Beth Israel Deaconess Medical Center | HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Introduction to Seizures

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Outline

- Definitions and epidemiology
- Differential diagnosis and seizure types
- Diagnostic workup
- Seizure first aid
- Seizure management

Seizures and TMS

- They are the most dramatic and medically dangerous acute complication of TMS
- IRB/ethics boards expect them to be addressed as a risk of TMS research
- The world of TMS research has expanded:
  - To researchers who are not physicians or who are not familiar with clinical neurological disorders
  - To labs that are not located proximate to medical facilities
  - To subject populations with known epilepsy or with neurological disorders that have an increased risk of seizures

What is a Seizure?

Seizure

- A clinical episode of neurologic dysfunction caused by the abnormal hypersynchronous activity of a group of neurons

What is Epilepsy?

Epilepsy Definition

International League Against Epilepsy

- Any disorder characterized by a tendency toward recurrent, unprovoked seizures
- A disease of the brain defined by any of the following 3 conditions:
  1. 2 or more seizures occurring >24h apart
  2. 1 unprovoked seizure and a probability of further seizures of at least 60% occurring over the next 10 years
  3. Diagnosis of an epilepsy syndrome
  - In practice, diagnosed after two unprovoked seizures

Fisher et al, 2024

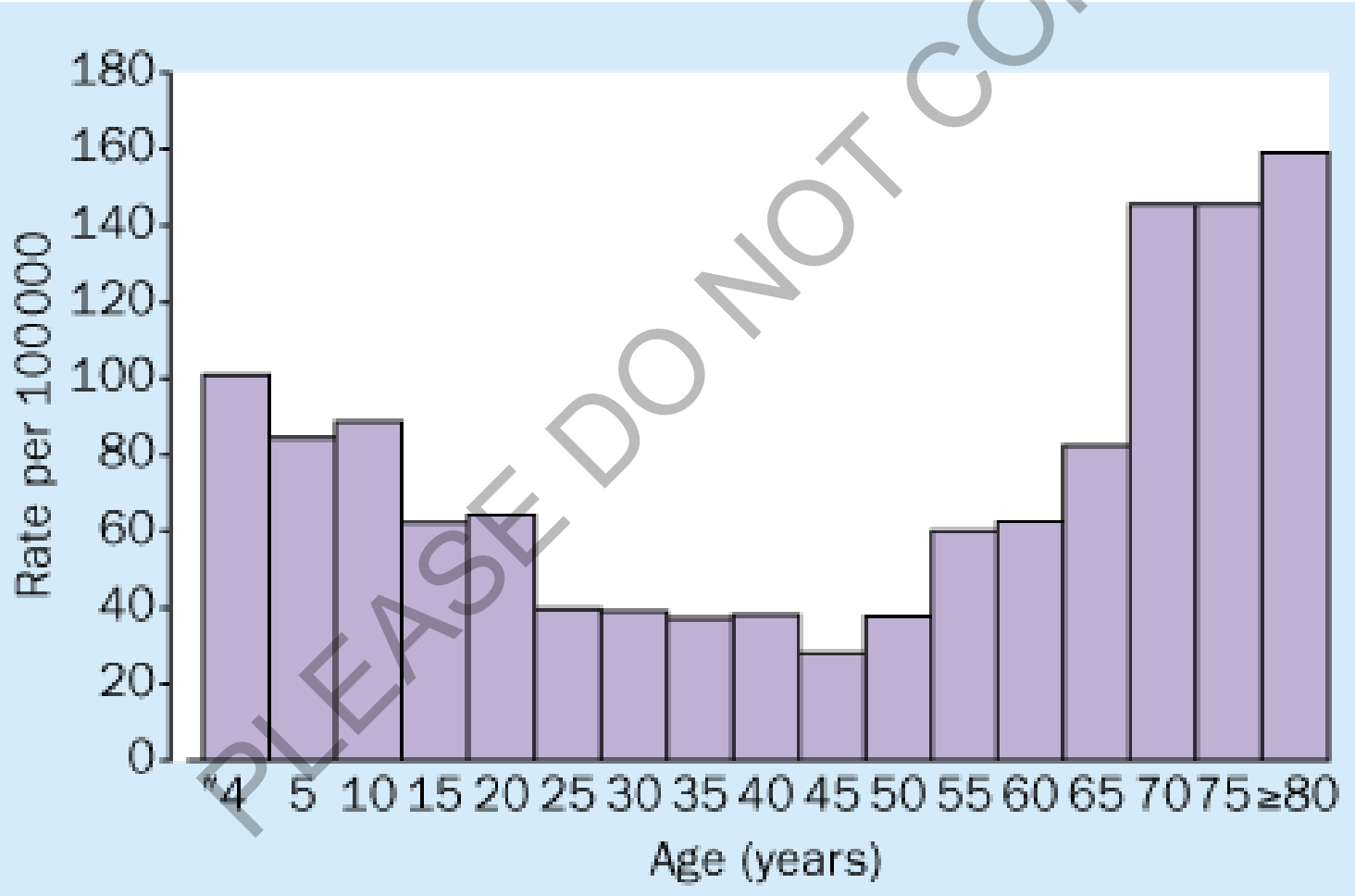
Seizures and epilepsy are quite common

- Prevalence of epilepsy in the general population is about 0.5% to 1%, or 1 in 100-200 persons

- Cumulative lifetime incidence of one or more seizures is 5-10%, including febrile seizures

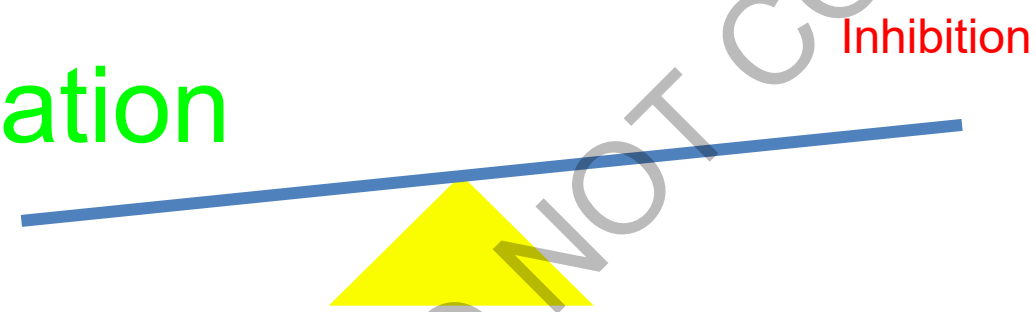
Annegers, 2001

The incidence of epilepsy is highest in the young and in the old



Stephen and Brodie, 2000

Seizures occur when an imbalance of excitation and inhibition exists in the nervous system



