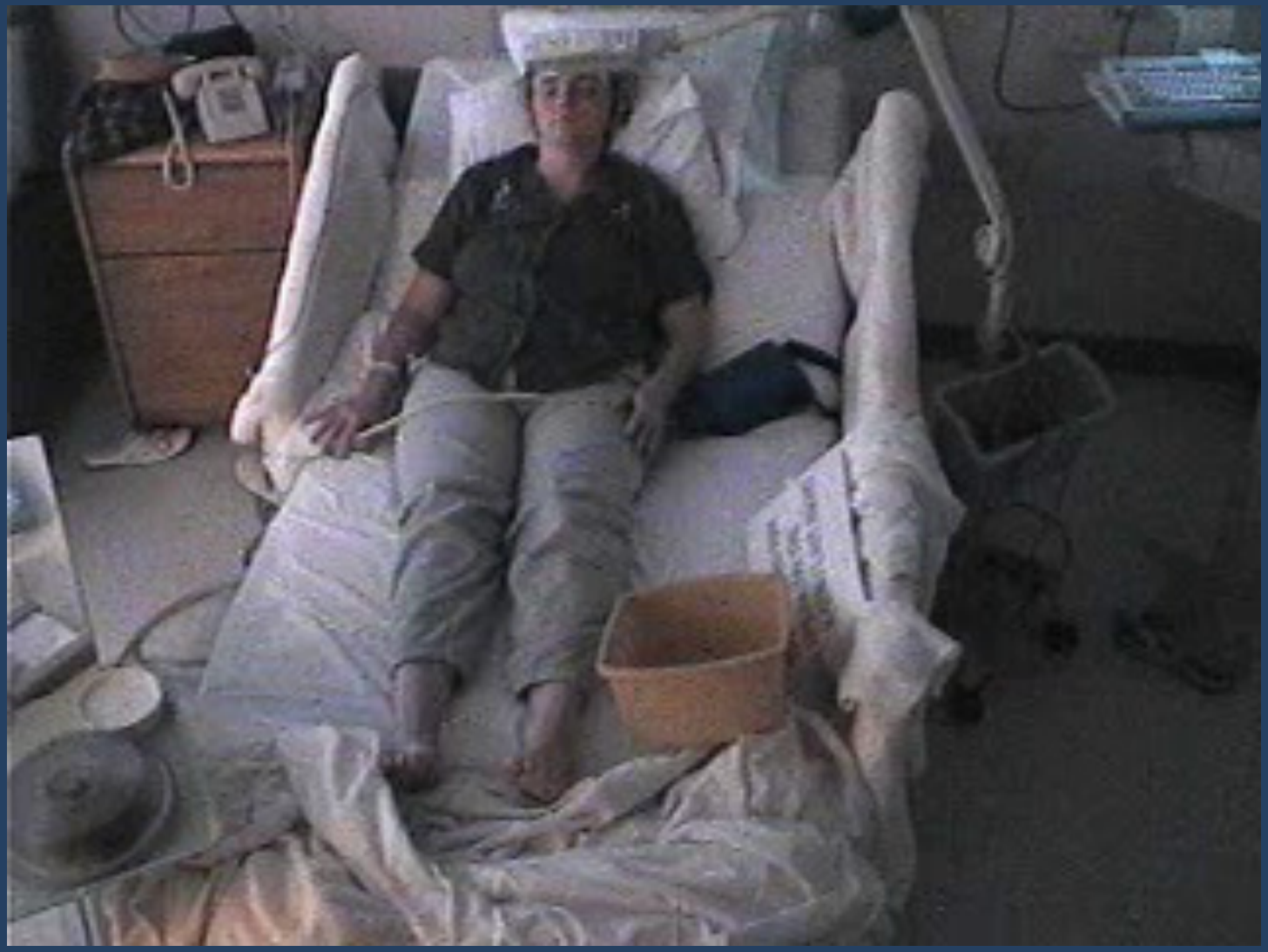

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