Psychogenic Non-Epileptic Seizures: Diagnosis and Management

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OVERALL OBJECTIVES:

1. Define psychogenic non-epileptic seizures (PNES)
2. Describe the process of diagnosing PNES
3. Identify key elements to delivering the diagnosis of PNES
4. Review treatment and barriers to treatment of PNES

Overview of Psychogenic Non-Epileptic Seizures (PNES)

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

Non-epileptic Paroxysmal Events

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

NES/PNES Terminology

- Hystero-epilepsy
- Hysterical seizures
- Pseudo-seizures
- Pseudo-epileptic seizures
- Stress seizures
- Dissociative seizures
- Medically unexplained transient loss of consciousness
- Psychogenic seizures
- Psychogenic non-epileptic seizures (PNES)
- Psychogenic non-epileptic events
- Non-epileptic seizures (NES)
- Non-epileptic attacks/NEAD
- Functional seizures
- Conversion disorder with seizures

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, dissociation, or anxiety)
- Not related to cortical hyperexcitability (i.e., ictal epileptiform discharges)

Definition of PNES

- **Not PNES when symptoms are entirely explained by:**
  - **Anxiety disorders (e.g., panic)**
  - **PTSD**
  - **Factitious Disorder or Malingering**
  - **Behavioral issues in context of developmental disability**
- **PNES:**
  - **Functional Neurological Symptom Disorder/Conversion**
  - **Somatic Symptom Disorder (aka Somatization Disorder)**
  - **Dissociative Disorder**

Conversion Disorder (300.11)
(*Functional Neurological Symptom Disorder*)

SIMPLE MOTOR

- With weakness or paralysis
- With abnormal movement
- With swallowing symptoms
- With speech symptoms

(F44.4)

COMPLEX MOTOR

- With attacks or seizures

(F44.5)

SENSORY

- With anesthesia or sensory loss
- With special sensory symptoms

(F44.6)

- With mixed symptoms

(F44.7)

Slide courtesy of Dr. George Tesar.

NES: Epidemiology

- Estimated prevalence ~ 30 per 100,000
- Reported incidence = 1 to 5 per 100,000 per year in those over 18 years
- 20-40% of epilepsy monitoring unit (EMU) discharge diagnoses

- Mean time to diagnosis = 7 years [Reuber et al. 2002]

NES: Patient Characteristics

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

Model for PNES Development

Contributing Factors	*Biological*	*Psychosocial*
Predisposing	Genetic	Childhood adversity, Trauma/abuse
Precipitating	Injury, Disease	Traumatic or stressful life-events
Perpetuating	Deconditioning, Physical disability	Emotional disorder, Illness beliefs, Ineffective coping strategies, Family conflict, Conflicting medical opinions

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 or personality traits (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)
- Anniversaries of past traumatic events

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), with recurrent marital discord (perpetuating).
2. 23yo with depression, anxiety, raised by alcoholic parents, taught that showing emotion was a sign of weakness (predisposing), with recent MVC leading to injury and job loss (precipitating), and chronic daily headache and fibromyalgia (perpetuating).
3. 65yo man with CAD s/p recent MI, now unable to work, recently developed NES. Pt recalled recent NES event triggered by seeing someone mowing his lawn for him, which served as a reminder of his disability (precipitating).

Contributing Factors by Age

1. Juvenile onset (< 18 years):
   - History of abuse
   - Academic failure
   - Epilepsy or FH of epilepsy
2. Adult onset (18 – 55 years):
   - Medical comorbidities
3. Late onset (> 55 years):
   - Male
   - Severe physical health problems
   - Less likely to report antecedent sexual abuse

Asadi-Pooya AA et al. Clin Neurol Neurosurg 2013; 115: 1697-1700.
Duncan R et al. Neurology 2006; 66: 1644-1647.

