Non-epileptic Paroxysmal Events

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Non-epileptic Paroxysmal Events

- Syncope
- Transient Ischemic Attack
- Migraine
- Sleep Disorders
- Movement Disorders
- Neuromuscular Disorders
- Panic Disorder
- Psychogenic Non-epileptic Seizures (PNES)

Syncope

- Defined as transient loss of consciousness due to global cerebral hypoperfusion
- Three major causes of syncope:
  - Reflex (neurally-mediated) syncope
  - Cardiac (cardiovascular) syncope
  - Orthostatic hypotension syncope
**Reflex Syncope**

- Prodromal phase: nausea, diaphoresis, pallor, abdominal discomfort
- Three subgroups:
  - Vasovagal: triggered by pain, fear or prolonged standing
  - Situational: triggered by micturition, coughing, sneezing, etc.
  - Carotid sinus: triggered by carotid sinus massage

**Cardiac Syncope**

- Shorter prodrome, if any
- May occur on exertion
- Resulting from brady- or tachyarrhythmias or structural heart disease
- 12-lead EKG for all patients with undiagnosed episodes of LOC

**Orthostatic Hypotension Syncope**

- Precipitated by fall in blood pressure following positional change
- Seen in autonomic neuropathy, diabetes, elderly
- Tilt-table testing: fall in BP without compensatory increase in HR
Syncopal Convulsions

- Myoclonus (multifocal and generalized) can accompany syncope (Lempert et al., noted myoclonus in 38/42 episodes, 90%)
- Also seen: head turns, oral automatisms, upward eye deviation, visual/auditory hallucinations
- Witnesses often overestimate the duration of “convulsions”
- Incontinence can occur


Transient Ischemic Attack

- Clinical features depend on arterial territory involved
- Typically last < one hour
- Symptoms are typically “negative” (weakness, numbness, aphasia, visual loss) but can be confused with postictal phase in epileptic seizures

Migraine

- Overlapping features can lead to diagnostic confusion
- Migralepsy: syndrome of migraine with aura; migraine is followed immediately by epileptic seizure (ICHD-3 migraine aura-triggered seizure: sz within 1 hr of migraine)
- Occipital lobe epilepsy: intractable headache with scintillating visual symptoms
**Migraine**

- Migraine auras are longer in duration than epileptic auras
- Migraine with brainstem aura
  - Dysarthric speech, vertigo, tinnitus, diplopia, paresthesias, ataxia, depressed consciousness
  - Headache can be minor
- Hemiplegic migraine
- Vestibular migraine

**Sleep Disorders**

- Narcolepsy/Cataplexy
- Parasomnias
  - REM Sleep Behavior Disorder
  - NREM-related
- Sleep-related Movement Disorders
  - Periodic limb movement disorder
  - Sleep-onset myoclonus

**Narcolepsy/Cataplexy**

- Excessive daytime sleepiness with “sleep attacks”
- Cataplexy
  - Transient weakness triggered by strong emotions
- Hypnagogic hallucinations
- Sleep paralysis
REM Sleep Behavior Disorder

- Complex behavior or vocalization during REM (last third of the night), correlating with dream mentation
- Movements are short, purposeful, not stereotyped, but can involve injury
- Pts typically recall dream content
- Evidence of REM sleep w/o atonia on PSG
- Responsive to clonazepam or dopaminergic agents

NREM-Related Parasomnias

- Sleepwalking (somnambulism)
- Sleep terrors (night terrors or pavor nocturnus)
- Sleep-related eating disorder
- Typically occur in the first third of the night, during NREM sleep
- Pts have no memory of the event
- Stereotyped movements are absent

Sleep-Related Movement Disorders

- Periodic limb movement disorder
  - May present with vigorous kicking or thrashing
  - History of restless legs syndrome common
  - Periodic intervals, every 20-40 seconds, characteristic flexion of the leg although arms may be involved
  - Stereotyped features are absent (no vocalizations or oral automatisms)
- Sleep-onset myoclonus or hypnic jerks
- Bruxism
  - Stereotyped teeth-grinding
**Episodes in Sleep in Infants**

- **Head Banging (Rhythmic Movement Disorder)**
  - Repetitive movements of head (trunk, or extremity) during sleep transitions
  - Can last 15-30 minutes
  - Benign, usually resolve spontaneously within 1-2 years
- **Benign Neonatal Sleep Myoclonus**
  - Typically bilateral, asynchronous, asymmetric, migrating, lasting minutes to hours, in all stages of sleep but not in wakefulness

**Movement Disorders**

- Tremors
- Tics
- Hemifacial spasm
- Paroxysmal dyskinesias
  - Paroxysmal kinesigenic dyskinesia/choreoathetosis
  - Paroxysmal exercise-induced dyskinesia
  - Paroxysmal non-kinesigenic dyskinesia
- Episodic Ataxia
  - Episodes of ataxia lasting seconds to minutes, AD, onset early childhood, various triggers

