2023 GW Epilepsy Board Review & Best Practices

Non-Epileptic Paroxysmal Disorders in Pediatrics

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DISCLOSURES

- **Disclosure of Financial Relationships**
  - **None**

- **Off-Label Usage**
  - **None**

Nonepileptic Paroxysmal Disorders

- can produce recurrent, paroxysmal changes of movement, consciousness or behavior.
- Heterogenous group (both neurological and nonneurological conditions).
- 25% in monitoring units have no epilepsy (Uldall et 2006, Hindley et al 2006, Bye et al 2000).
- Many are benign, require no treatment and can resolve spontaneously.

Non-epileptic paroxysmal disorders (ABPN Outline)

- **Behavioral, psychological and psychiatric disorders**
  - Daydreaming/inattention
  - Self gratification
  - Eidetic imagery
  - Tantrums and rage reactions
  - Out of body experience
  - Panic attacks
  - Dissociative states
  - Nonepileptic seizures
  - Hallucinations in psychiatric disorders

Non-epileptic paroxysmal disorders (ABPN Outline)

- **Syncope and anoxic seizures**
  - Vasovagal syncope
  - Reflex anoxic seizures
  - Breath-holding attacks
  - Hyperventilation syncope
  - Compulsive Valsalva
  - Neurologic syncope
  - Imposed upper airway obstructions
  - Orthostatic intolerance
  - Long QT and cardiac syncope
  - Hypercyanotic spells

Non-epileptic paroxysmal disorders (ABPN Outline)

- **Paroxysmal movement disorders**
  - Tics
  - Stereotypies
  - Paroxysmal kinesigenic dyskinesia
  - Paroxysmal nonkinesigenic dyskinesia
  - Paroxysmal exercise induced dyskinesia
  - Benign paroxysmal tonic upgaze
  - Episodic ataxias
  - Alternating hemiplegia
  - Hyperekplexia
  - Opsoclonus-myoclonus syndrome

Non-epileptic paroxysmal disorders (ABPN Outline)

- **Sleep related conditions**

- Sleep related rhythmic movement disorders
- Hypnogogic jerks
- Parasomnias
- REM sleep disorders
- Benign neonatal sleep myoclonic
- Periodic leg movements
- Narcolepsy-cataplexy

Non-epileptic paroxysmal disorders (ABPN Outline)

- **Migraine associated disorders**

- Migraine with visual aura
- Familial hemiplegic migraine
- Benign paroxysmal torticollis
- Benign paroxysmal vertigo
- Cyclical vomiting

Non-epileptic paroxysmal disorders (ABPN Outline)

- **Miscellaneous events**

- Benign myoclonus of infancy and shuddering attacks
- Jitteriness
- Sandifer syndrome
- Non-epileptic head drops
- Spasmus nutans
- Raised intracranial pressure