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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: Semiology

6-item bedside diagnostic tool:

- **To diagnose PNES with motor features similar to generalized motor seizures (to be used in ED)**

	EPILEPTIC	NONEPILEPTIC
EYES	Open	Closed
HEAD	Fixed, Unilateral Version	Side-to-side head movements
LIMBS	In phase / same direction	Out-of-phase limb movements
BODY (AXIS)	Straight / anterior flexion	Opisthotonus / arching
BODY (MOVEMENT)	No rotation	Intense rotation in bed
EVOLUTION	Continuous course	Fluctuating course

De Paola et al., Epilepsy & Behav 2016

Making the Diagnosis: VEEG

Simultaneous video and EEG:

- **Gold-standard for diagnosis**
- **To capture all typical events, as confirmed by witnesses**
- **Most helpful when there is motor activity or altered responsiveness**
- **Less useful for subjective symptoms (i.e., auras)**
- **Can be difficult in frontal lobe seizures and when EEG is obscured by movement/EMG**

Making the Diagnosis: Physiologic Measures

Some physiologic measures studied in PNES:

- **Serum prolactin (PRL)**
- **Serum cortisol**
- **Serum creatinine kinase**
- **Serum brain-derived neurotrophic factor (BDNF)**
- **Heart rate variability**

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

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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

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  - Presenting the Diagnosis
- Treatment
  - Stopping antiseizure medications
  - Referring for 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.

RCT for PNES

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.**

Cleveland Clinic PNES Program

Seizure Frequency

	Cleveland Clinic (N = 50)	Comparison Group[1] (N = 18)
Mean seizure reduction	72%	51-59%
Responder rate (≥ 50% reduction in seizure frequency)	92%	56-67%
Percent of patients seizure-free	48%	33-56%

The 50 patients treated with psychotherapy had a median duration of treatment of 12 sessions (range, 6–41). Of the 50 patients, 35 had PNES only, 11 had both PNES and epileptic seizures, and 4 had epilepsy only. Of the 48 who were having seizures prior to treatment, 46 had at least a 50% reduction in seizure frequency after treatment.

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

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)

Comorbid PNES and ES

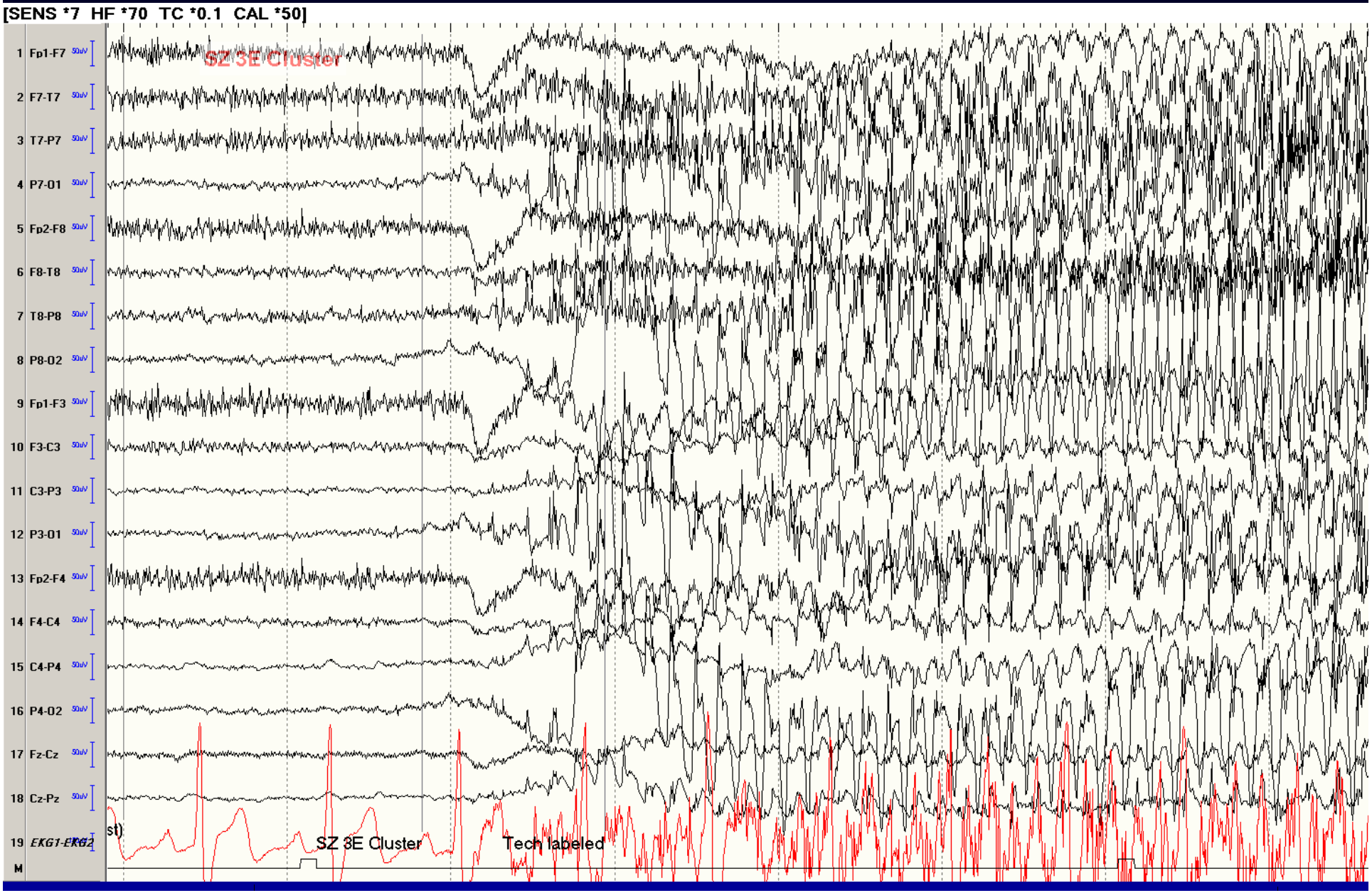
- Studies report 5-50% of pts with PNES also have ES (video-EEG)
  - Varying definitions of ES
- ES typically begins before PNES
- Similar semiology in 40-64% although PNES duration typically longer, with greater frequency; PNES is usually stereotyped and distinguishable from ES