**Neuromuscular Disorders**

- Hypokalemic periodic paralysis
  - Episodes of flaccid limb weakness, low serum potassium, last hours to days, triggered by carbohydrate meals, rest after exercise
- Hyperkalemic periodic paralysis
  - Myotonia may be present, episodes last minutes to hours
- Stiff person syndrome
  - Axial > distal muscle rigidity with episodic, severe spasms lasting hours to days
Panic Disorders

• Common symptoms: palpitations, diaphoresis, vertigo, dyspnea, chest pain, lightheadedness, nausea, numbness/tingling, fear of dying, trembling or shaking
• Duration: minutes to hours
• Average age of onset: late 20’s
• May be associated with agoraphobia
• Can occur in sleep

Behavioral Disorders

• Acute fugue
• Acute psychosis/hallucinations
• Phobias
• Autistic behaviors

Psychogenic Non-epileptic Seizures (PNES)

• Definition
• Epidemiology
• Patient Characteristics
• PNES Diagnosis
  - Making the Diagnosis
  - Presenting the Diagnosis
• Treatment
### Definition of PNES

- Transient/paroxysmal events that resemble epileptic seizures in clinical signs and symptoms
- Manifestations of psychological distress and/or psychiatric disorder (e.g., conversion, dissociative, or anxiety)
- Not related to cortical hyperexcitability (i.e., ictal epileptiform discharges)

### NES: Epidemiology

- Reported prevalence = 2 to 33 per 100,000
- Reported incidence = 3 per 100,000 per year in those over 18 years
- 20-50% of epilepsy monitoring unit (EMU) discharge diagnoses
- Mean time to diagnosis = 7 to 10 years

### NES: Patient Characteristics

- 80% occur in the 15-35 age group
  - Children and elderly also develop NES
- ~80% are women
- 5-10% also have epilepsy (up to 30% in those with intellectual disability and NES)
- Up to 50% will report an epilepsy risk factor (e.g., head trauma)
- ~70% have other psychiatric diagnoses
**Predisposing Factors**

- Childhood abuse (~25% of women with NES)
- Other significant past trauma (~90%)
- Family history of psychiatric disease
- Foster care
- Family dysfunction
- Psychiatric comorbidity (e.g., PTSD, depression, anxiety)
- Illness perceptions (e.g., alexithymia, inability to understand, process or describe emotions)

**Precipitating Factors**

- Also referred to as triggers
- Traumatic life events (death of loved one, serious medical illness/surgery, separation/divorce, job loss/financial stress, legal action)

**Perpetuating Factors**

- Avoidance/isolation
- Social/financial gain related to having seizures
- Misdiagnosis/mistreatment
- Family dysfunction/stress
- Ineffective coping strategies
PNES Case Examples

1. 35yo woman with prior history of childhood abuse (predisposing), whose own daughter has recently reached the age of the patient's own abuse (precipitating), now with recurrent marital discord (perpetuating).
2. 23yo with depression, anxiety, raised by alcoholic parents, taught that showing emotions was a sign of weakness (predisposing), with recent MVC leading to injury and job loss (precipitating), and ongoing family stressors and somatization traits such as chronic daily headache and fibromyalgia (perpetuating).

Overview of PNES

- Definition
- Epidemiology
- Patient Characteristics
- PNES Diagnosis
  - Making the Diagnosis
  - Presenting the Diagnosis
- Treatment

Making the Diagnosis

- Gold-standard: history and video-EEG during a typical seizure
- Consistency between neurologic and psychiatric history and video-EEG
- Separate from video-EEG, certain features of history and semiology are highly predictive
Making the Diagnosis: History

Predictors from history:
- At least two normal EEGs
- At least two seizures/week
- Resistance to at least two AEDs
- 85% PPV for PNES (Davis et al., 2004)

Davis BJ. Predicting nonepileptic seizures utilizing seizure frequency, EEG, and response to medication. Eur Neurol 2004;51:153-156.

Making the Diagnosis: History

Predictors from patient’s description of events:
- Focus on situations in which seizures have occurred or consequences of seizures
- Subjective seizure symptoms listed but not described in detail

Schwabe et al., 2008; Plug & Reuber, 2009

Making the Diagnosis: Semiology

Semiology that favors PNES:
- Long duration (“convulsive” seizures lasting > 10 minutes)
- “Convulsive” or “generalized motor” activity with retained responsiveness
- Out-of-phase limb movements and side-to-side head movements
- Variable amplitude of motor activity, distractibility
- Ictal crying
- Eyes-closed unresponsiveness

Less useful: flailing or thrashing, TB, UI, gradual onset, stereotyped events
Making the Diagnosis: VEEG

Simultaneous video and EEG:
- Of (all) typical events, as confirmed by witnesses
- Most helpful when there is motor activity or altered responsiveness
- Less useful for subjective symptoms (aura vs. PNES)
- Can be difficult in frontal lobe seizures and when EEG is obscured by movement/EMG