Examples

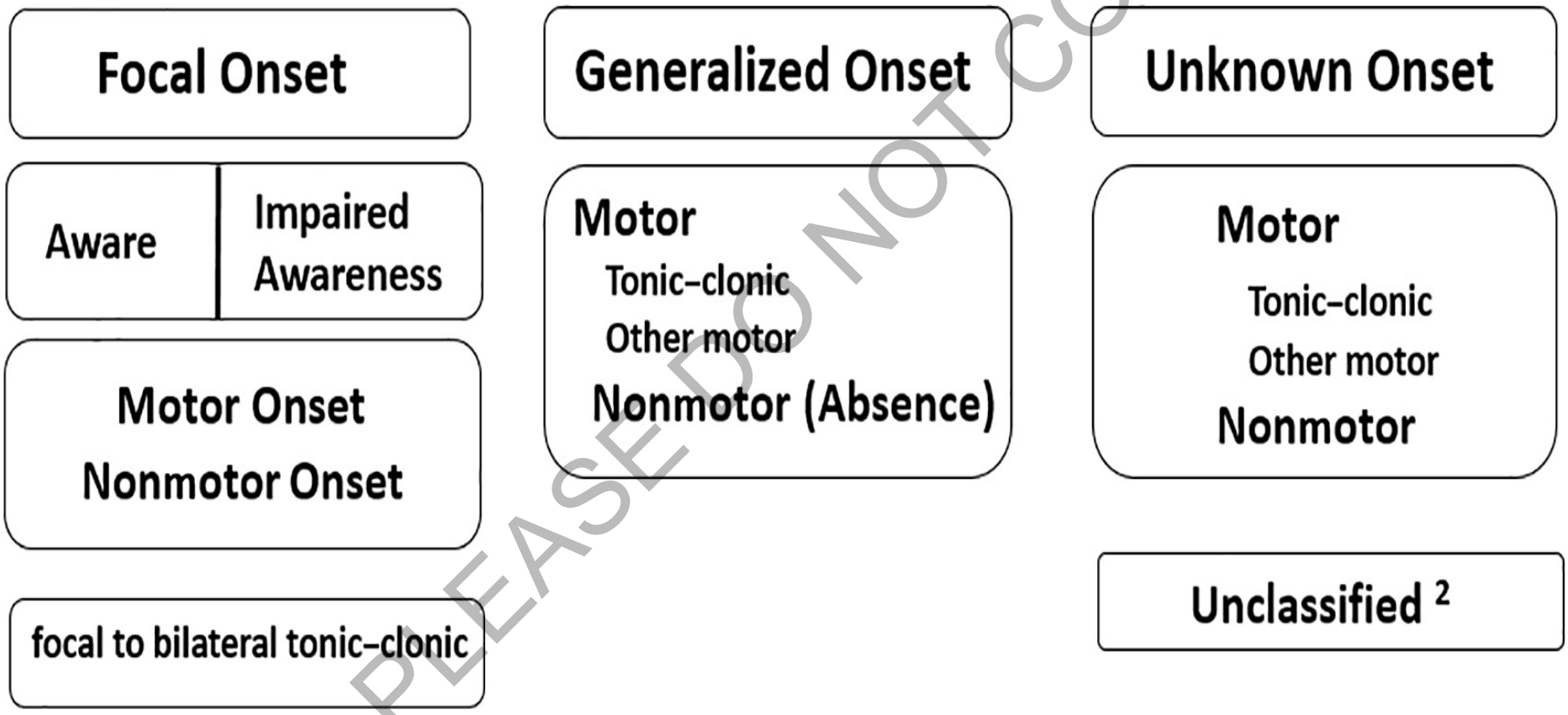
- hypoxic-ischemic brain injury
- developmental brain malformation
- traumatic brain injury
- neurosurgery
- brain tumors
- alcohol-related
- strokes
- CNS infections
- neurodegenerative diseases
- CNS demyelination/inflammation
- inborn errors of metabolism
- systemic illness

Modified from White, 2001

Seizures are classified by their origin in the brain and associated clinical features

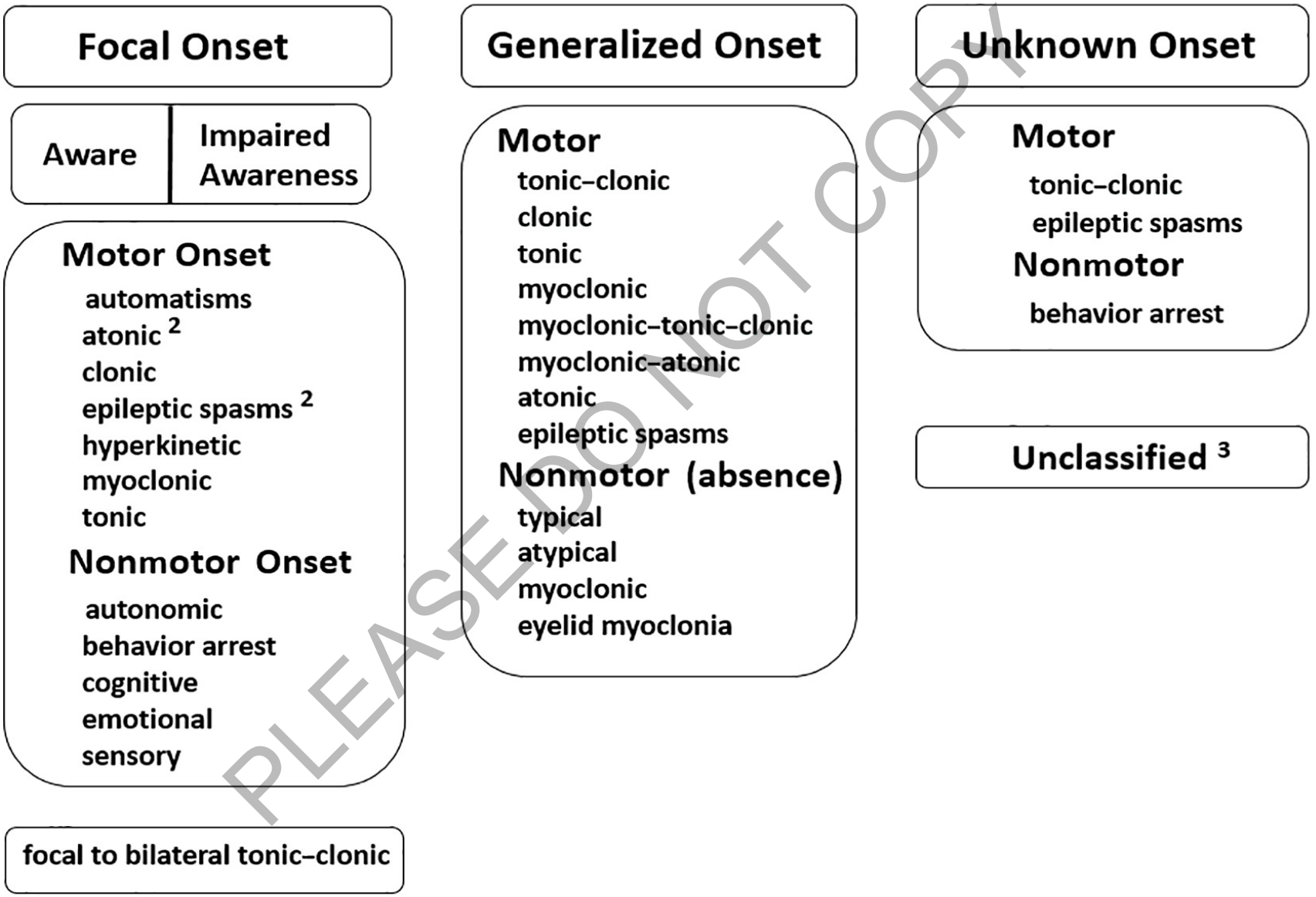
- Partial-onset or focal-onset
  - Simple partial
  - Complex partial
- Generalized-onset
  - Generalized tonic-clonic
  - Absence
  - Myoclonic
- All partial-onset seizures can become secondarily generalized