Patient AD

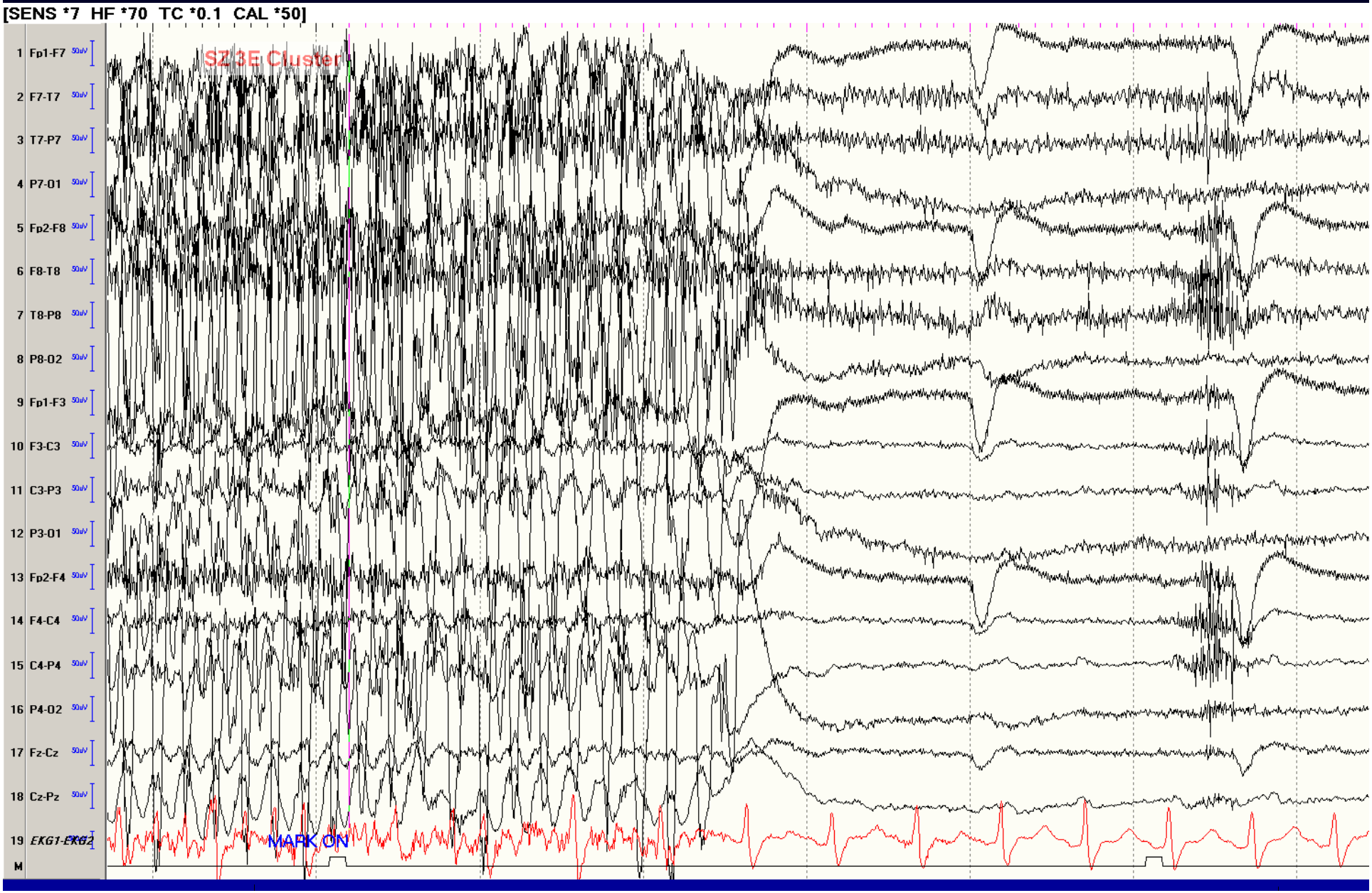
- 42yo LH man
- Seizure Onset: 23 years of age
- Medical History: hypothyroidism, HPL, psychotic disorder, h/o physical abuse with HT/concussion
- Exam: mild cognitive delay, psychomotor slowing
- Medically intractable (failed PHT, PHB, TPM, GBP, VPA, LTG), s/p VNS 2002

- Seizures
  - Automotor seizures (unresponsiveness with mouth movements) 2x/month
  - Convulsive motor seizures 3x/year