Making the Diagnosis: Physiologic Measures

Physiologic measures:
- Prolactin (PRL): elevated serum PRL in patients with GTC ES vs. PNES
- AAN: Twice normal elevation in serum PRL, drawn 10-20 min after ictal onset, c/t baseline, is useful adjunct to differentiate GTC (88% sens) and CPS (64% sens) ES from PNES
- False positives: DA antagonists, TCAs, syncope
- False negatives: DA agonists, status, frontal lobe ES
- Not reliable: serum cortisol, DST, salivary amylase

Overview of PNES: From the Neurologist’s Perspective

- Definition & Terminology
- Epidemiology
- Patient Characteristics
- PNES Diagnosis
  - Making the Diagnosis
  - Presenting the Diagnosis
- Treatment
Presenting the Diagnosis

- Typically, the role of the neurologist who has interpreted the video-EEG
- Having family members present may facilitate understanding
- Pts with PNES are less likely to accept that negative life experiences are relevant to seizures
- They also tend to have difficulty understanding and describing emotions; they are more aware of physical symptoms
- This often leads to resistance to efforts linking negative life experiences or emotional stress to apparently physical symptoms.

Presenting the Diagnosis

- Communicating the diagnosis effectively is crucial and can be therapeutic in the short-term (16-38% sz-free at 6 m wo further intervention)
- However, if process leaves patient angry or confused, PNES and other psychiatric symptoms may worsen
- Poor communication risks traumatizing the patient (yet again)
- Various strategies have been proposed; most important component, delivering diagnosis with empathy

Presenting the Diagnosis

- Acceptability and effectiveness of communication strategy:
  - Patient informational 27-page booklet covering common questions:
    - What are non-epileptic attacks?
    - What causes my attacks?
    - How can stress be the cause?
    - What about my other symptoms?
    - How are non-epileptic attacks treated?
    - What is psychological help?
    - What can I do to help myself get better?
  - Communication strategy for neurologists (one-page reminder sheet of key points to address)
  - 94% of patients found booklet easy to understand and stated their questions were answered by the doctor

Hall-Patch et al., Epilepsia 2010;51:70-78.
Presenting the Diagnosis

KEY POINTS Addressed in Communication Strategy:

- Genuine symptoms: these are real and can be frightening and disabling
- Give a name to the condition: let them know alternative names they may hear; reassure them this is a common and recognized condition
- Causes: not epilepsy; could be related to stress/emotions; vicious cycle of Worry → Stress → NES → more Worry
- Provide model: brain becomes overloaded and shuts down
- Treatment: AEDs not effective; psychological treatment is effective
- Expectations from Tx: NES can resolve, can expect improvement

Hall-Patch et al., Epilepsia 2010;51:70-78.

Presenting the Diagnosis

- Don’t discuss treatment until the patient at least acknowledges understanding of the diagnosis.
- Avoid phrases such as “psychiatric condition” and phrases that suggest the seizures are not real.
- Validate feelings of anger or confusion.
- Acknowledge that non-epileptic seizures can be easily confused with epileptic seizures.

Overview of PNES: From the Neurologist’s Perspective

- Definition & Terminology
- Epidemiology
- Patient Characteristics
- PNES Diagnosis
  - Making the Diagnosis
  - Presenting the Diagnosis
- Treatment
  - Stopping AEDs
  - Referring for Acute Mental Health Services
Treatment of PNES

- Formal psychosocial assessment early in the diagnosis
  - To identify relevant predisposing, precipitating and perpetuating factors
  - To identify need for pharmacotherapy for psychiatric comorbidities

- Psychotherapy should be implemented when indicated.

RCT for PNES

- Cognitive behavioral therapy informed psychotherapy (CBT-ip)
  - 12 weekly sessions, structured patient workbook
  - Promotes behavioral change and self-control, self-efficacy, tailored specifically for PNES patients

  Patients randomized to four treatment arms (N=38):
  - Medication (flexible-dose sertraline) only
  - CBT-ip only
  - CBT-ip with medication (sertraline)
  - Treatment as usual

LaFrance WC et al., JAMA Psych 2014; 71:997-1005.

Results:

- CBT-ip showed 51% seizure reduction and improvement in depression, anxiety, QOL and global functioning
- Combined arm (CBT-ip with sertraline) showed 59% seizure reduction and improvements in some secondary measures
- Medication only and treatment as usual did not show a reduction in seizures.
Treatment Challenges

- Effective treatments are available, but no guidelines for individualizing treatment (Reuber et al, 2005; LaFrance et al, 2013)
- Access to treatment is limited (Carton S et al, 2003)
- Failure to come for first session (Howlett S et al, 2007)
- Patient (and/or provider) unwillingness to accept diagnosis (Baxter S et al, 2012)

Conclusions

- Paroxysmal episodes of altered consciousness or involuntary movements can present a diagnostic challenge.
- In adults, the most common events misdiagnosed as epilepsy are syncope and psychogenic non-epileptic seizures (PNES).
- Video-EEG is the gold standard for diagnosing PNES.
- The neurologist/epileptologist plays an important role in presenting a diagnosis of PNES to the patient and initiating appropriate treatment.