Psychogenic NonEpileptic Versus Frontal Lobe Seizures

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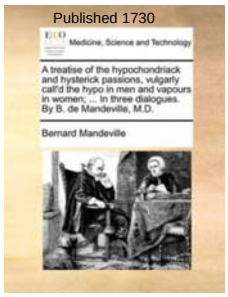
Psychogenic NonEpileptic Seizures(PNES)

- First Described 1711 by Philosopher, Bernard Mandeville. *A Treatise of the Hypochondriack and Hysterick Diseases*
- A reflection on hypochondria as well as on the global functioning of the human mind and on the place of the patient/physician relationship in the wider organization and impact on society.



So why talk about PNES?

- Large percentage of workload for Physicians (Neurologists, ED, PCP's)
- Large cost to patient (adverse effects of AED's, delay of appropriate mental Rx, employment diff/disability, risk of iatrogenic harm)
- Large cost to society (ED visits, hospitalizations, lab tests, disability)
  - Estimated $112k/pt or $900M/yr in US (2010)
  - Fewer than 40% of adults with PNES are expected to become seizure-free within 5 years after diagnosis.

Epidemiology PNES

- Incidence/Occurrence:
  - 2-33/100,000[1]
  - Similar to # of Multiple Sclerosis or Parkinson's disease
- Commonly misdiagnosed-80%
- 80% Pt's taking an AED prior to correct Dx
- Time to diagnosis 7-10 yrs. after symptom onset
- 3:1 female/male
- 83% begin in young adulthood, 15-35 yo: less common in very young/very old

Asadi-Pooya, A.A. Neurol Sci (2017) 38: 935. https://doi.org/10.1007/s10072-017-2887-8

Modern Definition of PNES

- An observable abrupt paroxysmal change in behavior, consciousness, autonomic/motor/sensory function, resembling an epileptic seizure, but without organic cause and without the accompanying neurophysiologic (EEG) changes.
- Gold Standard for Diagnosis is captured event on vEEG using techniques such as activation procedures (e.g., photic stimulation and hyperventilation) or presenting the triggering stimulus, accompanied by strong clinical history.

More on epidemiology

- 10-15% of Pt's with PNES also have epilepsy
- PNES when preceded by ES Neurologists tend to use ambiguous language, such as "thought to be" or "suggestive of" to describe their impressions of patients overall, even those with definitive PNES. Ambiguous language may lead to miscommunication across providers and inappropriate health care.
- Confused with or given other diagnosis if organic or physiological symptoms. (i.e increased heart rate)

Differential diagnosis of PNES

Physiologic non-epileptic: ("seizure mimics")

- Syncope (cardiac/non-cardiac)
  - Convulsive syncope
- Metabolic (Hypoglycemia)
- Dizziness/Vertigo
- Migraine
- Sleep Disorders (Narcolepsy)
- Movement Disorders (Paroxysmal Dyskinesia)
- Transient Ischemic Attacks

Psychogenic non-epileptic:

- Panic Attacks
- Malingering
- Intermittent Explosive Disorder
- Breath-holding Spells

Diagnosis

- History
  - Psychosocial h/o, recent/remote stressors (91% PNES Pt's)
  - PMH chronic pain, fibromyalgia, IBS; recent/multiple surgeries, +Family h/o seizures
  - **Semiology**
- Post-ictal Labs: CK↑,
  - Prolactin 20-30 min after onset: 96% specific for GTC if elevated three-fold
  - Not specific for CPS vs. NES or repetitive seizures not sensitive
- MRI: abnormal in 10% PNES

Diagnosis: vEEG Monitoring

- **Gold standard-** 80% Specific & Sensitive
  - Why not routine?
    - 30% patients w/ES normal rEEG
    - 33% patients w/PNES have abnormal EEG
  - Without vEEG: Neurologists ~50% specificity in Dx & Tx
  - vEEG rectifies an incorrect Dx and prompts Tx change in 80% pts w/PNES

Limitations of Video EEG

- Comprehensive EMU program not readily available at many institutions with continuous eyes-on EEG
- Frontal lobe sz, Focal sz with awareness, Deep temporal focus may not be present on EEG despite ES
- Appropriate cognitive testing during the event limited & not timely for untrained professionals-Despite patient event or alarm button pressed by patient or family member
- Length of time to capturing habitual sz or event longer than staffing capabilities
- Insurance pre-authorizations not given