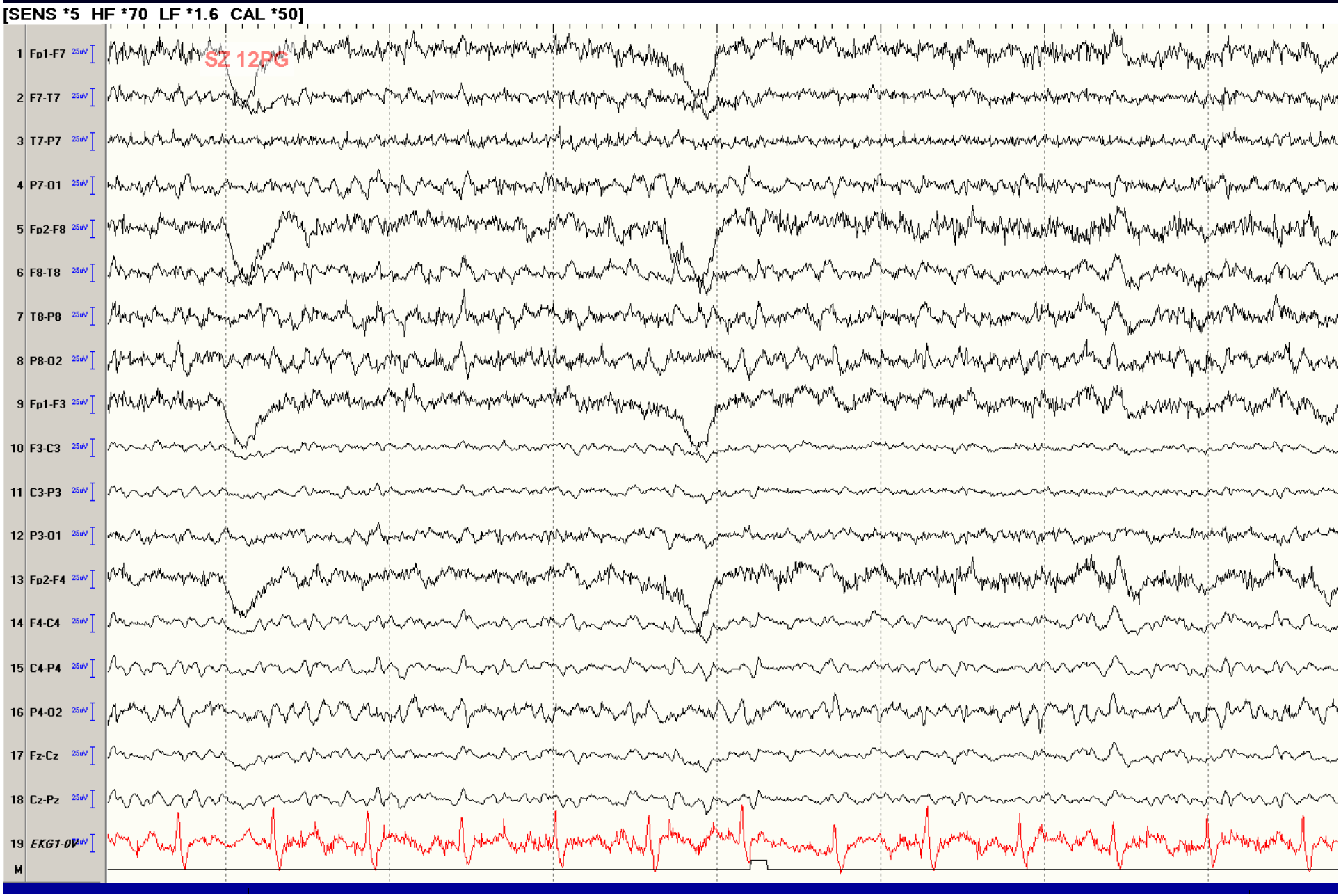
Days 1-5 in EMU: 11 clusters of PNES



First 5 days in EMU: 11 clusters of PNES



