Differential Diagnosis of Epilepsy

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Outline

Introduction

Paroxysmal event in children

Paroxysmal event in adult
Diagnosis: Rely on clinical history

- Description of onset, course, offset of paroxysmal symptoms
- Precise circumstances
- Past medical history
- Family history
- Current medication

Witness

Paroxysmal events in children

1. Generalized paroxysms and drop attacks
2. Jerks and abnormal posture
3. Ocular abnormalities
4. Sleep disorder

Generalized paroxysms and drop attacks

- **Neonates**
  - Apnea
  - Hyperekplexia

- **Infants**
  - Hyperekplexia
  - Reflex anoxic seizures
  - Breath-holding spell
  - Benign paroxysmal vertigo
  - Pathologic startle

- **Children and adolescents**
  - Benign paroxysmal vertigo
  - Pathologic startle
  - Compulsive Valsalva
  - Alternating hemiplegia
  - Familial hemiplegic migraine
  - Syncope (long QT, vasovagal, vagovagal, orthostatic, migraine induced)
  - Psychogenic seizures
  - Cataplexy

Jerks and abnormal postures

- Neonates
  - Jitteriness
  - Paroxysmal dystonic choreoathetosis

- Infants
  - Jitteriness
  - Sandifer
  - Paroxysmal dystonic choreoathetosis
  - Benign myoclonus of early infancy
  - Benign paroxysmal torticollis
  - Psychologic disorders

Jerks and abnormal postures

- children and adolescents
  - Tics
  - Paroxysmal dyskinesia
  - Benign paroxysmal torticollis
  - Benign paroxysmal vertigo of childhood
  - Episodic ataxia
  - Psychologic
Oculomotor abnormalities

- Neonates
  - Paroxysmal tonic upward gaze

- Infants
  - Paroxysmal tonic upward gaze
  - Oculomotor apraxia
  - Spasmus nutans
  - Opsoclonus

- Children
  - Daydreaming

Sleep disorder

- Neonates and Infants
  - Benign neonatal sleep myoclonus
  - Sleep transition disorders

- Children and adolescents
  - Non-REM partial arousal disorders
  - REM sleep disorders
  - Narcolepsy
  - Sleep transition disorders

Benign neonatal sleep myoclonus

- Repetitive, usually bilateral rhythmic jerks of upper and lower limb during NREM sleep
- Mimic clonic seizure
- Lack of autonomic symptom
- Occur only during sleep
- Suppress by awakening
- Spontaneous remission at 2-3 month

Hyperekplexia

- Rare neurogentic disorder
- Presented in newborn period
- Majority have dominantly inherited disorder
- Defect in alpha or beta subunit of strychnine-sensitive glycine receptor
- Exaggerated startle responses, hyperreflexia, hypertonia
- Elicit by tapping nose → startle reflex with head retraction
- Trigger → bathing, awakening, auditory, tactile stimuli

Jitteriness

- Equal backward and forward movements of limbs
- Spontaneous or triggered by touch and loud sound
- Suppression by stimulus removal or relaxation affecting limb
- Lack of autonomic symptom
- Possible etiology
  - Hypocalcemia
  - Hypoglycemia
  - Drug withdrawal
  - HIE

Breath-holding spell

- **Type**
  - Pallid type or white episode
  - Blue type: prolonged expiratory apnea

- 6-18 months

- Trigger (injury, frustration, anger) → cry, apnea, cyanosis → +/- syncope, tonic posturing

Shuddering

- Common infantile form of tremor
- Typically occur at 6 months of age
- Rapid tremor/shivering of head, shoulder and trunk
- While seated
- Duration few seconds
- No associated loss of awareness

Tics

- Most common voluntary movement in children
- Can be temporary voluntary suppressed
- Sense of relief when they are expressed
- Motor, vocal or sensory
  - Common motor tics
    - Eye blinking, facial grimace, head and neck craning, arm twitching, shoulder shrugging, lip lapping
    - Exacerbation by emotion
    - Typically wax and wane
    - Disappear in sleep
  - Vocal tics
    - Squeaking, chirping, coughing, sniffing
  - Sensory tics
    - Unusual or uncomfortable sensation: tingling, itching

