

DIFFERENTIAL DIAGNOSIS OF EPILEPSY AND SEIZURE MIMICS

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DISCLOSURES

- None

ALWAYS QUESTION THE DIAGNOSIS

- What is a seizure?
 - A sudden and temporary change in the electrical and chemical activity in the brain which leads to a change in movement, behavior, level of awareness, or emotions
- Seizure semiology can vary broadly based on etiology of seizure, zone of onset, and spread
 - Wide range of positive and negative motor and non-motor manifestations depending on areas of origin may be seen
- What is epilepsy?
 - At least two unprovoked seizure occurring greater than 24 hours apart OR one unprovoked seizure with probability of future seizures similar to that of two unprovoked seizures (>60%) in the next 10 years (ILAE).
 - The diagnosis of epilepsy continues to carry prominent stigma and discrimination and has significant impact daily life and employment
- Of patients seen in epilepsy centers 20-30% are found to have been misdiagnosed due to wide variety of paroxysmal conditions that can lead to referral
- Misdiagnosis has important implications on driving, work, and other aspects of life along with psychological burden and possible

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TABLE 2-1 Events That May Potentially Mimic Seizures

► Physiologic Events
Syncope (orthostatic/arrhythmia, others)
Migraine (complex)
Transient ischemic attacks
Transient global amnesia
Dizziness/vertigo
Sleep disorders
Waxing and waning delirium
Intermittent movement disorders
► Psychiatric-Based Events
Panic/anxiety attacks
Conversion, psychogenic nonepileptic seizures
Dissociative states
Hyperventilation syndrome
Acute psychosis
Malingering

TABLE 2-2 Yearly Incidence of Episodic Events

Episodic Events	Number/ 100,000
Syncope	3000
Dizziness	2600
Migraine	730
Epilepsy	50
Transient ischemic attack	23
Transient global amnesia	3

Modified from Fisher RS. Imitators of epilepsy. New York: Demos, 1994.

SUSPECTING THE DIAGNOSIS

- History!
 - Description of events including frequency, duration, post-ictal state, provoking factors, comorbidities
- Imaging
- Cardiac monitoring
 - Tilt table testing
 - Telemetry, ILR
- Inpatient and home video EEG monitoring

PSYCHOGENIC NON-EPILEPTIC EVENTS (PNEE)

- Behavioral events that look like epileptic seizures.
 - They are NOT epileptic and are instead caused by psychological factors
- DSM divides physical symptoms resulting from psychological factors as
 - 1) Somatoform disorders – conversion disorder and somatization disorder
 - 2) Factitious disorder
 - 3) Malingering
- Previously referred to as pseudoseizure, non-epileptic seizure, psychogenic seizure
- History of abuse is common although underlying psychopathology relates to poor coping mechanisms
 - Comorbidities may include depression, anxiety, fibromyalgia, PTSD, or personality disorder
- Most common condition misdiagnosed as epilepsy (>90%) with delay to correct diagnosis often being 7-10 years

PSYCHOGENIC NON-EPILEPTIC EVENTS (PNEE)

- Historical features include
 - Resistance to seizure medications
 - Very high frequency or duration of events
 - Specific triggers such as certain movement or sounds or getting upset
 - Variable semiology
 - Pelvic thrusting or back arching
 - Ictal stuttering
 - Ictal eye closure
- Video EEG monitoring with goal of recording episodes is "gold standard" for diagnosis
 - May be inpatient epilepsy monitoring unit (EMU) or home
 - PNEE may occur co-morbid with epilepsy
- The most important part of initiating treatment is delivery of diagnosis to patient and family
- Cognitive behavioral therapy is most studied treatment plan
- Correct diagnosis leads to reduced resource utilization