PNES Versus ES

Semiology	PNES	Frontal-Lobe Seizures
Level of Consciousness/Situational onset	Awake, Often in front of Caregiver, family and/or physicians or techs	Occur out of sleep 2am to noon, Complete or Partial unresponsiveness
Movement	"Flailing limbs", pelvic thrusting, supine posture head in midline position, Rocking side to side, Asynchronous Mvt, Irregular and waxing waning character of limb movement	Head and eye movement to one side, Abnormal body posturing, such as one arm extending, repetitive movements such as rocking, bicycle pedaling, pelvic thrusting
Facial Expression	Eyes Closed, Resistance to opening	Eyes Open Wide-out of sleep

PNES Versus ES

Semiology	PNES	Frontal-Lobe Seizures
Pupillary light reflex	Usually retained	Commonly absent
Tongue Biting (tip/side)	Occasional/Rare	Rare/Common
Ictal Behavior	Vocalization Uncommon	Explosive screams, including profanities, or laughter,
Vital Sign Changes	Tachycardia	Tachycardia >30% increase from baseline in ES
Post-Ictal Behavior	Weeping or Whimpering	Nose Wiping or Cough

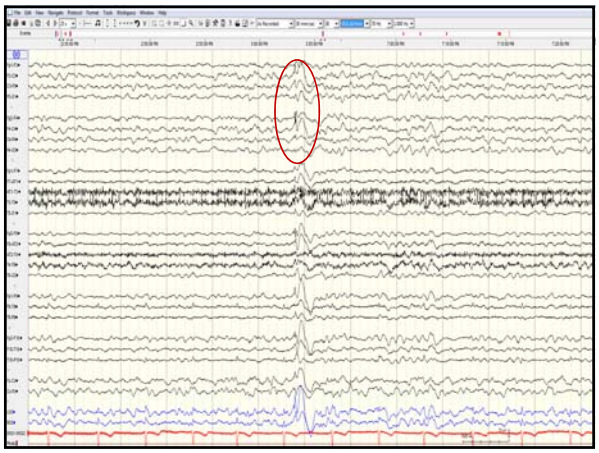
PNES Versus ES

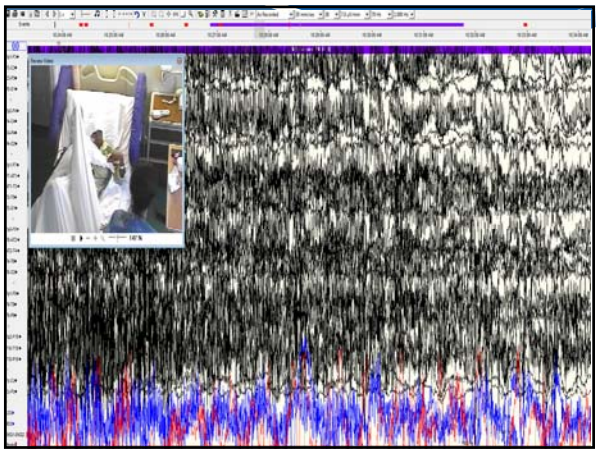
Semiology	PNES	Frontal-Lobe Seizures
Post-ictal Speech Pattern	Whispering, stuttering, emotional, comprehensible	Arrested, Flat, empty, often incomprehensible
Length of Event	Extended; > 1 min to 5 minutes	Brief; <30 seconds
Rapid Post-Ictal reorientation	Common	Rare
EEG	EMG with no ictal activity	Focal onset with rapid secondary generalization

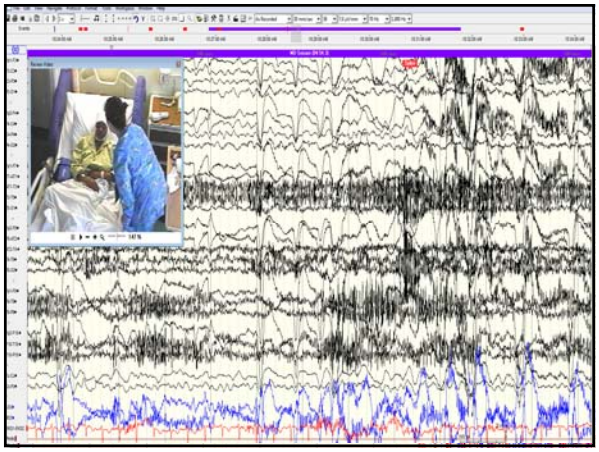
Teddy Bear Sign

- The presence of a stuffed animal brought by the (adult/adolescent) patient to the EMU was studied in 903 patients:
  - 383 pts. True PNES without ES
  - 23 had Teddy Bear Sign
  - Positive Predictive Value for PNES of 87% (19), with a high specificity (99%) but low sensitivity (5.2%)
- Same study found ictal stuttering to be equally specific and equally insensitive

Burneo JG, Martin R, Powell T, *et al.* Teddy bears: an observational finding in patients with nonepileptic events. Neurology 2003; 61:714–715.