Paroxysmal kinesogenic dyskinesia

- Rare hyperkinetic movement disorder
- Age of onset → below 20 years (6-15 years)
- Boy: girl → 4:1
- Often a family history
- Brief intermittent dyskinetic movements
- Dystonic, athetosis, ballism or combination
- Brief, unilateral or bilateral
- Usually no loss of consciousness
- Triggered by sudden voluntary movement
- Variability in pattern of severity and localization

Stereotypies or repetitive movement

- Often in neurologically impaired children
- Head banging
- Head rolling
- Body rocking
- Hand flapping

Paroxysmal event in adult
Consequence of misdiagnosis

- Psychosocial and socioeconomic problem
  - Loss of employment
  - Driving restriction

- Being treated with inappropriate or ineffective drugs, potentially resulting in side effects or teratogenicity

Paroxysmal event

- Seizure
- Syncope
  - Vasovagal
  - Cardiogenic
- Metabolic
  - Hypoglycemia
  - Electrolyte disturbances
  - Toxicity (drug, alcohol)
- Neurologic
  - Sleep disorder
    - Parasomnias
    - Narcolepsy/Cataplexy
  - Migraine
  - Vertigo
  - Transient ischemic attacks
  - Transient global amnesia
  - Psychogenic nonepileptic seizures
  - Movement disorder

Transient loss of consciousness

Secondary disturbance of CNS function
- Circulation
  - Cardiac
  - Neurovasogenic syncope
  - Carotid sinus hypersensitivity
  - Hypovolemia

Primary disturbance of CNS function
- Metabolic/endocrine
  - Hypo/hyperglycemia
  - Electrolyte disorder
- Epileptic
  - Focal
  - Generalize
  - Unclassified
- Psychiatric
  - Panic disorder
  - Hyperventilation
  - PNES
  - Factitious
  - Malingering

Seizure

- Typically paroxysmal and episodic resulting in suddenly occurring but transient behavioral, somatosensory, motor, or visual symptom or sign

- Abnormally excessive cortical neuronal activity

- May be provoked by certain influences (trauma, brain hemorrhage, metabolic, drug exposures) or occur spontaneously

Clinical symptoms and signs of epilepsy

- Ictal (during a seizure)
- Interictal (between seizure episodes) manifestations
- Postictal (immediately following seizure termination)
Syncope
Syncope

- Abrupt, transient, self-limiting loss of consciousness
- Usually associated with loss of postural tone
- Transient global cerebral hypoperfusion
- Relatively rapid onset
- Spontaneous, complete, relatively prompt recovery

Syncope

- Most common non-neurologic disorder mimicking epilepsy

- Vasovagal/neurovasogenic → most common

- Cardiogenic → most dangerous

- Autonomic failure

- Hypotensive causes

Vasovagal/neurocardiogenic syncope

- Benign form of syncope
- Often provoked by triggers
  - Positional change, physical exertion, valsalva maneuvers (lifting, toileting), strong emotional triggers (sight of blood)
- Prodromal subjective symptoms
  - Lightheaded dizziness, diaphoresis, nausea
- Brief, seconds to a few minutes LOC
- Convulsive movements are frequent during syncopal attacks
- Infrequent confusion and loss of continence following recovery of consciousness
Neural mediated syncope: clinical example

- Vasovagal syncope

- Carotid sinus syncope
  - Hypotension and/or cardiac inhibition are triggered by stimulation of carotid baroreceptors in the neck
  - Common in older patient

- Situational syncope (including cough, swallow, micturition, defecation, hair brushing, stretch, swallow)

Cardiogenic syncope

- Arrhythmia or structural cardiac disease
- History of heart disease
- Exercise related
- Occurred from supine position
- Shorter history of attacks
- Absence of pre-syncopal symptom
- Abrupt onset and offset
- Less frequently involve long prodromes
- Sometimes with a prodrome of dyspnea and chest pain
Autonomic failure