Days 6-8 in EMU: 8 Epileptic Seizures



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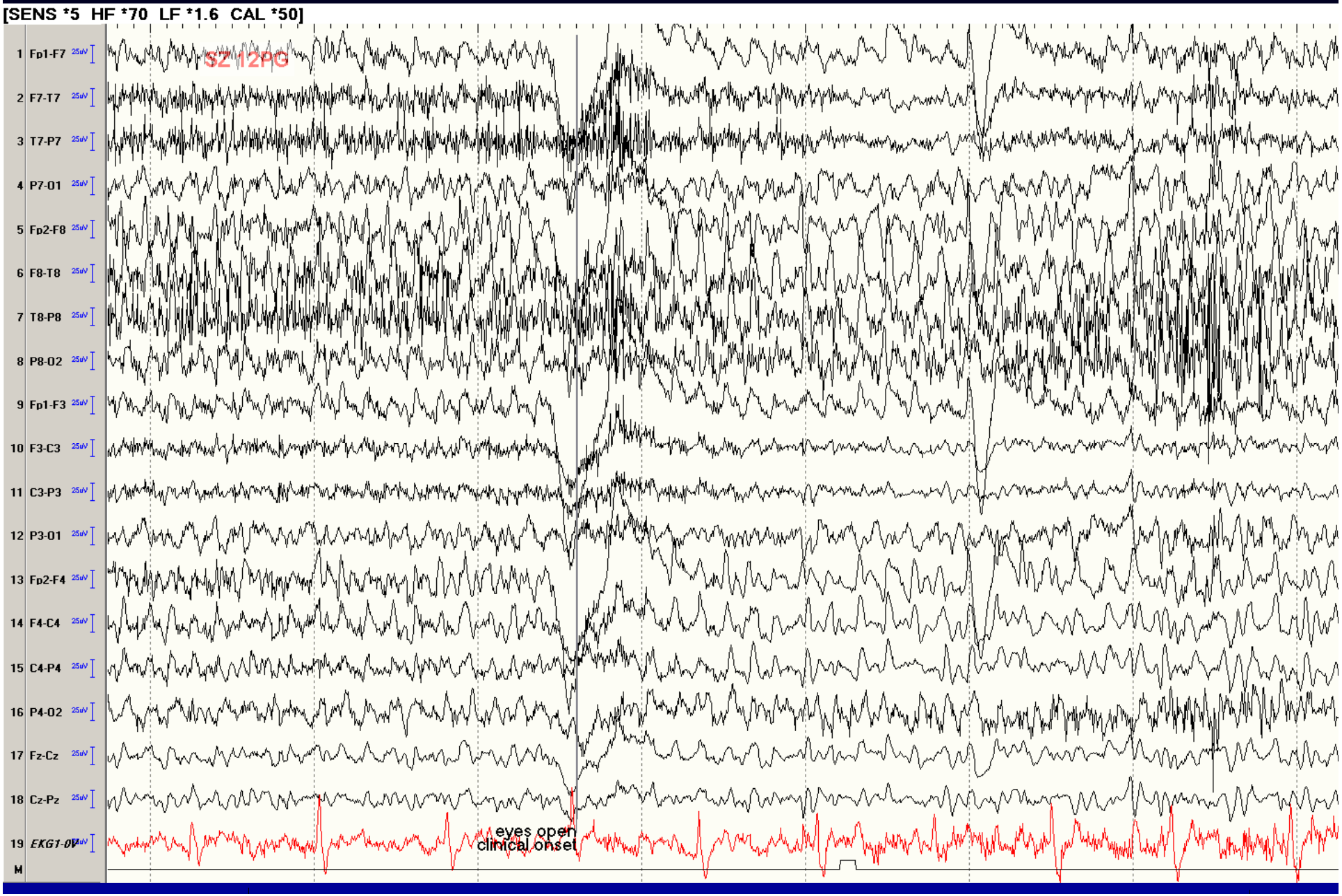