ILAE 2017 Classification of Seizure Types Basic Version [1]



Epilepsia, Volume: 58, Issue: 4, Pages: 522-530, March 2017

ILAE 2017 Classification of Seizure Types Expanded Version [1]



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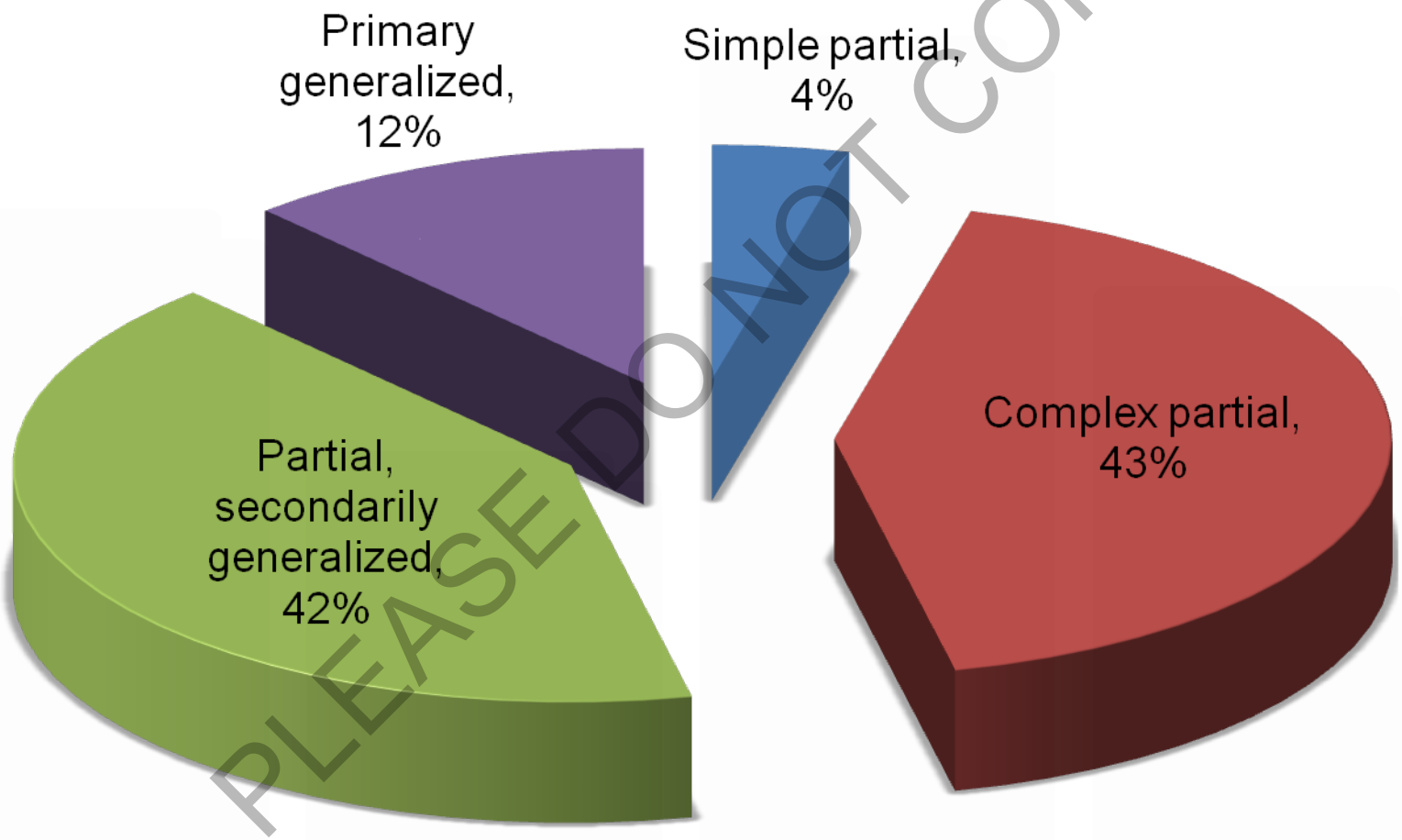
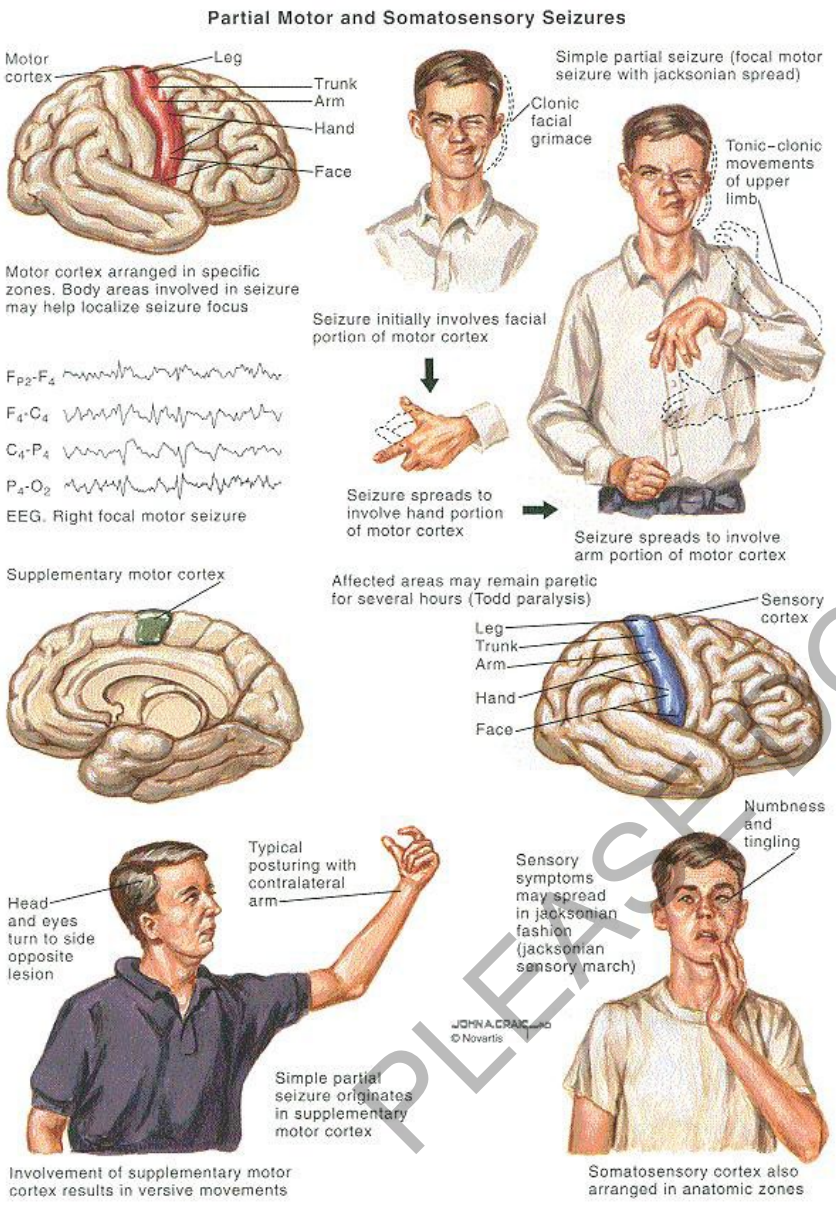
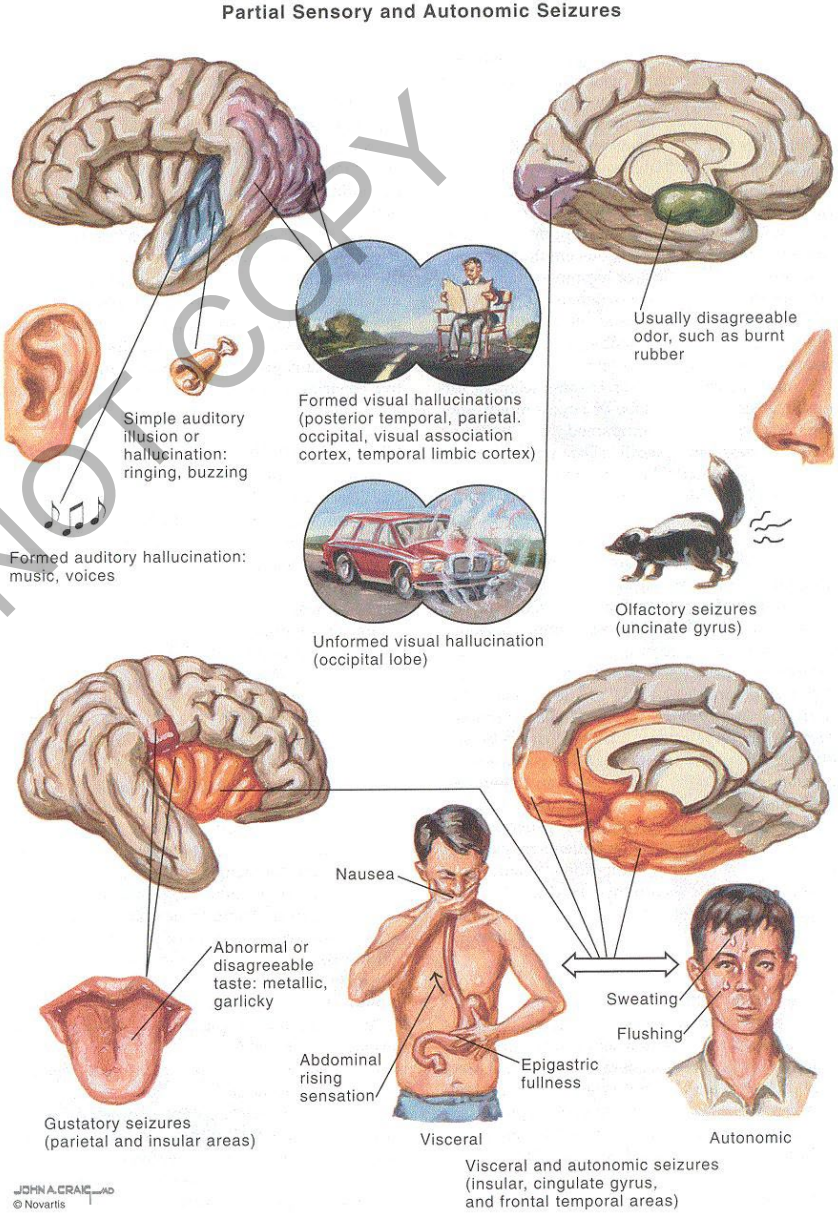
Most seizures in adults are partial-onset