EXAMPLES OF SOME NONEPILEPTIC PAROXYSMAL DISORDERS

Non-epileptic paroxysmal disorders

- **Paroxysmal movement disorders**
- Tics
- Stereotypies
- Paroxysmal kinesigenic dyskinesia
- Paroxysmal nonkinesigenic dyskinesia
- Paroxysmal exercise induced dyskinesia
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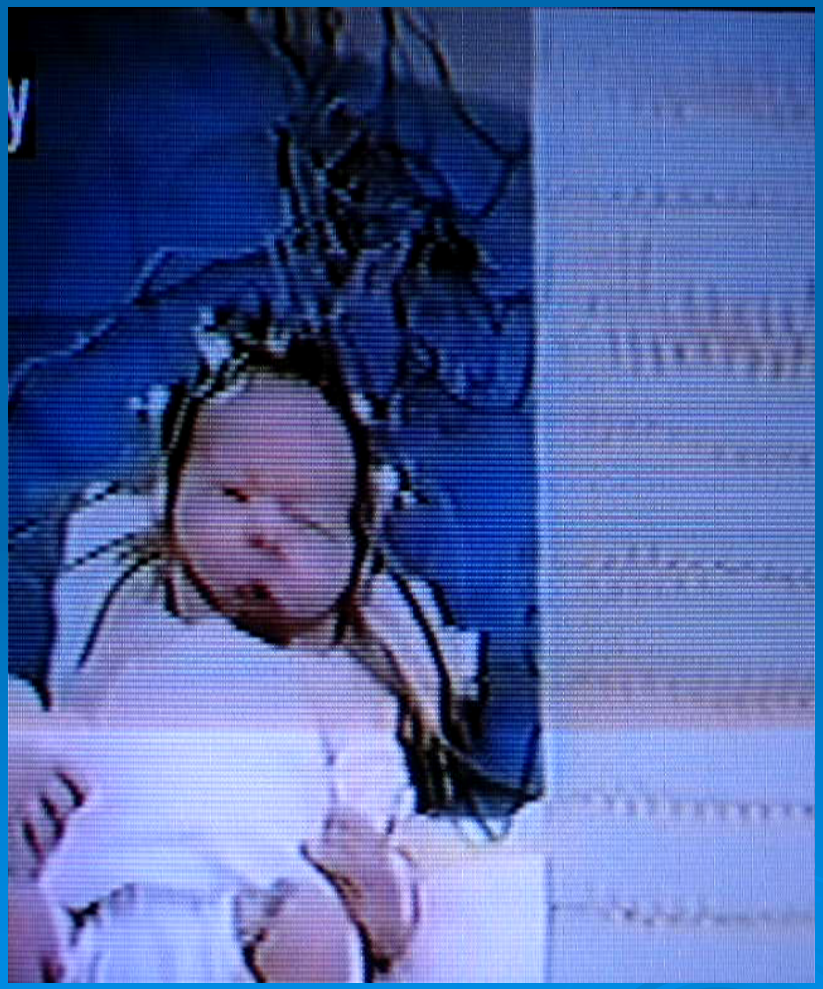
- Episodic ataxias
- Alternating hemiplegia
- Hyperekplexia
- Opsoclonus-myoclonus syndrome

Hyperekplexia

- "Stiff baby syndrome or startle disease"
- rare
- hyperactive startle reflex (falling)
- triad: *generalized stiffness*
  nocturnal myoclonus
  tonic spasms with auditory/tactile stimuli
- gene mutations affecting glycine receptor (GLRA1, GLRB) (Sotero de Meneses 2002)
- can be dominant or recessive
- Tx: clonazepam; valproic acid (Andermann F et.al. Brain Dev 1988)

Hyperekplexia video 1



Paroxysmal dyskinesia

Paroxysmal kinesogenic dyskinesia (PKD)

- Repetitive attacks of dystonia or choreoathetosis
- precipitated by movement.
- Can be sporadic or familial
- Chromosome 16p11.2
- Duration: seconds to minutes
- EEG: normal
- Tx: low dose AED (carbamazepine, phenytoin).