- Mechanism → insufficient vascular tone → orthostatic hypotension
  - Decrease of SBP $\geq 20$ mmHg and/or diastolic $10$ mmHg within 3 minutes of standing

- Primary: MSA, pure autonomic failure
- Secondary: DM, neuropathy
- Drug: antidepressant, beta blocker
## Syncope versus seizure

<table>
<thead>
<tr>
<th>Background</th>
<th>Favor syncope</th>
<th>Favor seizure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting</td>
<td></td>
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</tr>
<tr>
<td>Prodrome</td>
<td>Previous presyncope or syncope</td>
<td>Previous seizures, cortical abnormality on MRI</td>
</tr>
<tr>
<td></td>
<td>Prolonged sitting or standing, rising to upright posture, dehydration</td>
<td>Stress, sleep deprivation, drug withdrawal (alcohol, benzodiazepine), photic trigger</td>
</tr>
<tr>
<td>Attack</td>
<td>Nausea, palpitations, dyspnea, warm sensation, light-headedness, greying of vision, hearing becoming distant</td>
<td>Symptom indicate temporal, frontal, parietal or occipital focus</td>
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<tr>
<td></td>
<td>Pallor, motionless collapse</td>
<td>Tongue biting, head turning, unusual posturing, urinary incontinence, cyanosis</td>
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<tr>
<td>Recovery</td>
<td>Follow fall, small amplitude, synchronous, shorter</td>
<td>Before LOC, unilateral, more massive, last longer</td>
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<tr>
<td></td>
<td>Loss of consciousness remembered</td>
<td>Confusion, headache, not recall</td>
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</table>
Case

- Young woman with history of right hippocampal sclerosis presented with paroxysmal event

- Dizziness, blurred vision, abnormal motor activity
Psychogenic nonepileptic seizures
PNES

- Behavioral events closely resembling epileptic seizures
- Lacking typical clinical and electrophysiologic features of epilepsy
- Especially common presentations in EMU, 30% to 50% of admissions
- Ictal video-EEG telemetry remains the gold standard for diagnosis

PNES: clinical

- Prolonged spell duration (often > 1 minute)
- Non-stereotyped
- Eye closure
- Bizarre voluntary movements
- Asynchronous movement
- “yes-yes” type head nodding or “no-no” type side-to-side head shaking
- Prominent pelvic thrusting
- Ictal crying/weeping

PNES: clinical

- Atypical non-anatomic spread of movements
  - Clonic-type movements, may begin in a leg, spread to head, then to arm
- Memory recall for period of unresponsiveness
- Resist eyelid opening
- Guarding of hand drooping over face
- Evidence of visual fixation

Seizure

- Unresponsiveness
- Postictal-type behavioral alteration, confusion
- Very severe tongue biting
- Impaired corneal reflex
- Extensor plantar response

Migraine
Epilepsy and migraine are often easily discriminated.

Distinguishing migrainous visual auras from occipital seizure symptoms can cause diagnostic confusion.

<table>
<thead>
<tr>
<th>Migraine</th>
<th>Epilepsy</th>
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</thead>
<tbody>
<tr>
<td><strong>Aura duration</strong></td>
<td><strong>Seconds to few minutes</strong></td>
</tr>
<tr>
<td>5-60 min</td>
<td>Bright, multi-coloured curved or rounded shapes, might arise in one hemifield and move</td>
</tr>
<tr>
<td><strong>Visual aura</strong></td>
<td><strong>Tingling/numbness/heat/pain,</strong> rapid distal to proximal spread, frequent evolve to CPS or GTCs</td>
</tr>
<tr>
<td>Flickering, uncoloured zigzags, central onset, spreading peripherally, might leave scotoma</td>
<td><strong>Variable feature, often mild</strong></td>
</tr>
<tr>
<td><strong>Somatosensory aura</strong></td>
<td><strong>Common</strong></td>
</tr>
<tr>
<td>Tingling/numbness of hand, slowly spreading to ipsilateral face, tongue</td>
<td></td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td></td>
</tr>
<tr>
<td>Usually present, unilateral, pulsating, worse on exertion, moderate or severe intensity, often with photophobia, phonophobia</td>
<td></td>
</tr>
<tr>
<td><strong>Confusion</strong></td>
<td></td>
</tr>
<tr>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>
Transient ischemic attack
Cerebrovascular disease: TIA