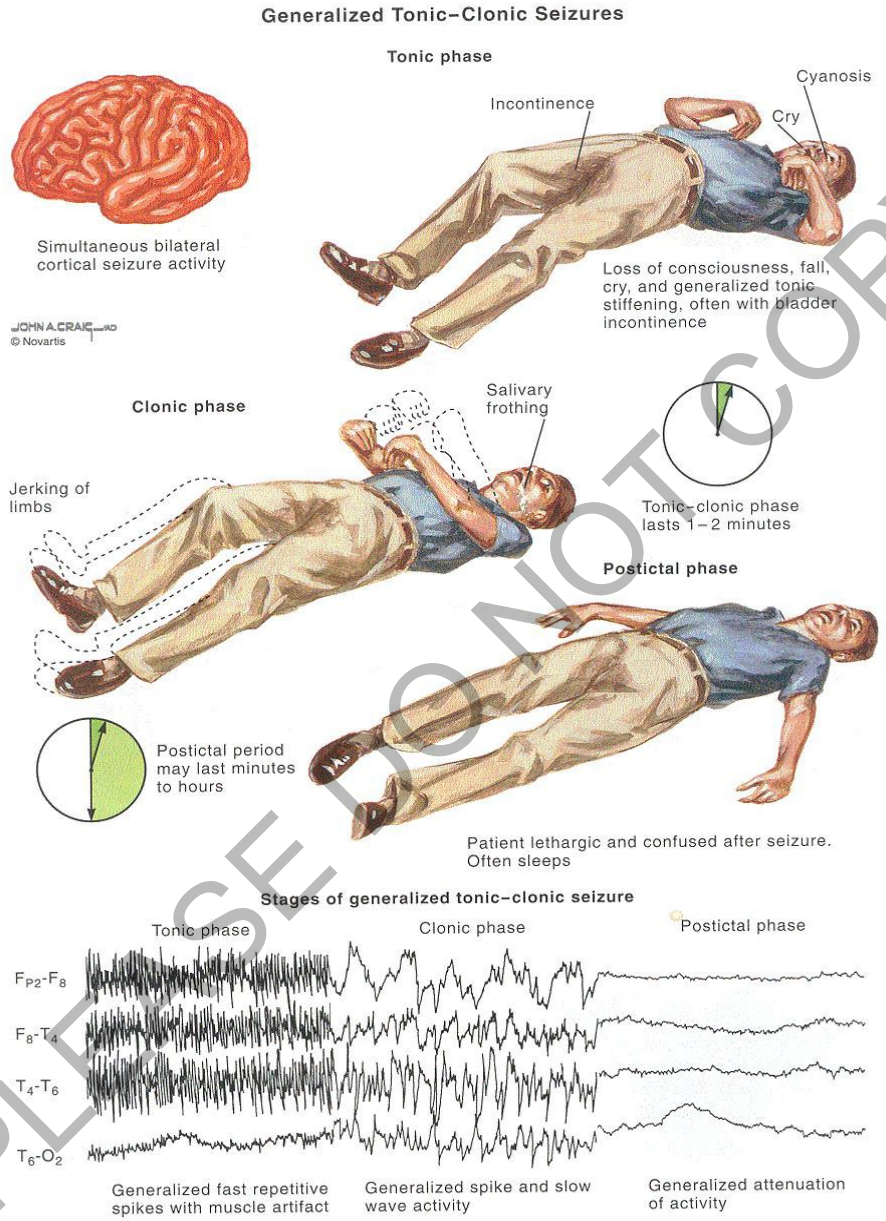
Seizure types in the elderly population

Holt-Seitz et al., 1999





Netter F, Ciba collection of medical illustrations



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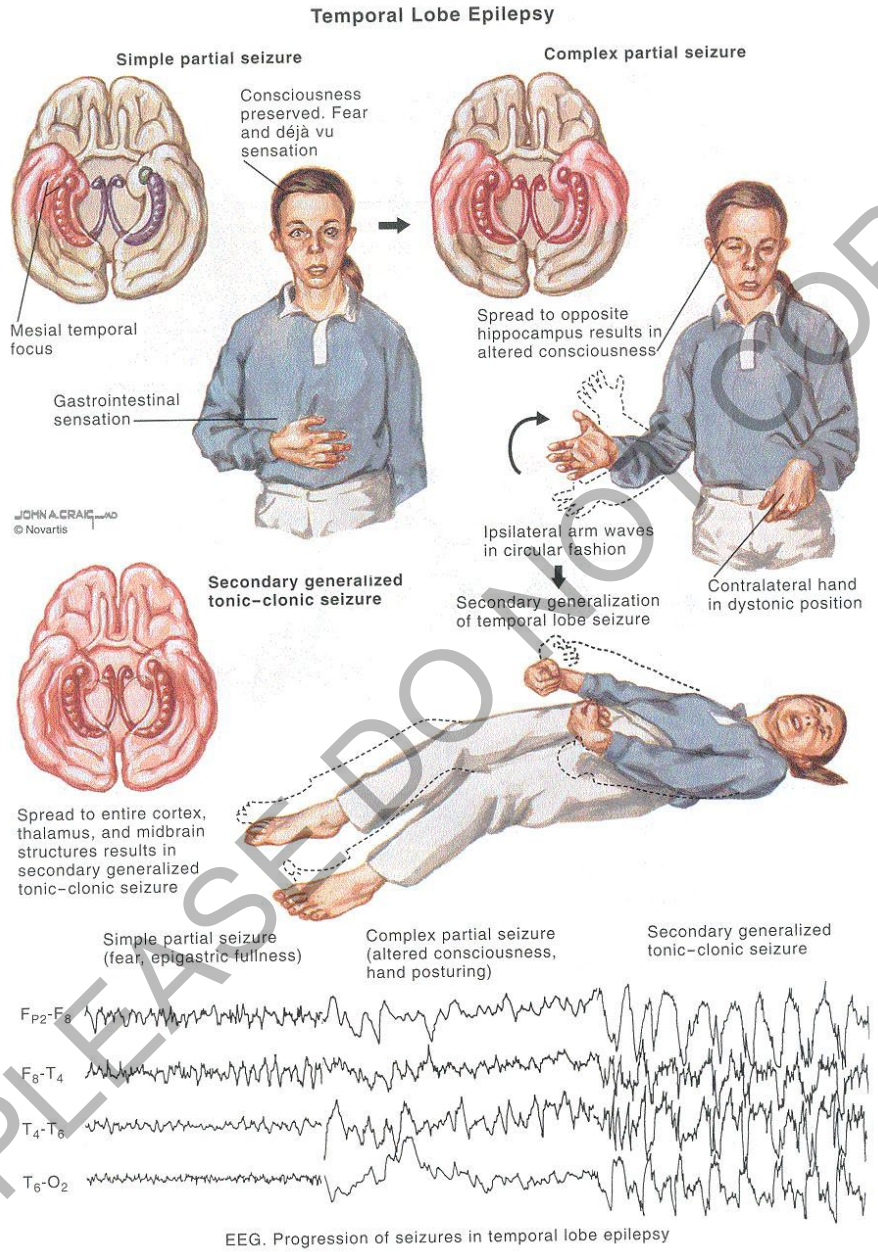