VASCULAR MIMICS

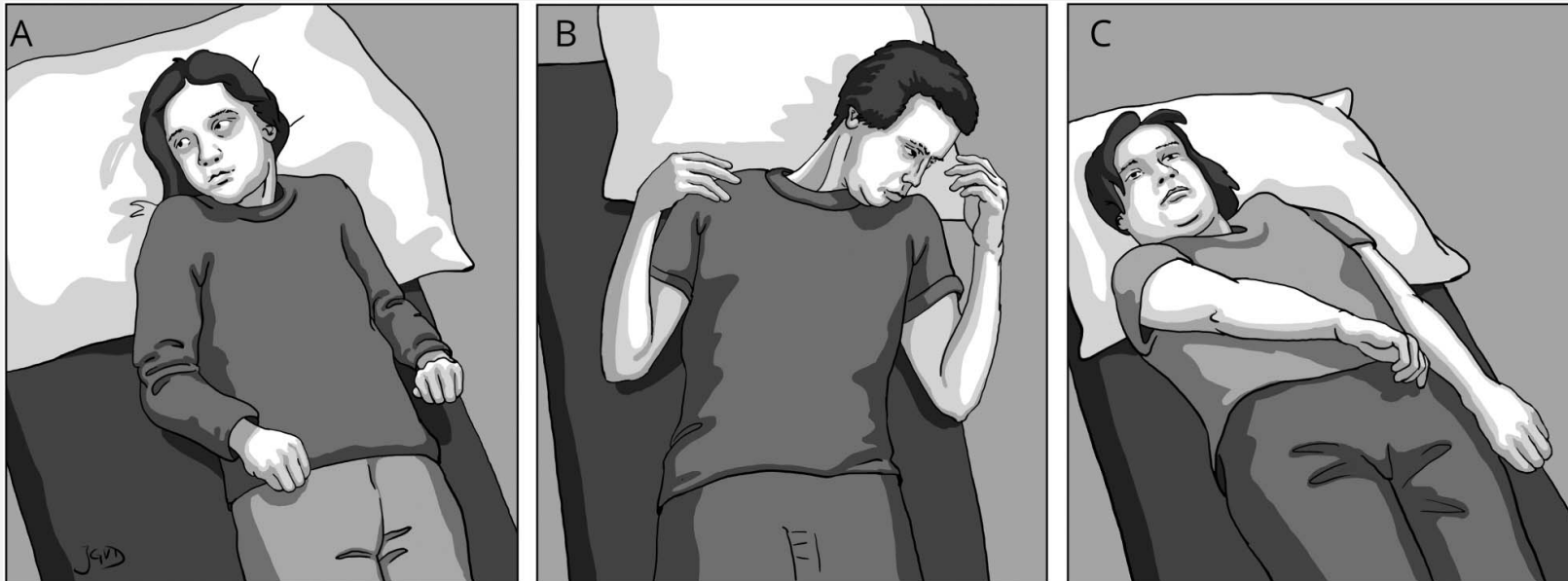
- Syncope
- TIA
- Bowhunter
- Amyloid Spell

SYNCOPE

- Syncope is defined as abrupt, transient, and complete loss of consciousness associated with inability to maintain postural tone with spontaneous and rapid recovery due to cerebral hypoperfusion
 - May be secondary to systemic vasodilation or decreased cardiac output
- Historical features include events are typically brief with more prolonged loss of consciousness (>60 seconds) suggestive of seizure and more prolonged recovery to cognitive baseline suggestive of seizure
- Accounts for over 1% of all ER visits with 25% admitted and 10% given observation status

SYNCOPE

- Motor signs are often common to both seizures and syncope with 40-90% of all syncope having convulsive features (Shmueli 2018, Lempert 1991)
 - Myoclonic jerks occur in 51% often occurring repeatedly for a minute or longer
 - Tonic postures occur in 65%
 - Posturing may even suggest lateralizing features such as head and eye version or arm extensions and pronation
 - Myoclonus results from hypoperfusion of cortex and posturing from hypoperfusion of brainstem



SYNCOPE

- Reflex (Neurogenic) Syncope – most common
 - Carotid Sinus Hypersensitivity
 - Stimulation of carotid sinus such as with shaving, tight collars, neck turns can cause ventricular pause or drop in SBP which is reproducible with massage
 - Situational
 - Valsalva such as cough or micturition syncope
 - Vasovagal
 - Most common type of syncope accounting for 85% of syncope in people under 40 with lifetime incidence of 33%
 - Associated with physiologic signs such as sweating, nausea, vomiting, palpitations
 - Requires intact autonomic nervous system making it less likely in conditions like Parkinson's disease.