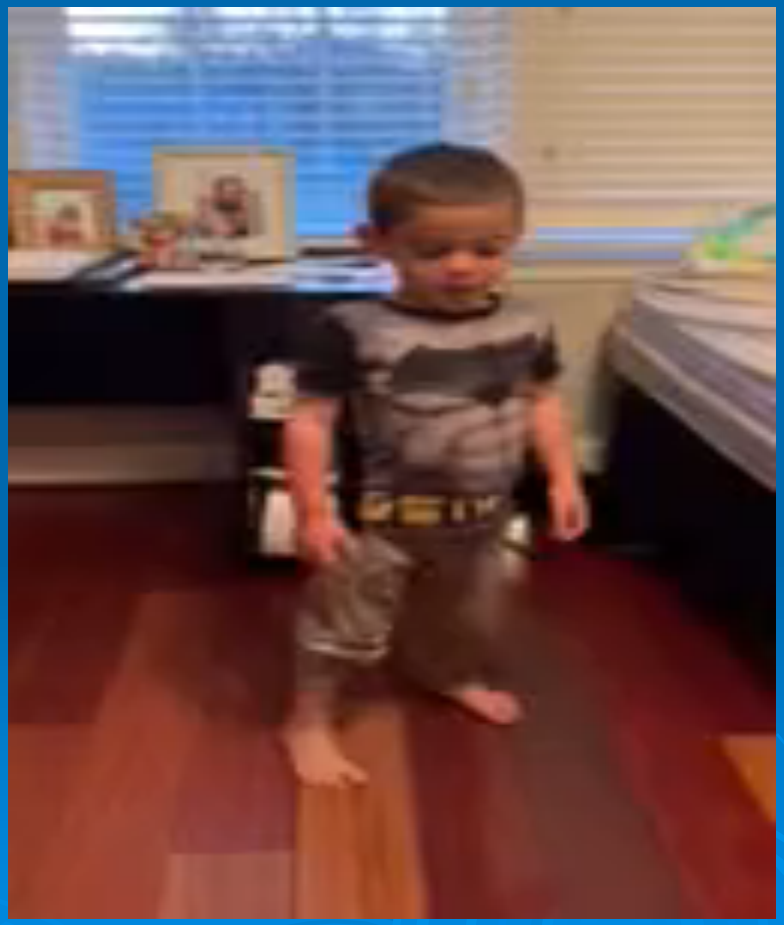
Paroxysmal dyskinesia

- **Paroxysmal nonkinesogenic dyskinesia (PNKD)**
- Onset childhood and adolescence
- Movements may involve trunk, lips, jaw or tongue.
- movements last longer (10 mins to several hours).
- Familial with AD inheritance; spontaneous cases reported
- Does not respond to anticonvulsants.

- **Paroxysmal Exercise-induced dyskinesia (PED)**
- Rare
- Triggered by prolonged exercise
- Focal dystonia,hemidystonia,or generalized dyskinesia
- Tx: AEDs. L-Dopa, trihexyphenidyl, acetazolamide.

(Muchau J Neurol Neurosur Psychiatry 2000)

Paroxysmal Dyskinesia



Video courtesy of Dr. Laura Tochen

Stereotypies

- Patterned repetitive movements that recur frequently.
- more common in children with autism and with mental retardation; can be seen in normal children.
- Head banging, head rolling, body rocking.
- Movements stops when distracted.
- Treatment: behavioral modification techniques.

Stereotypies

Alternating hemiplegia

- Intermittent attacks of paroxysmal episodes of weakness, hypertonicity or dystonia.
- Attacks begin before 18 months of age.
- Precipitated by emotional factors or fatigue.
- Last minutes of hours.
- Treatment: flunarizine (calcium blocker)

(Bourgeois et. Al. J Pediatr 1993 ; Silver et .al. Neurology 1993)

Opsoclonus myoclonus

- Rare
- Rapid, conjugate, multidirectional , oscillating eye movements usually continuous.
- Paraneoplastic syndrome caused by neuroblastoma and ganglioneuroblastoma.

(Rossor T et al. 2022; Losher W. 1993; De Deyn PP et al. 1992)

- Tx:removal or neural crest tumor and immunomodulatory tx

Non-epileptic paroxysmal disorders

Migraine associated disorders

- Migraine with visual aura
- Familial hemiplegic migraine
- Benign paroxysmal torticollis
- Benign paroxysmal vertigo
- Cyclical vomiting

Migraines

- Dilemma: acute neurologic events without significant headaches.

Confusional migraine

- confusion, hyperactivity, partial or total amnesia, disorientation, lethargy, vomiting
- several minutes to hours
- Clears up following sleep
- Headache +/- visual sxs before.
- r/o encephalitis, substance abuse, metabolic causes, and vasculitis

Migraines

Migraines with Visual Aura

"Alice in Wonderland "

- distortions of perception, change in size and shape of body parts, distortion of surroundings.
- confused with temporal lobe or occipital seizures; encephalitis, vasculitis

Benign paroxysmal torticollis

- Sudden, repetitive episodes of head tilting or turning to one side with rotation of the face to opposite side.
- Minutes to days
- child is responsive
- etiology unknown.
- family hx of torticollis or migraine
- Ddx: neoplastic conditions of the posterior fossa, cervical cord, neck

Benign paroxysmal torticollis

Benign paroxysmal vertigo

- Sudden or repeated attacks of dysequilibrium usually < a minute.
- child unable to walk, associated with nystagmus, diaphoresis, nausea and vomiting.
- child alert and responsive.
- EEG: normal
- (+) family history of migraine.
- Subsequently develop typical migraines.

(Drigo P, et al. Brain Dev. 2001)

Cyclic Vomiting

- Acute, recurrent episodes of intense nausea with vomiting, lasting for hours to days.
- Later evolves to migraine.
- Unknown cause. Multifactorial (aberrant brain-gut pathways,mitochondrial enzymopathies, GI motility disorders, Calcium channel abnormalities) – *Drossman et al. Gastroenterology 2016*

- Family history of migraines.
- Extensive GI work up
- Tx: abortive and preventive

Non-epileptic paroxysmal disorders

Syncope and anoxic seizures

- Vasovagal syncope
- Reflex anoxic seizures
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Syncope

- Transient interruption of cerebral blood flow resulting in loss of consciousness.
- Majority are neurally mediated (Mcleod KA 2003).