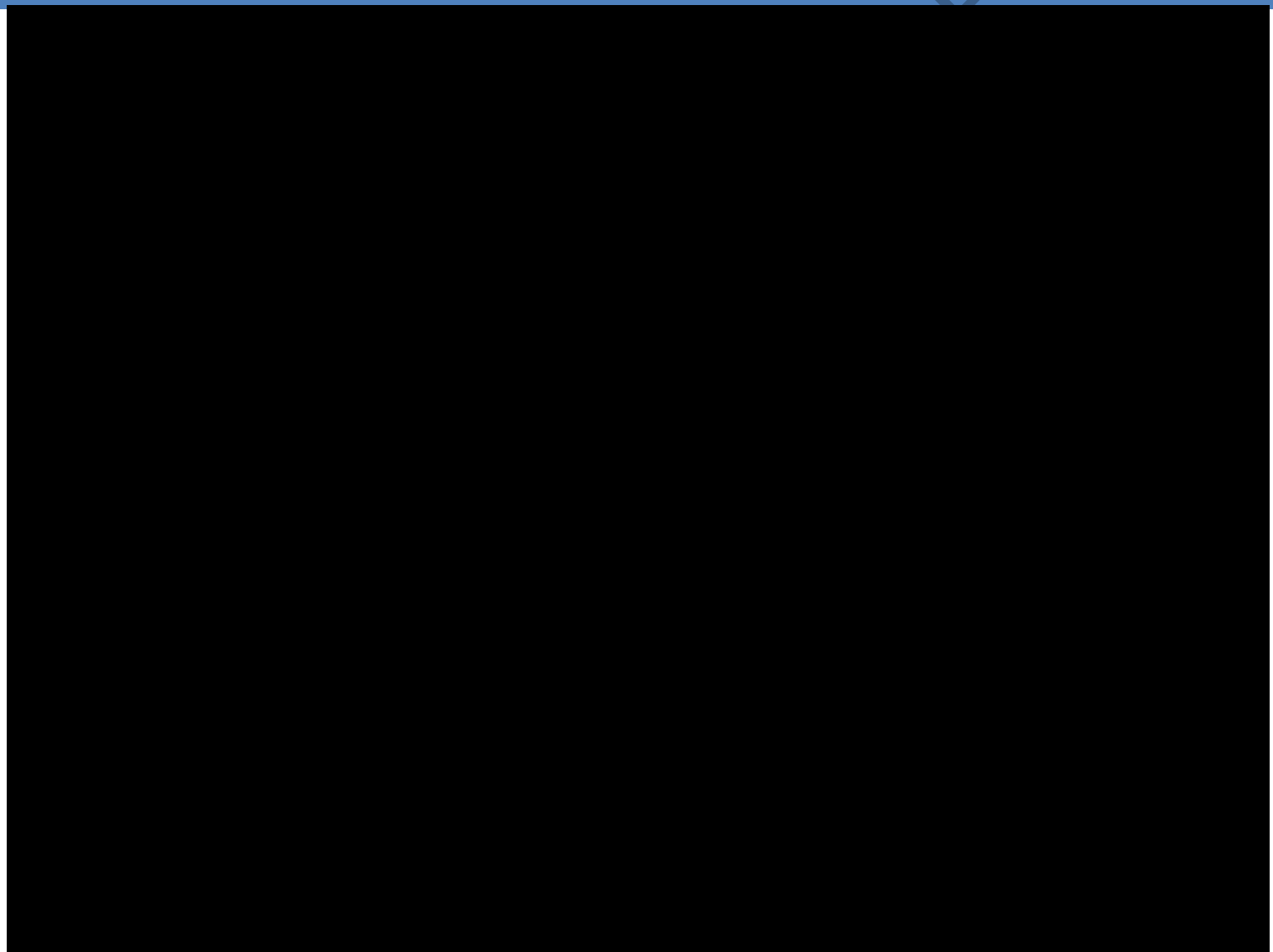


EEG. Progression of seizures in temporal lobe epilepsy

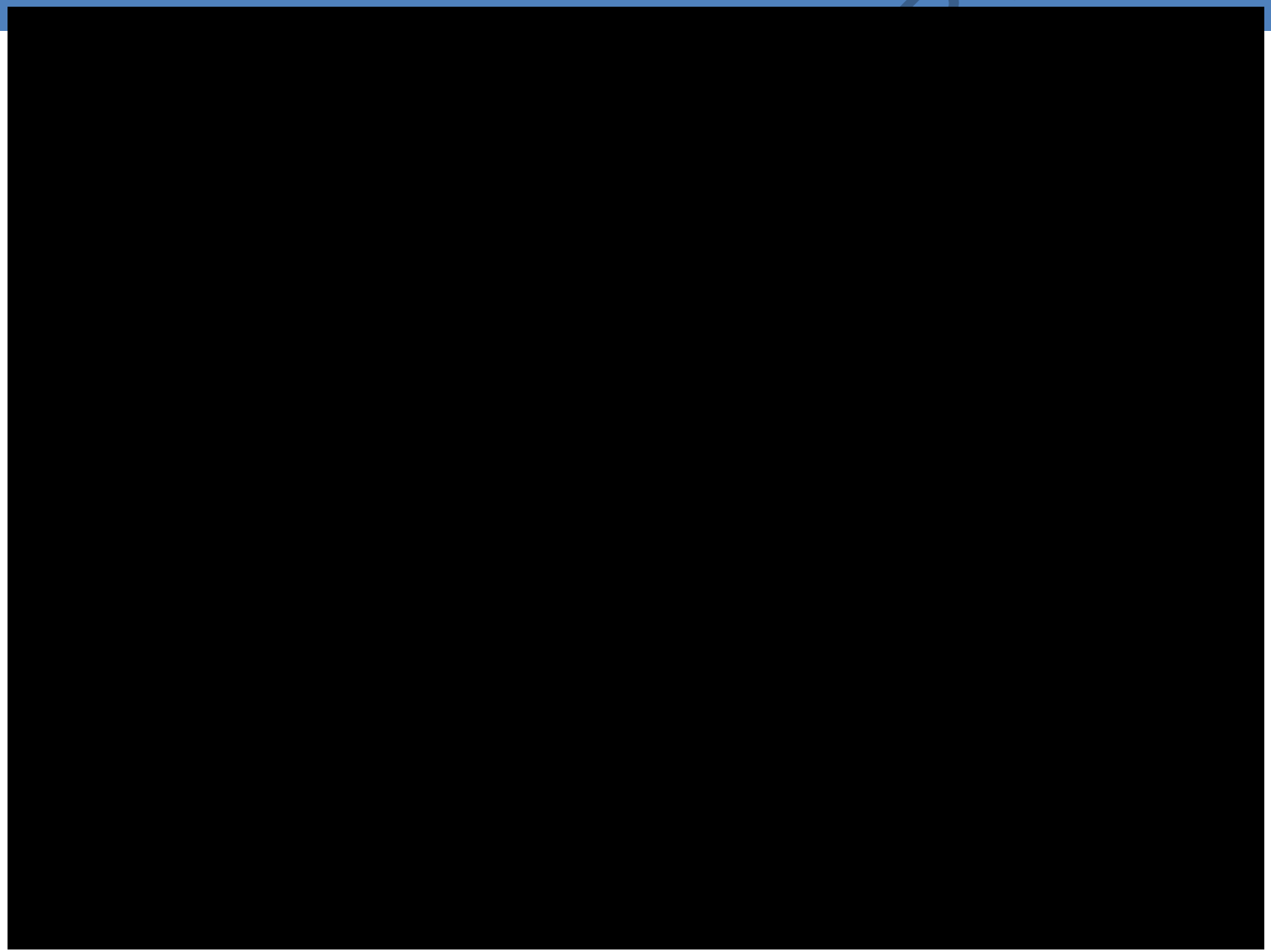
Netter F, Ciba collection of medical illustrations