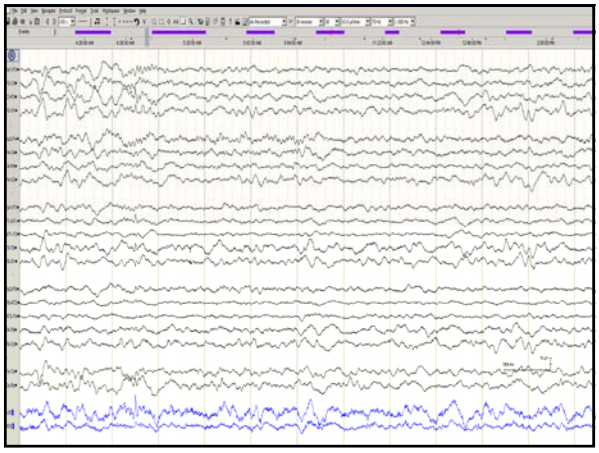


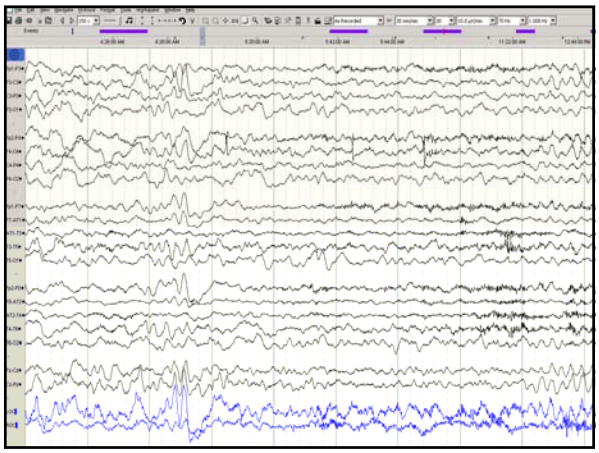
EEG findings in patients with Frontal Lobe seizures?

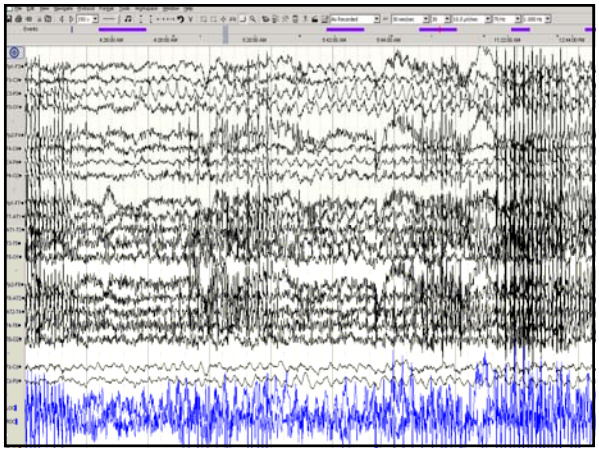
- Not uncommon for an EEG to be normal in frontal lobe epilepsy (FLE)
  - Up to 40% of patients with FLE have no epileptiform abnormalities in the interictal period
  - 30-40% of patients have no epileptiform discharges in the ictal period
  - Patients are often misdiagnosed as "hysterical" and referred to Psychiatry since routine EEGs are frequently normal and the event description consists of bizarre behavior

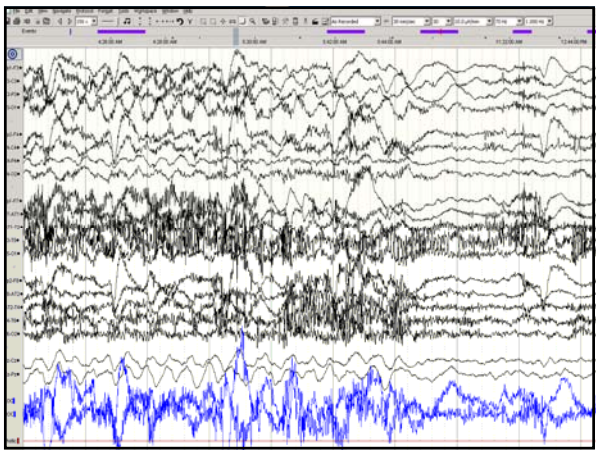
What Are Other Manifestations of Seizures From This Area?

- Various Semiology's.
  - primary motor cortex: focal motor clonic seizures, which frequently generalize
  - supplementary motor area (SMA): characteristic asymmetric tonic appearance (fencing posture).
  - frontal operculum: prominent mastication, swallowing and salivation with preserved consciousness
  - dorsolateral frontal cortex can be tonic or clonic with prominent head and eye deviation.
- Bizarre seizures with complex behavior, emotionality, vocalizations and hypermotor movements can arise from various frontal regions, including medial frontal, frontopolar, orbitofrontal or anterior cingulate.









