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

- 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.
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

- **Focal Onset**
  - **Aware**
    - Impaired Awareness
  - **Motor Onset**
    - Nonmotor Onset
    - focal to bilateral tonic-clonic

- **Generalized Onset**
  - **Motor**
    - Tonic-clonic
    - Other motor
  - **Nonmotor (Absence)**

- **Unknown Onset**
  - **Motor**
    - Tonic-clonic
    - Other motor
  - **Nonmotor**

- **Unclassified**
ILAE 2017 Classification of Seizure Types Expanded Version

Focal Onset
- Aware
- Impaired Awareness

Motor Onset
- automatisms
- atonic
- clonic
- epileptic spasms
- hyperkinetic
- myoclonic
- tonic

Nonmotor Onset
- autonomic
- behavior arrest
- cognitive
- emotional
- sensory

focal to bilateral tonic-clonic

Generalized Onset
- Motor
  - tonic-clonic
  - clonic
  - tonic
  - myoclonic
  - myoclonic-tonic-clonic
  - myoclonic-atonic
  - atonic
  - epileptic spasms
- Nonmotor (absence)
  - typical
  - atypical
  - myoclonic
  - eyelid myoclonia

Unknown Onset
- Motor
  - tonic-clonic
  - epileptic spasms
- Nonmotor
  - behavior arrest

Unclassified

Epilepsia, Volume: 58, Issue: 4, Pages: 522-530, March 2017
Most seizures in adults are partial-onset

Seizure types in the elderly population

- Complex partial, 43%
- Partial, secondarily generalized, 42%
- Primary generalized, 12%
- Simple partial, 4%

Holt-Seitz et al., 1999
Generalized Tonic–Clonic Seizures

**Tonic phase**
- Loss of consciousness, fall, cry, and generalized tonic stiffening, often with bladder incontinence

**Clonic phase**
- Jerking of limbs
- Salivary frothing

**Postictal phase**
- Postictal period may last minutes to hours
- Patient lethargic and confused after seizure, often sleeps

**Stages of generalized tonic–clonic seizure**
- Tonic phase
- Clonic phase
- Postictal phase

- Generalized fast repetitive spikes with muscle artifact
- Generalized spike and slow wave activity
- Generalized attenuation of activity

Netter F, Ciba collection of medical illustrations
Temporal Lobe Epilepsy

Simple partial seizure
- Consciousness preserved. Fear and déjà vu sensation
- Mesial temporal focus
- Gastrointestinal sensation

Complex partial seizure
- Spread to opposite hippocampus results in altered consciousness
- Ipsilateral arm waves in circular fashion
- Centralateral hand in dystonic position

Secondary generalized tonic-clonic seizure
- Spread to entire cortex, thalamus, and midbrain structures results in secondary generalized tonic-clonic seizure

Simple partial seizure (feeling of déjà vu)
- Complex partial seizure (altered consciousness, hand posturing)

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**
- Restrain.
- Put any objects in their mouth.
- Rescue medicines can be given if prescribed by a health care professional

Learn more: [epilepsy.com/firstaid](http://epilepsy.com/firstaid)

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

[Epilepsy Foundation](http://epilepsy.com)
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

<table>
<thead>
<tr>
<th>Seizure</th>
<th>TIA</th>
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<tbody>
<tr>
<td>- Sudden onset</td>
<td>- Sudden onset</td>
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<tr>
<td>- Possible warning / “aura”</td>
<td>- Rapid recovery of focal neurological deficit</td>
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<tr>
<td>- Possible postictal state</td>
<td>- Preserved consciousness</td>
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<tr>
<td>- Automatisms</td>
<td>- “Negative” neurological symptoms</td>
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<tr>
<td>- “Positive” neurological symptoms</td>
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<tr>
<td>- Possible tongue bite/incontinence/limb jerking</td>
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<table>
<thead>
<tr>
<th>Syncope</th>
<th>Acute confusion</th>
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<tr>
<td>- Gradual onset</td>
<td>- Waxing and waning</td>
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<tr>
<td>- Presyncopal warning</td>
<td>- Inattention</td>
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<tr>
<td>- Change in color / appearance</td>
<td>- No focal neurological deficit</td>
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<tr>
<td>- Brief loss of consciousness, with rapid recovery</td>
<td>- Drowsiness / decreased alertness / delirium</td>
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<td>- Loss of tone</td>
<td>- Asterixis / myoclonus</td>
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PLEASE DO NOT COPY
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.

<table>
<thead>
<tr>
<th>Classical</th>
<th>Newer</th>
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<tr>
<td>1857 – Bromides</td>
<td>1993 – Felbamate (FBM), Gabapentin (GBP)</td>
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<tr>
<td>1912 – Phenobarbital (PB)</td>
<td>1995 – Lamotrigine (LTG)</td>
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<tr>
<td>1937 – Phenytoin (PHT)</td>
<td>1997 – Topiramate (TPM), Tiagabine (TGB)</td>
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<td>1954 – Primidone</td>
<td>1999 – Levetiracetam (LEV)</td>
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<td>1958 – ACTH</td>
<td>2000 – Oxcarbazepine (OXC), Zonisamide (ZNS)</td>
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<td>1960 – Ethosuximide (ESM)</td>
<td>2005 - Pregabalin (PGB)</td>
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<tr>
<td>1963 – Diazepam</td>
<td>2008 – Lacosamide (LCM), Rufinamide (RUF)</td>
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<tr>
<td>1974 – Carbamazepine (CBZ)</td>
<td>2009 – Vigabatrin (VGB)</td>
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<td>1975 – Clonazepam (CZP)</td>
<td>2011 – Ezogabine</td>
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<tr>
<td>1978 – Valproate (VPA)</td>
<td>Clobazam</td>
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<td>2012 – Perampanel</td>
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<tr>
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<td>2013 – Eslicarbazepine</td>
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<td>2016 – Brivaracetam</td>
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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