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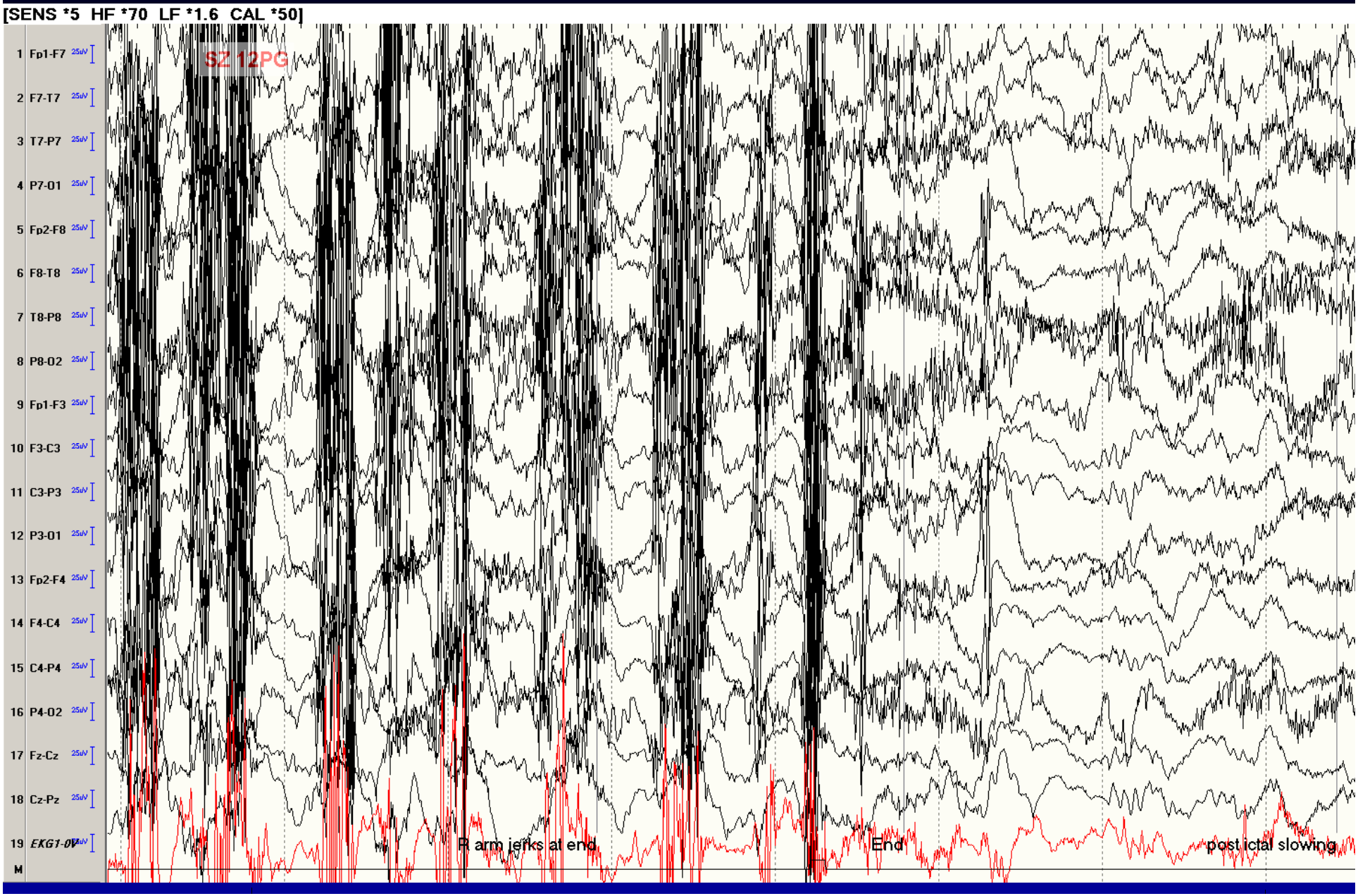