SYNCOPE

- Cardiac
 - Arrhythmia
 - Bradycardia, tachyarrhythmia, sinus pauses
 - May be preceded by palpitations but less commonly involve prodrome of nausea, vomiting, sweating
 - Structural
 - Tamponade, Hypertrophic cardiomyopathy, Infiltrative disease (amyloid/sarcoid)
 - Valvular
 - Atrial, Mitral, pulmonic stenosis – may have murmur on exam
- Vascular
 - Acute myocardial infarct, Aortic dissection, Pulmonary embolism

SYNCOPE

- Autonomic failure
 - May be seen in diabetes mellitus, Parkinson's disease, Lewy body dementia, multiple sclerosis, spinal cord lesion
- Drug induced
 - Anti-cholinergics, diuretics, anti-hypertensives, dopaminergics, opiates, antipsychotics, tricyclic antidepressants
- Postural Orthostatic Tachycardia Syndrome (POTS)
 - Most common in women in early adulthood
- Volume depletion

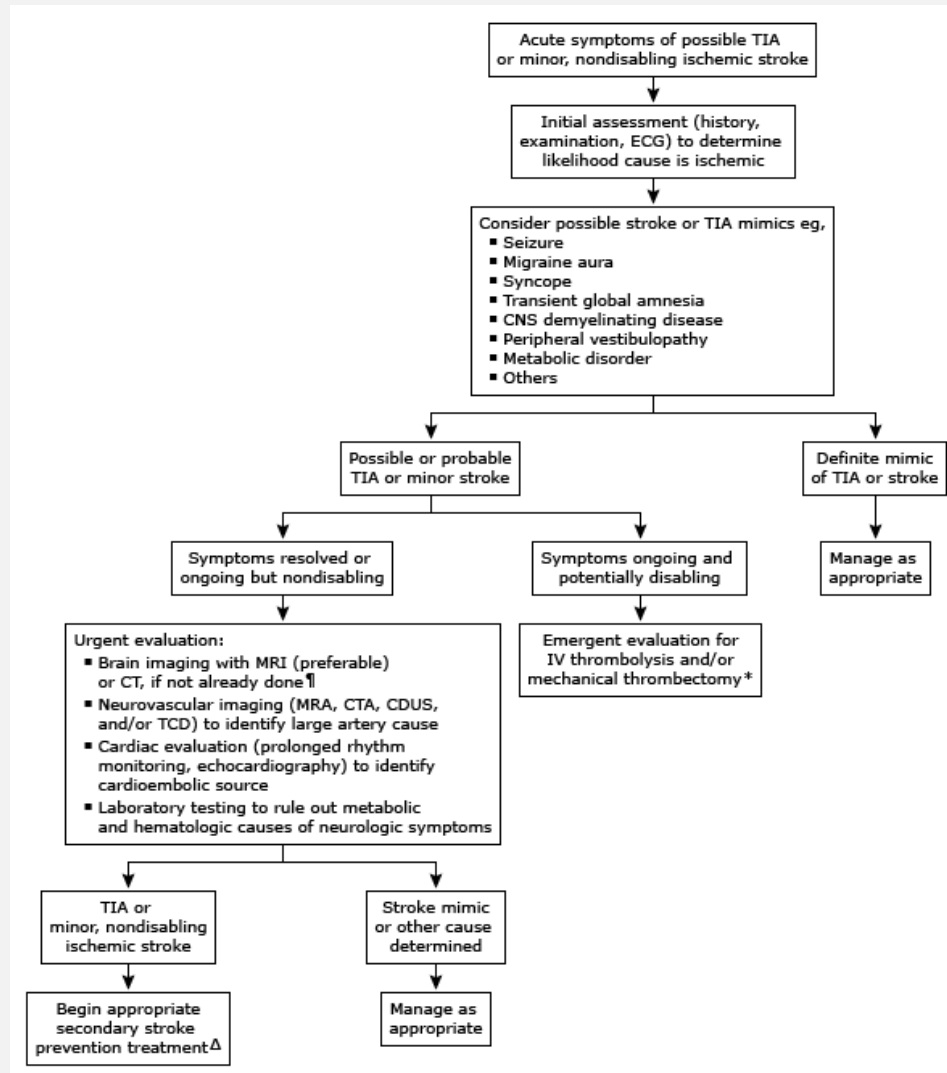
SYNCOPE

- Evaluation
 - History!
 - Orthostatic vital signs
 - Supine, 1/3/5 minutes standing
 - Drop SBP>20, DBP>10, or increase HR>20
 - Tilt table testing