- Clinical depend on duration of ischemia and arterial territory involved, depending on anatomic localization

- Typically last from minutes to 1 hour

- Rarely associated with loss of consciousness

- More frequently cause “negative” symptoms
  - Numbness, weakness, visual loss, aphasia

- Epileptic seizures
  - More often involve “positive” symptoms and signs and shorter duration

Limb shaking TIA

- Repetitive limb-shaking convulsive movements
- Lack of Jacksonian march or aura
- No LOC
Cerebrovascular disease VS seizure

- Symptomatic seizures from irritation of neighboring cerebral cortical tissue may all follow acute ischemia.

- Postictal “negative” signs (aphasia and hemiparesis), frequently complicate seizures, leading to diagnostic confusion with stroke.
Cerebrovascular disease: EEG

- Ictal video-EEG sometimes helpful in differentiating TIAs from seizures

- TIAs or stroke: focal cerebral slowing or normal findings

- Partial seizure: focal evolving rhythmic activity
Delirium
Encephalopathy (delirium)

- State of generalized confusion caused by a systemic disorder

- Often occurring when vulnerable patient with mild cognitive impairment or dementia
  - Change in medication
  - New acute change associated with systemic infection, inflammation, exposure to toxins or metabolic disturbance

Delirium

- Hallmarks are disorientation and inattention
  - Acutely disoriented, unable to accurately name current location or date
  - Incapable of concentrating well enough to execute serial calculations or spell words backward

- Confusion may resemble ictal or postictal behavior
  - Staring with disorientation, inattention, variable responsiveness; stupor with reduced vigilance; unusual movements (myoclonic jerks)
Delirium

- May also have acute symptomatic seizures resulting in further diagnostic confusion

- EEG most often shows diffuse nonspecific non-epileptiform background slowing or even epileptiform-appearing patterns such as diffuse triphasic waves
Sleep disorder
Parasomnias are unpleasant or undesirable behavioral or experiential phenomena.

- Occur predominantly or exclusively during sleep.
- Often occupy particular sleep stages and show predisposition for transition periods between sleep states.

Sleep disorders

- Non-rapid eye movement (REM) arousal disorder parasomnias
  - Confusional arousals
  - Sleep terrors
    - Cry or scream, vigorous motor activity, and behavioral and autonomic features of intense fear
  - Sleep walking

- REM sleep behavior disorder
Non-REM parasomnias: EEG

- May show no change other than arousal

- Occasionally shows generalized or frontal dominant rhythmic delta or theta patterns lasting a few seconds following arousal
Nocturnal seizures

- Highly stereotyped complex motor behavior
- Arousals with tonic or dystonic posturing, oral, limb, or trunk automatisms, violent coordinated movements, bicycling movement, thrashing, grunting, vocalization
- Stereotyped aura, distinctive somatic sensation or “breath stuck in throat” feeling
- Often in first 30 min of N2 sleep
- Often cluster with multiple attacks per night
- Often recollected by individual
Nocturnal seizure

- Ictal EEG
  - Frontal lobe seizures show little change, often obscured by muscle and movement artifact
    - Diagnosis relies upon observation of stereotyped typical hypermotor behaviors
  
  - Temporal lobe seizure show prominent focal evolving rhythmic activity
REM sleep behavior disorder

- Characterized by complex motor behavior paralleling dream content causing enactment of dream

- Behaviors are often violent
  - Dream of being attacked or chased
  - While in their dream they are defending themselves
  - Kicking, punching, yelling, swearing, or jumping out of bed
  - May injure themselves or bed partner