Focal aware (Simple partial seizures) do not impair awareness or consciousness

Focal impaired awareness (complex partial seizures) of temporal lobe origin have distinct characteristics

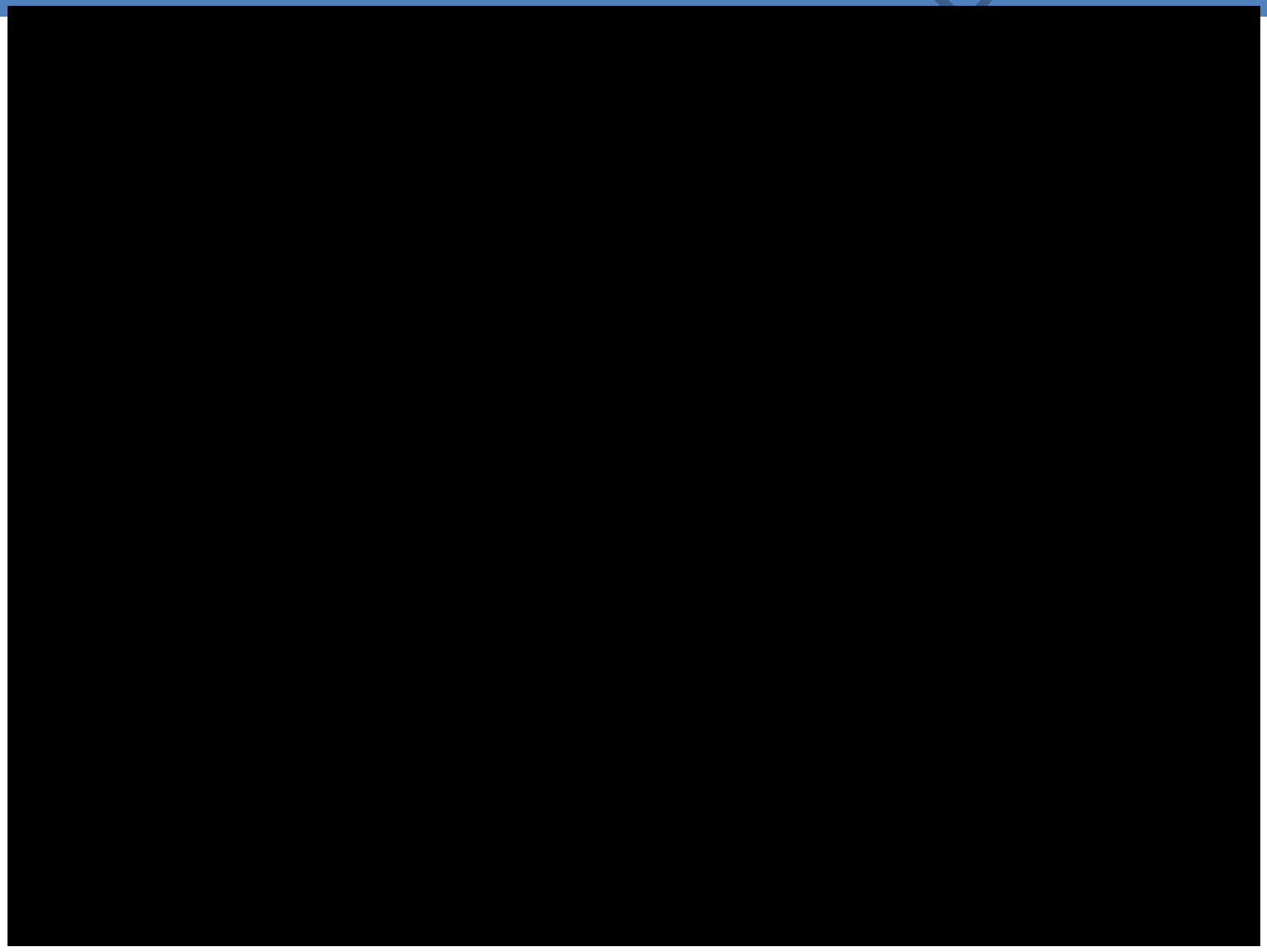


Some focal impaired awareness have minimal associated motor activity



Focal-onset seizures can progress to generalized seizures

The generalized tonic-clonic phase has a very typical appearance



Acute response to seizures

There is little to do acutely during a seizure for most types of seizures

- Absence, myoclonic, focal aware (simple partial) seizures
  - Usually no intervention necessary except reassurance when event ends
- Focal impaired awareness (complex partial) seizures
  - Allow event to run its course while preventing patient from encountering harm
  - Patients may become hostile or violent if actively restrained
- Generalized tonic-clonic seizures
  - Lay patient on side
  - Remove nearly objects that may cause harm
  - Do not place anything inside the mouth

Seizure first aid

Seizure First Aid

How to help someone having a seizure

1

STAY with the person until they are awake and alert after the seizure.