Syncope - Causes

A. Secondary to known precipitating events.
1. Neurocardiogenic
a. Vasovagal – fear, pain, unpleasant sights
b. Reflex – cough, micturition, carotid sinus pressure, swallowing.
2. Decreased Venous return
- Orthostatic, soldier's syncope, Valsalva
B. No clear precipitating event.
1. Cardiac – arrhythmia, obstructive outflow
2. Cerebrovascular insufficiency
3. Psychogenic

Pellock's Pediatric Epilepsy 2017.

Syncope versus seizures

	Syncope	Seizures
Setting	usually provoked	unprovoked
Prodrome/aura	presyncope	déjà vu, olfactory
EEG	high voltage delta flattening of EEG	spike waves
Recovery	fast, back to baseline	prolonged confusion/ lethargy

*** **Convulsive Syncope** - occurs in more prolonged cerebral hypoperfusion.

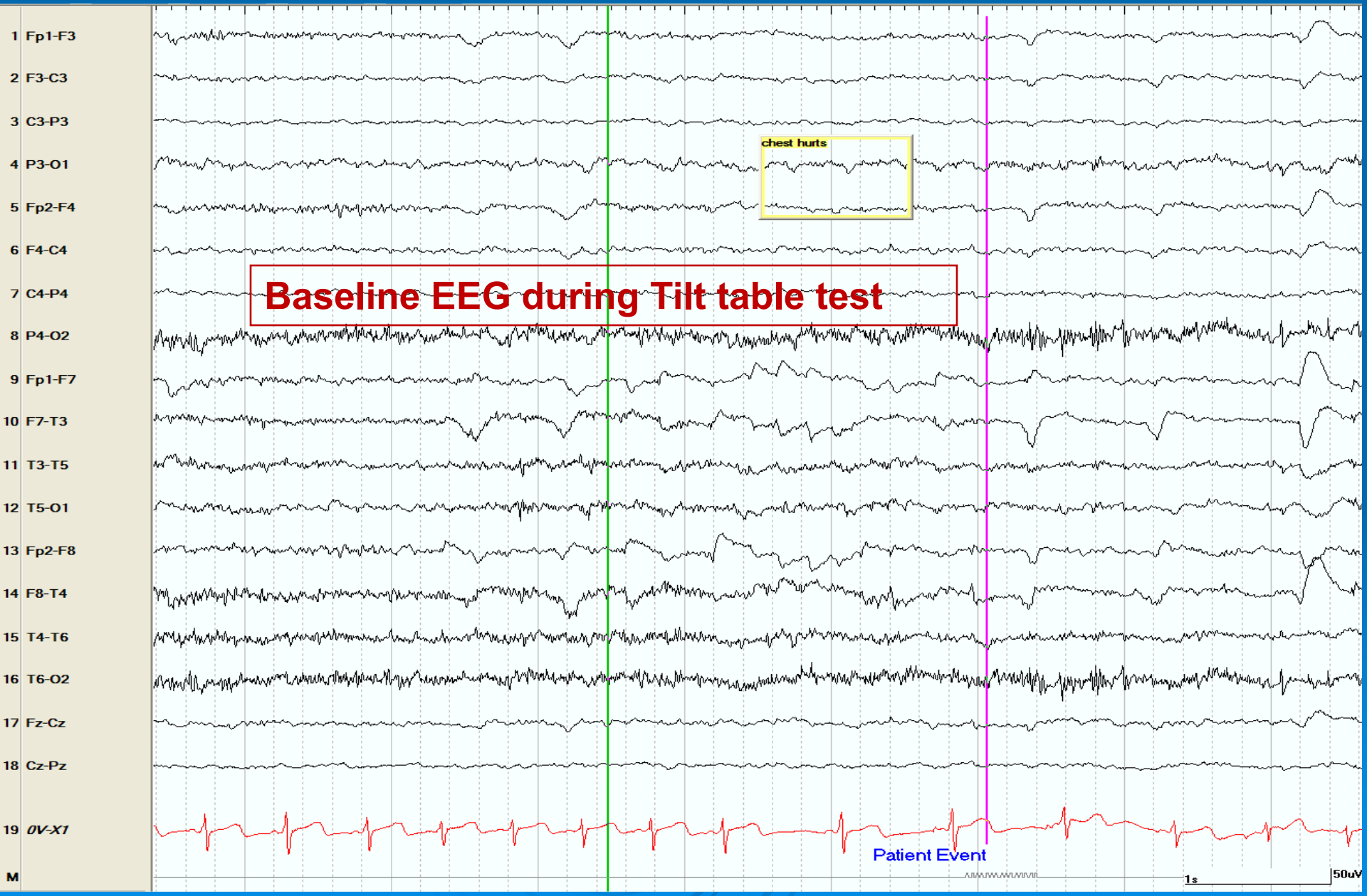
Syncope

Neurocardiogenic syncope

- a. Vasovagal syncope
  - Most prevalent
  - Occurs in response to an emotion or setting (blood drawing, hot weather, anxiety).
  - Prodome: warmth, nausea, tunnel vision