 - Protocols may include pharmacologic challenge such as sublingual nitroglycerin
 - Typically done with concurrent EEG to evaluate for slowing indicative of hypoperfusion
 - Extended EKG monitoring
 - Typically done in association with video EEG

TRANSIENT ISCHEMIC ATTACK (TIA)

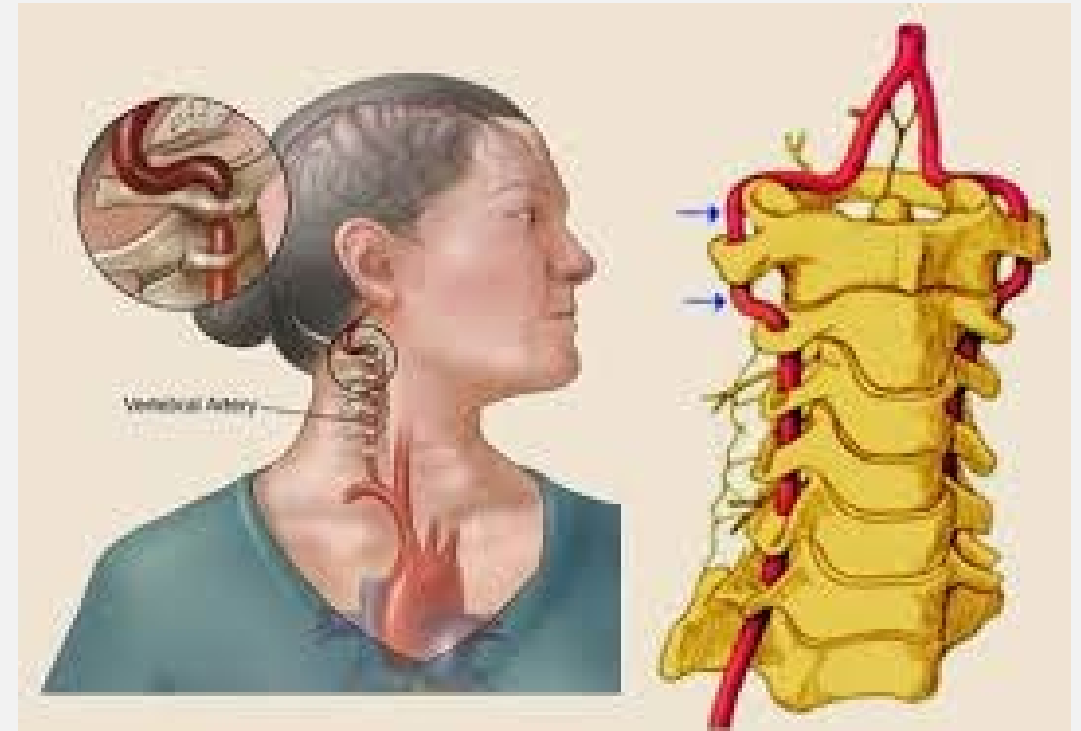
- Transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia without acute infarct lasting minutes up to <1 hour.
- Signs and symptoms focal but may vary widely depending on area of the brain to which they localize.
 - FAST (face, arm, speech, time)
 - May also include diplopia, monocular vision loss, dizziness, or balance
- Symptoms may fluctuate depending on adequacy of perfusion
- Symptoms are typically “negative” indicating absence or loss of function
 - “Limb shaking TIA” consist of myoclonic or rhythmic motor activity due to ischemia from artery stenosis supplying motor cortex
- Event or events typically cluster over an acute or subacute period of time and do not continue over months to years without fixed deficit