✓**Time** the seizure ✓Remain **calm**
✓Check for **medical ID**

2

Keep the person **SAFE**.

✓Move or guide away from **harm**

3

Turn the person onto their **SIDE** if they are not awake and aware.

✓Keep **airway clear**
✓**Loosen tight clothes** around neck
✓Put **something small and soft** under the head

Call 911 if...

- Seizure lasts longer than 5 minutes
- Person does not return to their usual state
- Person is injured, pregnant, or sick
- Repeated seizures
- First time seizure
- Difficulty breathing
- Seizure occurs in water

Do NOT

✗ Do **NOT** restrain.

✗ Do **NOT** put any objects in their mouth.

✓**Rescue medicines can be given** if prescribed by a health care professional

Learn more: **epilepsy.com/firstaid**

EPILEPSY FOUNDATION | epilepsy.com

24/7 Helpline: 1-800-332-1000

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Life-threatening complications of isolated seizures are rare

- Vast majority of generalized tonic-clonic seizures last 1-2 minutes
- Emesis, aspiration, face-down positioning
- Cardiac arrest or prolonged respiratory arrest, anoxia

Generalized seizures > 2 minutes

- ABC's:
  1. Airway
  2. Breathing
  3. Circulation
- Lorazepam 2mg IV/IM/IN
- Call neurology

What are the initial elements of evaluating a possible seizure?

- History
  - Details of the event
  - Past history of seizure-like symptoms or similar events
  - History of head trauma, febrile seizures, CNS infection
  - Family history of seizures
- Exam
  - General exam: evidence of head injury, meningismus, tongue bite
  - Neurologic exam: evidence suggesting a focal brain lesion
- Labs
  - Evidence of infection or metabolic disturbance: CBC, electrolytes, toxicologic screen, drug levels

Many paroxysmal events can appear similar to seizures clinically

- Syncope / orthostatic hypotension
- TIA
- Confusion/delirium
- Medication side effects
- Cardiac arrhythmia
- Migraine (without headache)
- Hallucinations
- Myoclonus
- Transient global amnesia
- Vertigo
- Movement disorder
- Nonepileptic seizure

The initial clinical diagnosis is based on some distinguishing features

Seizure

- Sudden onset
- Possible warning / "aura"
- Possible postictal state
- Automatisms
- "Positive" neurological symptoms
- Possible tongue bite/incontinence/limb jerking

TIA

- Sudden onset
- Rapid recovery of focal neurological deficit
- Preserved consciousness
- "Negative" neurological symptoms

Syncope

- Gradual onset
- Presyncopal warning
- Change in color / appearance
- Brief loss of consciousness, with rapid recovery
- Loss of tone

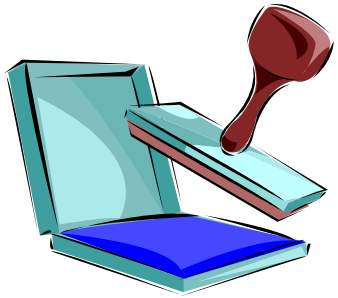
Acute confusion

- Waxing and waning
- Inattention
- No focal neurological deficit
- Drowsiness / decreased alertness / delirium
- Asterixis / myoclonus

Further neurodiagnostic testing could be indicated in certain cases

- Neuroimaging (MRI/CT)
  - All new partial-onset seizure patients should have a nonurgent MRI
  - If acute neurologic lesion is suspected, or injury sustained during a seizure, obtain an urgent CT or MRI
- EEG
  - New onset seizure patients
  - Can help to clarify partial- vs. generalized-onset and prognosticate risk of recurrence

What about the neurology triad?



- MRI / CT
  - If acute neurologic lesion is suspected, obtain an urgent CT or MRI
  - All new partial-onset seizure patients should have a non-urgent MRI
- EEG
  - All new seizure patients should have an EEG
  - Can help to clarify partial- vs. generalized-onset and prognosticate risk of recurrence
- LP
  - Should be performed if CNS infection is suspected
  - Does not need to be automatically performed after any unexplained seizure

A single seizure does not generally warrant antiepileptic drug treatment

- The risk of recurrence after a single unprovoked seizure in next two years is 25-40%
  - Depends on seizure type, EEG findings
- The risk of recurrence after two unprovoked seizures is 80% or more
  - Most neurologists do treat after two episodes

Berg and Shinnar, 1991

There are many antiepileptic drugs, some of which have multiple indications

Classical

- 1857 – Bromides
- 1912 – Phenobarbital (PB)
- 1937 – Phenytoin (PHT)
- 1954 – Primidone
- 1958 – ACTH
- 1960 – Ethosuximide (ESM)
- 1963 – Diazepam
- 1974 – Carbamazepine (CBZ)
- 1975 – Clonazepam (CZP)
- 1978 – Valproate (VPA)

Newer

- 1993 – Felbamate (FBM), Gabapentin (GBP)
- 1995 – Lamotrigine (LTG)
- 1997 – Topiramate (TPM), Tiagabine (TGB)
- 1999 – Levetiracetam (LEV)
- 2000 – Oxcarbazepine (OXC), Zonisamide (ZNS)
- 2005 - Pregabalin (PGB)
- 2008 – Lacosamide (LCM),
  Rufinamide (RUF)
- 2009 – Vigabatrin (VGB)
- 2011 – Ezogabine

  Clobazam
- 2012 – Perampanel
- 2013 – Eslicarbazepine
- 2016 – Brivaracetam
- 2018 - Epidiolex (6/25/2018)

Status epilepticus is a medical emergency

- Either a state of continuous seizure activity or a state in which seizures are recurring so frequently that there is no recovery in between

- The operational definition (when to begin acting) is 5 minutes

There are many precipitating risk factors for status epilepticus

- Preexisting epilepsy
  - Medication noncompliance
  - Sleep deprivation or alcohol
  - Worsening underlying disease
- Metabolic / toxic disturbances
  - Hyperglycemia, hyponatremia, etc.
  - Drug intoxication
- Structural neurological causes
  - Acute stroke, hemorrhage
  - Head trauma

Summary

- Seizures are quite common in the population, but rare as a direct complication of TMS
- Most seizures in adults are focal-onset, but can become secondarily generalized
- Seizures have some distinguishing characteristics, but can still be confused with other types of events
- There is little to do other than ensure safety in the setting of an acute seizure
- The vast majority of seizures stop by themselves, but any lasting 5 minutes or more should be treated as a medical emergency

Questions