- When roused, affected individuals are aware they were dreaming vividly
REM sleep behavior disorder

- Impairment of normal mechanisms that prevent most muscle activity (extraocular and respiratory muscles) during REM sleep

- Polysomnography showed frequent rapid phasic muscle jerks and heightened chin and limb muscle tone during REM sleep

- More common in second half of sleep, more REM sleep occurs

- Uncommon below age of 50 years
Narcolepsy

- Disorder of regulation of sleep and wakefulness
- Mostly starting in adolescence
- Selective loss of hypocretin-secreting neuron in hypothalamus
Narcolepsy: Tetrad

- Excessive day time sleepiness
- Cataplexy (70%)
- Sleep paralysis
- Sleep-related hallucinations
Cataplexy

- Sudden loss of muscle tone after emotional stimuli such as laughter or anger with retained consciousness

- Last several seconds or minutes

- Reversible loss of knee muscle stretch reflexes during an attack, followed by recovery of reflexes between attacks

- DDx atonic or astatic seizure
Sleep-related hallucinations

- Auditory (telephone ringing), visual (figures or animals, sometimes threatening), or somatosensory experiences

- Occurrence at sleep onset and offset
Vertigo
Vertigo DDx

- Non-epileptic
  - Vestibular
  - Brainstem
  - Migraine

- Epileptic vertigo (rare)
  - Seizures involving temporo-parieto-occipital junction

Summary table
<table>
<thead>
<tr>
<th>Type</th>
<th>Premonitory symptom</th>
<th>Characteristic</th>
<th>Duration</th>
<th>Postspell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure with loss of awareness</td>
<td>Variable aura or brief (10-30s) Sensory march</td>
<td>staring, automatism, variably preserved posture</td>
<td>30-180sec</td>
<td>Common, amnesia, aphasia, sleepiness, confusion, incontinence</td>
</tr>
<tr>
<td>Absence seizure</td>
<td>None</td>
<td>Staring, automatism</td>
<td>&lt;10sec</td>
<td>None</td>
</tr>
<tr>
<td>Tonic-clonic seizure</td>
<td>Variable aura</td>
<td>Brief tonic posturing, clonic</td>
<td>1-3 min</td>
<td>Requisite Amnesia, sleep, incontinence, tongue biting, injury</td>
</tr>
<tr>
<td>Psychogenic spell</td>
<td>variable</td>
<td>Variable responsiveness, non stereotyped unusual movements</td>
<td>Often prolonged (&gt;5-10 min)</td>
<td>Variable, often none</td>
</tr>
<tr>
<td>Syncope</td>
<td>Frequent, light headed, dizziness</td>
<td>Falling, eye closure, variable movement</td>
<td>1-5 minutes</td>
<td>Variable, often none</td>
</tr>
</tbody>
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Chen DK, LaFrance WC Jr. Diagnosis and Treatment of Nonepileptic Seizures. Continuum (Minneap Minn) 2016;22(1):15-37
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<th>Duration</th>
<th>Postspell</th>
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<tr>
<td>Migraine</td>
<td>Prolonged sensory march (minutes)</td>
<td>Often positive symptoms (paresthesia, photopsia)</td>
<td>20-60 min.</td>
<td>Headache</td>
</tr>
<tr>
<td>TIA</td>
<td>Rapid sensory march (1-10sec)</td>
<td>Often negative symptoms (dead, numbness, weakness)</td>
<td>&lt;60 min</td>
<td>None</td>
</tr>
<tr>
<td>Parasomnia</td>
<td>None</td>
<td>Vocalization, confusion, ambulation</td>
<td>minutes</td>
<td>Amnesia, confusion</td>
</tr>
<tr>
<td>Cataplexy</td>
<td>Emotional provocation</td>
<td>Muscle atonia, preserved consciousness or sleep attack</td>
<td>Seconds to minutes</td>
<td>None</td>
</tr>
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