TRANSIENT ISCHEMIC ATTACK (TIA)



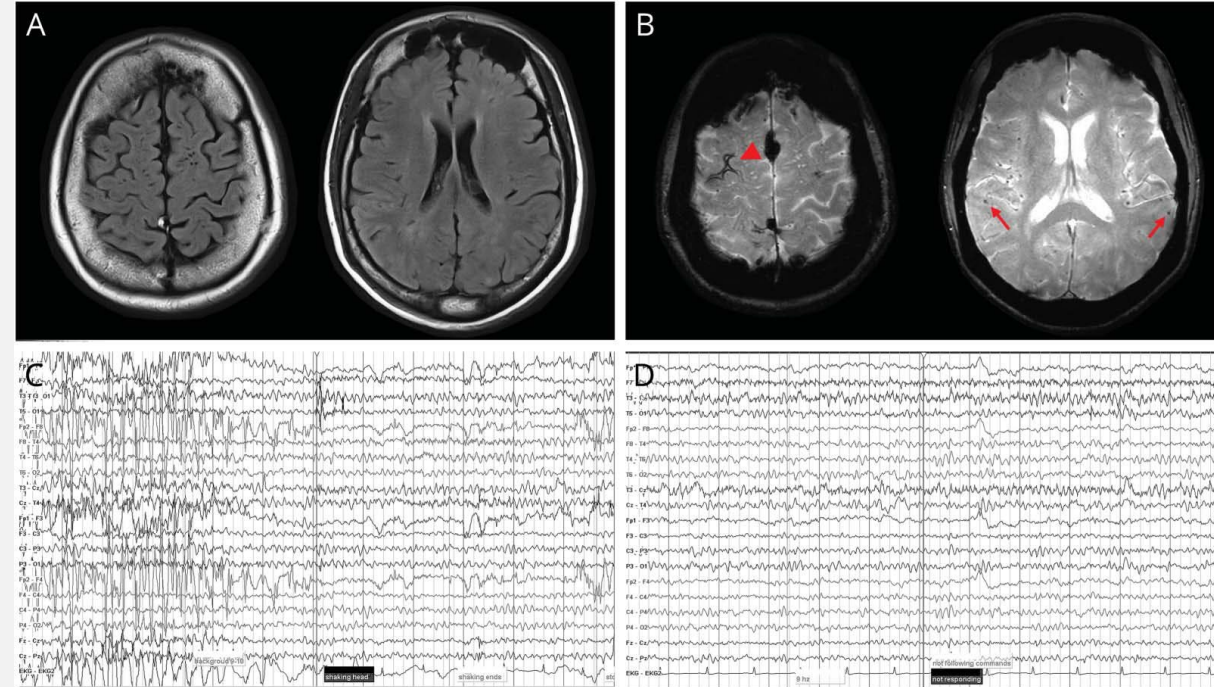
BOWHUNTER SYNDROME

- Rotational vertebral artery syndrome in which vertebrobasilar insufficiency occurs due to vertebral artery compression by transverse process of cervical vertebrae during head rotation
- Common symptoms include drop attacks, vision change, dysarthria, vertigo
- Osteophytes are most common etiology although may occur by atherosclerosis or dissection
- Evaluation includes transcranial doppler or angiogram with evocative maneuvers
- Treatment may be conservative (anticoagulation and avoidance) or surgical (c-spine decompression, stent placement in asymptomatic vertebral artery for improved perfusion)