***Decreased venous return: Autonomic activation → parasympathetic cardioinhibitory response → vasodepression.*

EEG - Syncope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3 C3-P3
4 P3-O1
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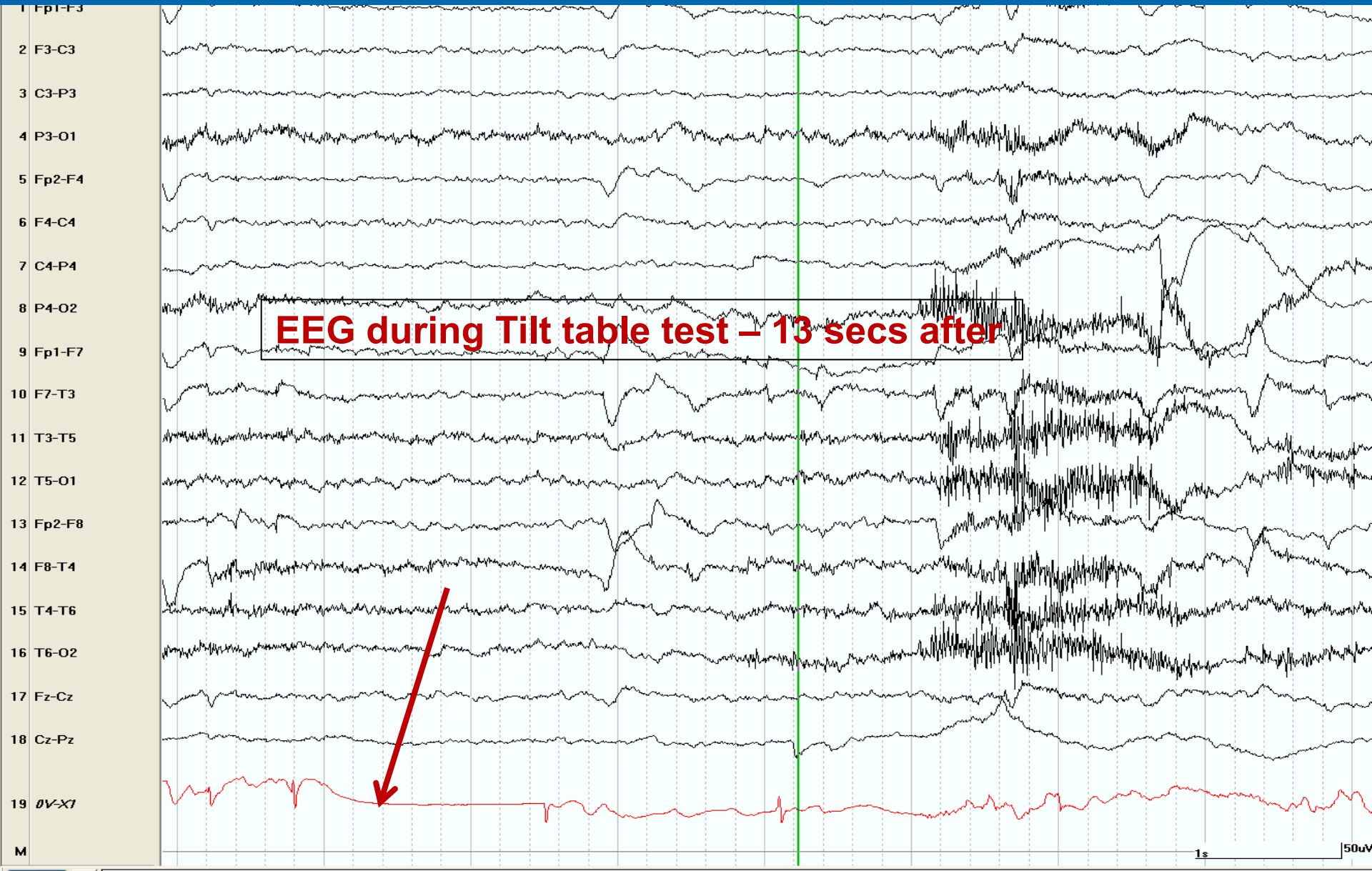