What Are Some Common Etiologies of Epilepsy Syndromes From This Area?

- 50% of frontal lobe epilepsies (FLE) are associated with an underlying structural abnormality on MRI
  - focal cortical dysplasia
  - vascular malformation
  - Neoplasia
  - Trauma
  - other developmental lesions
  - Hypoxia
  - Infection
- In the remaining 50% of patients with FLE, no cause is identified.

Proposed Model for Developing PNES?

Psychological etiology- Causative factor: physical and/or sexual abuse, PTSD

Vulnerability- Predisposing factors: personality d/o with severe panic or anxiety with poor coping skills, depression

Shaping factors- Family member with seizures, Having witnessed seizures in others (i.e. healthcare worker), PMH as child of szs.

Trigger- Create circumstances or situations that provoke PNES through psychological mechanisms, such as dissociation and somatization.

Prolongation Factors- Above explain why the seizures persist and PNES may become a chronic disorder.

Psychological factors

- Dissociation
  - A sense of detachment from your emotions, or emotional numbness
  - Mechanism of sparing emotional pain
- Somatization (d/o of communication/emotion)
  - Distress conveyed physically rather than verbally
  - Emotions experienced as physiologic reactions rather than feelings

What Is The Treatment of Patient's Epilepsy?

Frontal-Lobe

- AED's-carbamazepine, oxcarbazepine, levetiracetam, lamotrigine, lacosamide, topiramate, and zonisamide
- There is no one "right" AED for FLE, and drug choice should be tailored to each individual patient (based on age, gender, other medical conditions, other medications, side effect profile).
- If MRI reveals a focal cortical dysplasia in the right frontal lobe, what other treatment options could be considered?
- Surgical Candidate
- Responsive Neurostimulation

Treatment for PNES

18th Century Treatment

- Dr. Mandeville:

"In order to it, I would for one Month prescribe a Course of Exercise, and no Medicines at all."

19th Century Treatment

- Gowers: aversive therapies during attacks
  - Closing nose & mouth
  - Electric shocks to the skin
  - Hydrotherapy "more than one jugful"
  - Pulling pubic hair
  - Injection of "apomorphia" to induce vomiting
- Charcot
  - Ovarian Compression
  - Hypnosis

21st Century Treatment of PNES?

PNES

- Emphasize that the necessary first step of intervention is to is communicate to the patient in a non-accusative, open way the diagnosis of PNES.
- PNES often result from a mismatch of traumatic experience and inability to cope, so simply telling patients that they do not have epilepsy may traumatize them further.
- Psychotherapy
  - Behaviour modification
  - Anxiety or Anger Training
- Pharmacotherapy Management
  - Panic disorder, Major mood disorder, ADHD or psychoses (Depression)

21st Century Treatment of PNES?

- Difficult Challenge
- PNES not "claimed" by either neurology or psychiatry
  - Dx by Neurology
  - Tx by Psychiatry
- No randomized controlled trials in these >200 years for effectiveness of Tx
- Current Tx: case reports, uncontrolled trials, retrospective f/u studies

21st Century Treatment of PNES?

1. **Definitive diagnosis and explanation**
   - Patient, family, psychiatrist/therapist, PCP
2. Psychotherapy (CBT in 12 sessions, 2009 study)
   - 11 of 17 pts event free by end of 12 wks
   - mean scores on scales of depression, anxiety, somatic symptoms, quality of life, and psychosocial functioning improved over 12 wks
3. Withdraw AEDs in PNES only pts
4. Education of self employed maneuvers to stop PNES
5. SSRI's – if indicated for mood d/o
6. Rx: psychiatric disease

PNES Prognosis

- Worse than patients w/ES- Probably Poor Overall
  - 1/3 sz free, 1/3 reduced, 1/3 unchanged/chronic
  - Some reports of 50-70% sz free following dx
  - Highly correlated w/px of personality d/o (40%)
- Longest f/u study: mean 4 yrs post dx
  - 2/3 still had sz
  - 1/2 still dependent on SSI disability
  - Only 16% event free
- Little to No data on employment, QOL, HC utilization
  - QOL px worse for intractable NES than for intractable ES

Take home points

- Probably >30% patients with intractable seizures have PNES
- Prior to vEEG, physicans make preliminary Dx of PNES based on
  - Suspicious history
  - Testing during events +/-
  - Presence of: preserved awareness, eye flutter, others can influence
  - Absence of: eye opening/widening, abrupt onset, post ictal confusion/sleep
- All intractable epilepsy patients should be referred to tertiary epilepsy center for the **GOLD STANDARD vEEG.**

QUESTIONS