Differential Diagnosis of Epilepsy

Suda Jirasakuldej ,Montida Veeravigrom
King Chulalongkorn Memorial Hospital
Faculty of medicine Chulalongkorn University

Outline

- Introduction
- Paroxysmal event in children
- Paroxysmal event in adult

Diagnosis: Relies on clinical history

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

- **Witness**

Obeid M, Mikati MA. Expanding spectrum of paroxysmal events in children: potential mimickers of epilepsy. Pediatr Neurol. 2007 Nov;37(5):309-16.

Paroxysmal events in children

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

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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

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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
- children and adolescents
  - Tics
  - Paroxysmal dyskinesia
  - Benign paroxysmal torticollis
  - Episodic ataxia
  - Psychologic

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Oculomotor abnormalities

- Neonates
  - Paroxysmal tonic upward gaze
- Infants
  - Paroxysmal tonic upward gaze
  - Oculomotor apraxia
  - Spasmus nutans
  - Opsoclonus
- Children
  - Daydreaming

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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

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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

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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

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Jitteriness

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

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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

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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

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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

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Paroxsymal 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

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Stereotypies or repetitive movement

- Often in neurologically impaired children

- Head banging
- Head rolling
- Body rocking
- Hand flapping

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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

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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

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Transient loss of consciousness

Secondary disturbance of CNS function

Circulation

Cardiac
Neurovasogenic syncope
Carotid sinus hypersensitivity
Hypovolemia

Metabolic/endocrine

Hypo/hyperglycemia
Electrolyte disorder

Primary disturbance of CNS function

Epileptic

Focal
Generalize
Unclassified

Psychiatric

Panic disorder
Hyperventilation
PNES
Factitious
Malingered

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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

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Clinical symptoms and signs of epilepsy

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

Syncope

- Most common non-neurologic disorder mimicking epilepsy
- Vasovagal/neurovasogenic → most common
- Cardiogenic → most dangerous
- Autonomic failure
- Hypotensive causes

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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

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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)

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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 >/= 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

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

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

Perez DL, LaFrance WC Jr. Nonepileptic seizures: an updated review. CNS Spectr. 2016 Jun;21(3):239-46.

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

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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

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Seizure

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

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Migraine

Migraine

- Epilepsy and migraine are often easily discriminated
- Distinguishing migrainous visual auras from occipital seizure symptoms can cause diagnostic confusion

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

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

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Limb shaking TIA

- Repetitive limb-shaking convulsive movements
  - Lack of Jacksonian march or aura
  - No LOC
  - Follow maneuver causing carotid compression

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

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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

Sleep

- 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

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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

- Spontaneous arousal from non-REM sleep, N2 or N3 (slow-wave) sleep
- Nonstereotyped confused behavior w/w/o vocalization or sleepwalking
- Crying or sobbing, waxing and waning, interactive behavior
- Indistinct offset
- Prolonged duration > 2 minutes
- Tend to occur in the first third of the night
- Rare to have more than one or two parasomnia episodes per night
- Failure to wake after event
- No recall

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

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Summary table

Seizure VS non epileptic

Type	Premonitory symptom	Characteristic	Duration	Postspell
Seizure with loss of awareness	Variable aura or brief (10-30s) Sensory march	staring, automatism, variably preserved posture	30-180sec	Common, amesia, aphasia, sleepiness, confusion, incontinence
Absence seizure	None	Staring, automatism	<10sec	None
Tonic-clonic seizure	Variable aura	Brief tonic posturing, clonic	1-3 min	Requisite Amnesia, sleep, incontinence, tongue biting, injury
Psychogenic spell	variable	Variable responsiveness, non stereotyped unusual movements	Often prolonged (>5-10 min)	Variable, often none
Syncope	Frequent, light headed, dizziness	Falling, eye closure, variable movement	1-5 minutes	Variable, often none

Chen DK, LaFrance WC Jr. Diagnosis and Treatment of Nonepileptic Seizures. Continuum (Minneap Minn) 2016;22(1):15-37.

Seizure VS non epileptic

Type	Premonitory symptom	Characteristic	Duration	Postspell
Migraine	Prolonged sensory march (minutes)	Often positive symptoms (paresthesia, photopsia)	20-60 min.	Headache
TIA	Rapid sensory march (1-10sec)	Often negative symptoms (dead, numbness, weakness)	<60 min	None
Parasomnia	None	Vocalization, confusion, ambulation	minutes	Amnesia, confusion
Cataplexy	Emotional provocation	Muscle atonia, preserved consciousness or sleep attack	Seconds to minutes	None

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Thank you