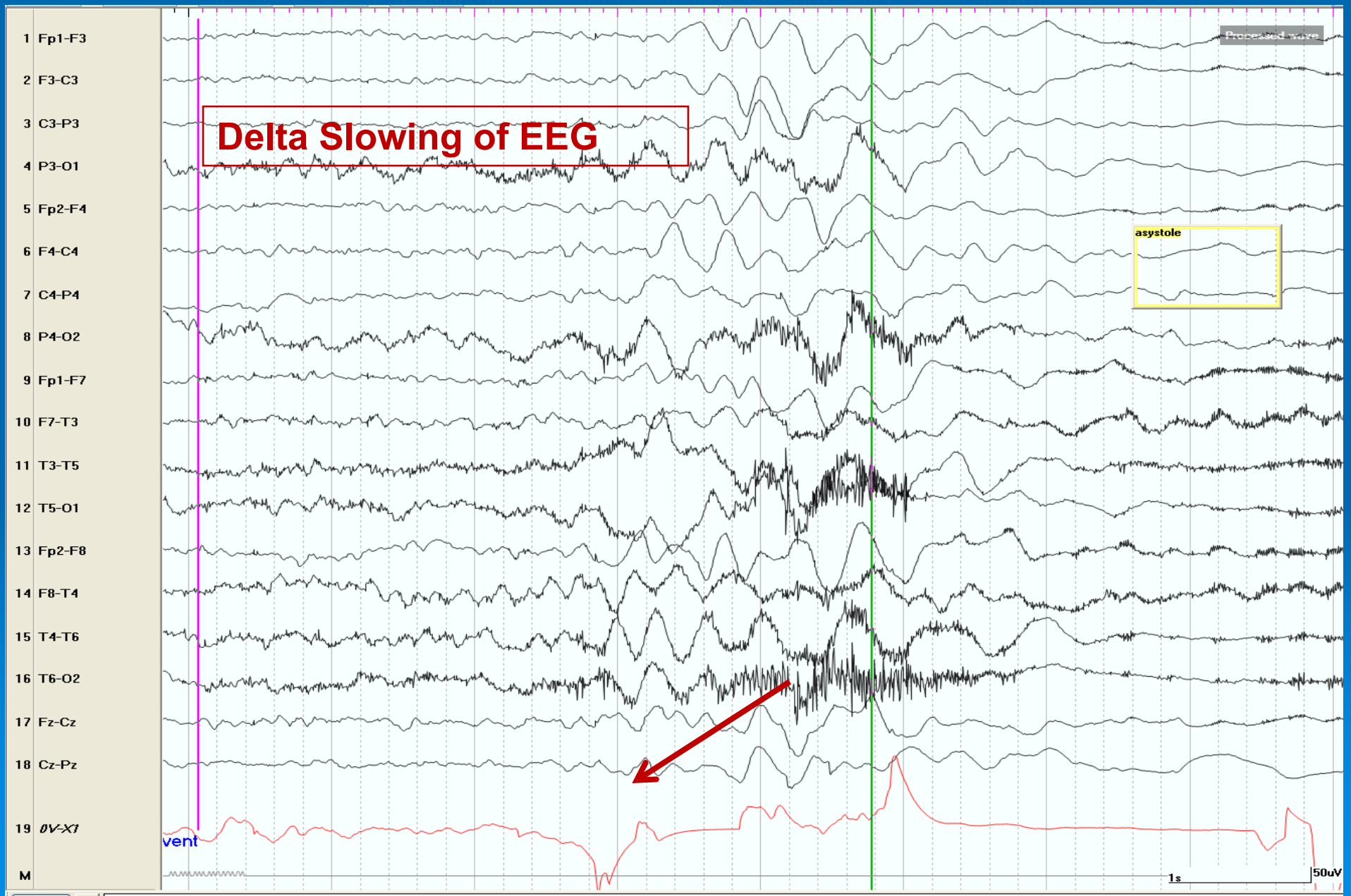
6 F4-C4
7 C4-P4
8 P4-O2
9 Fp1-F7
10 F7-T3
11 T3-T5
12 T5-O1
13 Fp2-F8
14 F8-T4
15 T4-T6
16 T6-O2
17 Fz-Cz
18 Cz-Pz
19 0V-X1
M
chest hurts
Baseline EEG during Tilt table test
Patient Event
1s
50uV