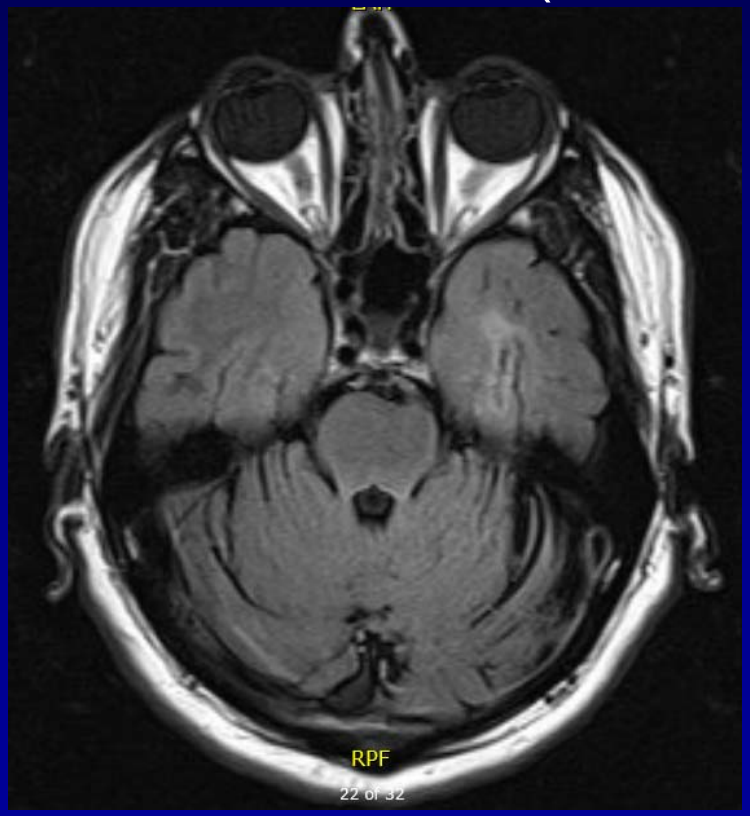
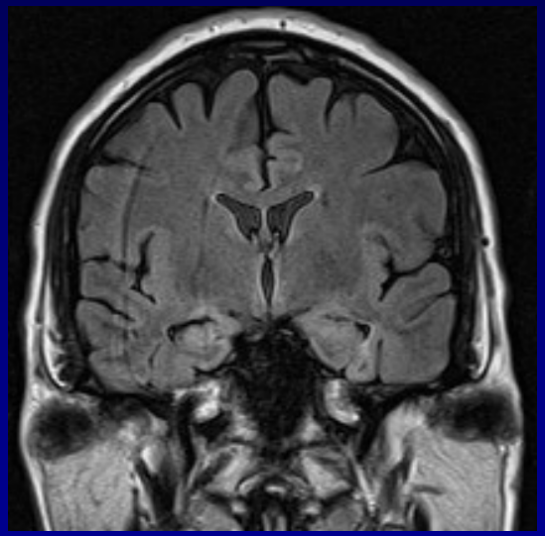