AMYLOID SPELLS

- Cerebral Amyloid Angiopathy (CAA) is characterized by accumulation of amyloid beta-peptide in small to medium cerebral vessels
- “Amyloid Spells” occur in about 20% with increased risk in the setting of superficial siderosis and last seconds up to 30 minutes
- Positive symptoms due to cortical spreading depression 2/2 hemosiderin include limb shaking
- Negative symptoms due to vessel occlusion and spasms include numbness, inability to speak, weakness, loss of consciousness
- EEG during episodes is normal
- Episodes sometimes improve with blood pressure control, limited evidence for seizure medications



MIGRAINE AURA

- ICDH-3 description of **migraine** is recurrent headache disorder manifesting in attacks lasting 4-72 hours.
 - unilateral location, pulsating quality,
 - moderate or severe intensity,
 - aggravation by routine physical activity
 - association with nausea and/or photophobia and phonophobia
- Aura may occur hours to days before the headache phase
 - May be visual (occipital), sensory (parietal), or psychic (temporal)
- Pathology is related to **cortical spreading depression** (CSD) in which an efflux of K^+ and glutamate depolarizes adjacent neurons and glia leading to neuronal swelling
 - Glutamate increases production of NO causing vasodilation
 - Wave of depolarization spreads at 1-2mm/minute with lasting inhibition of cortical activity lasting up to 30 minutes

MIGRAINE AURA

- **Migraine with typical aura**

- Aura consists of **visual and/or sensory and/or speech/language symptoms**, but no motor weakness, characterized by gradual development, duration of each symptom no longer than one hour, a **mix of positive and negative features** and complete reversibility.

- **Hemiplegic migraine**

- Aura consisting of both of the following:
 - fully reversible motor weakness
 - fully reversible visual, sensory and/or speech/language symptoms.
- Hemiplegia occurs at onset versus Todd paralysis which occurs after

- **Migraine with brainstem aura**

- Aura symptoms clearly originating from the brainstem, but **no motor weakness**.
- at least two of the following fully reversible brainstem symptoms:
 - a) dysarthria
 - b) vertigo
 - c) tinnitus
 - d) hyperacusis
 - e) diplopia
 - f) ataxia not attributable to sensory deficit
 - g) decreased level of consciousness (GCS ≤ 13)

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TRANSIENT GLOBAL AMNESIA (TGA)

- Clinical syndrome of sudden onset of anterograde more than retrograde amnesia lasting from less than an hour up to 24 hours
 - Most common in those over 50 years with incidence 24 per 100,000
 - Presentation may include nausea, vomiting, headache, dizziness
 - Often brought on by heightened physical or emotional state such as exertion, Valsalva, sexual activity, high altitudes, exposure to extreme temperatures
 - Lifetime recurrence up to 25%
 - MRI not required for diagnosis but may include punctate DWI lesion in the hippocampus in the first 24 hours
 - Hypothesized mechanism is jugular venous hypertension from increased thoracic pressure

INTRACRANIAL PRESSURE

- Adults with Chiari malformations may have drop attacks with Valsalva or modest exertion due to transient increases in intracranial pressure that cause dysfunction of the ascending reticular activating system
- IIH compression of dural venous sinuses can lead to syncope
 - 15% of cases may lack headaches and the condition may present without papilledema
- Cerebral venous sinus thrombosis may result in intracranial pressure fluctuations and syncope

SLEEP DISORDERS

- Non REM (N2/slow wave sleep) parasomnias
 - Night Terrors
 - Awakening in terrified state unable to communicate with poor responsiveness to voice or difficulty with full arousal lasting up to 15 minutes
 - Risk factors include psychoactive drugs or alcohol
 - Sleep Walking (Somnambulism)
 - Patient wanders about without recollection
 - 15% children, 0.7% adults
 - Enuresis
 - Confusional arousals
 - Slow awakening with confusion
- REM parasomnias
 - REM behavior disorder
 - Flailing, kicking, punching, yelling, running
 - Most common in men over 50 and associated with Parkinson's disease and Lewy Body Dementia
 - Nightmares