EEG - 13 seconds after



EEG - Syncope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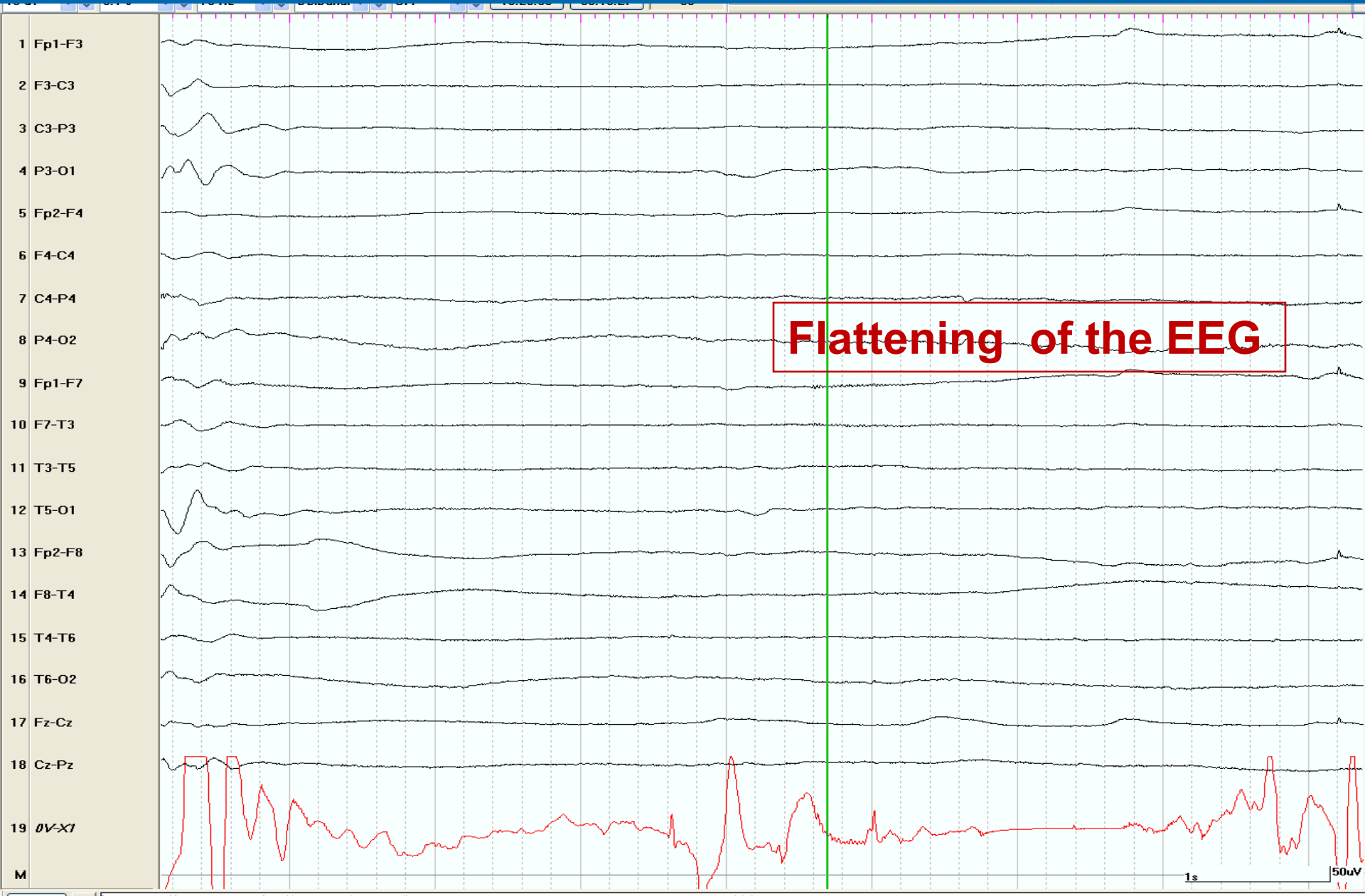
11 T3-T5
12 T5-O1
13 Fp2-F8
14 F8-T4
15 T4-T6
16 T6-O2
17 Fz-Cz
18 Cz-Pz
19 0V-X1
M
Delta Slowing of EEG
asystole
vent
1s
50uV