Patient AD

EMU evaluation 2014:

- First five days: 11 clusters of PNES
- Video-EEG continued to capture 2nd seizure type
- Next 3 days: 8 ES (4 R Temp, 3 L Temp, 1 Bitemp)
- Interictal SW (70% L FT, 30% R FT)





MRI BRAIN 10/2014

"Focal encephalomalacia involving left fusiform gyrus with abnormal T2/FLAIR signal extending into the mesial aspect of the left inferior temporal gyrus, possible R MTS

Patient AD

- PNES was treated (psychiatry and psychology), psychosocial stressors addressed, psychosis controlled

- Girlfriend was able to tell the difference between seizure types
  - PNES 1-2x/month but then none for 3 months
  - ES 2x/month

- **PMC OPTIONS**
  1) No surgery, given concern for bilateral independent seizures
  2) Left temporal lobectomy to remove the area of encephalomalacia and surrounding areas of abnormal signal. If bilateral temporal lobe epilepsy, will have limited success. Dominant temporal lobe makes him at risk for memory decline post-operatively.
  3) Invasive evaluation would not offer additional information; the options would remain the same

Patient AD

- Underwent LEFT anterior temporal lobectomy 5/2015
- Surgical pathology c/w focal cortical dysplasia
- Neuropsychological testing showed decline but pt denied new memory difficulties post-op:

INDEX	11/2014 pre-op	11/2015 post-op
Verbal Comprehension	63 (extremely low)	70 (borderline)
Perceptual Reasoning	75 (borderline)	77 (borderline)
Working Memory	77 (borderline)	77 (borderline)
Processing Speed	71 (borderline)	81 (low average)
Auditory Immediate Memory	89 (low average)	80 (low average)
Auditory Delayed Memory	89 (low average)	83 (low average)
Auditory Delayed Recognition	90 (low average)	80 (low average)
Visual Immediate Memory	88 (low average)	71 (borderline)
Visual Delayed Memory	99 (low average)	81 (low average)

- As of 3/2020, no ES since surgery, rare PNES, remains on antiseizure medications.

Comorbid PNES and ES

- Coexistence of PNES is not an absolute contraindication to epilepsy surgery, but needs to be considered very carefully.
- Case series by Reuber et al., 2002:
  - 13 pts with PNES + ES had surgery
  - 11 pts improved: 7 completely sz-free; 2 w/ PNES, 2 w/ ES
  - 2 pts did not improve: ES better but PNES worse
- De novo PNES after epilepsy surgery
  - 2-4%, typically in 1st 6 months, regardless of ES outcome

Conclusions

- PNES care is complex and requires effective communication between neurology, psychology and psychiatry.
- Video-EEG is the gold standard for diagnosis.
- Barriers to care include resistance to PNES diagnosis, inadequate access to mental health providers trained to treat PNES
- The neurologist has a crucial role in delivering the diagnosis, and needs to communicate clearly and with empathy.
- Effective treatment is available.
- PNES is not an absolute contraindication to epilepsy surgery in a patient with coexistent focal epilepsy.