EEG - Syncope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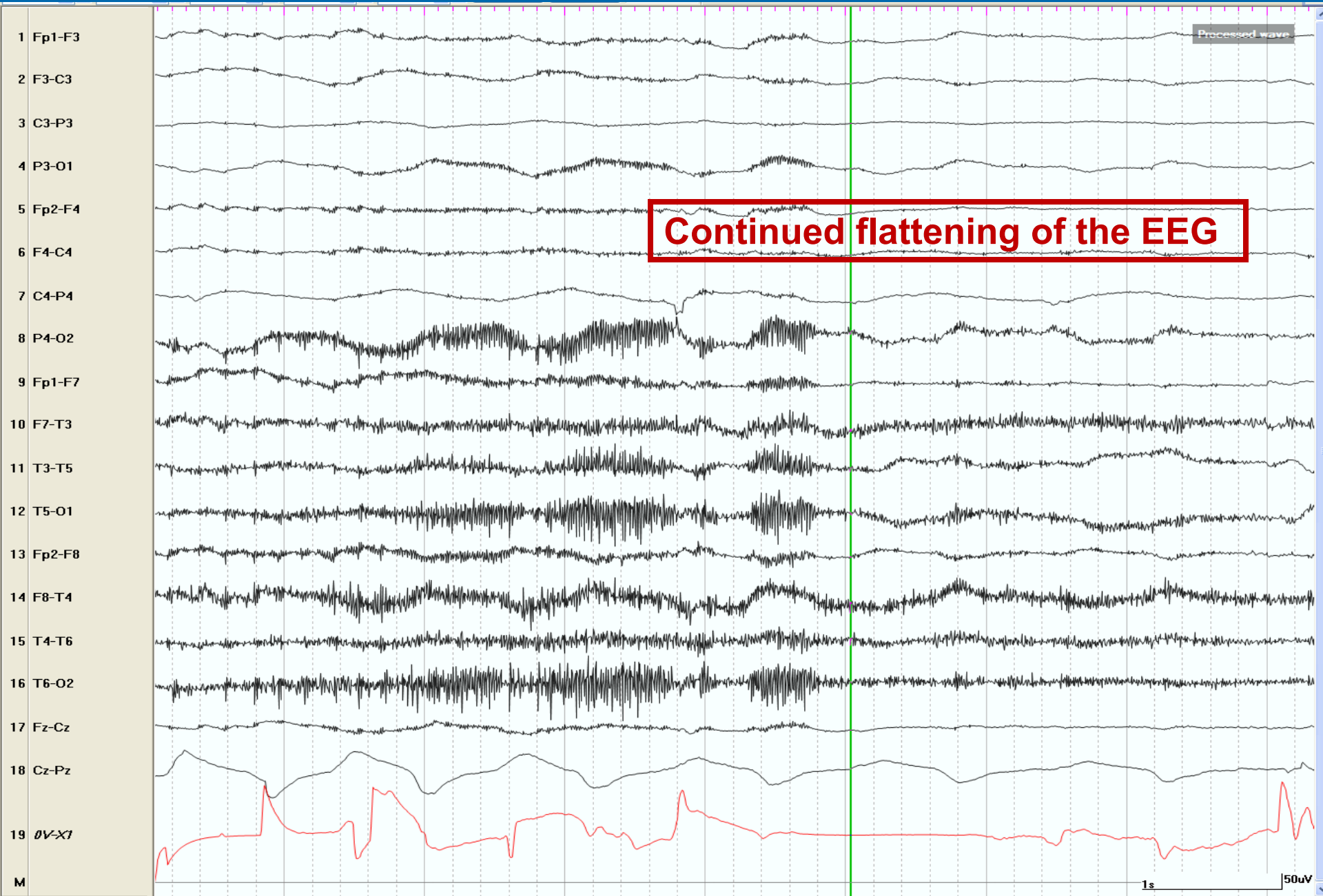
11 T3-T5
12 T5-O1
13 Fp2-F8
14 F8-T4
15 T4-T6
16 T6-O2
17 Fz-Cz
18 Cz-Pz
19 0V-X1
M
Flattening of the EEG
1s
50uV

EEG - Syncope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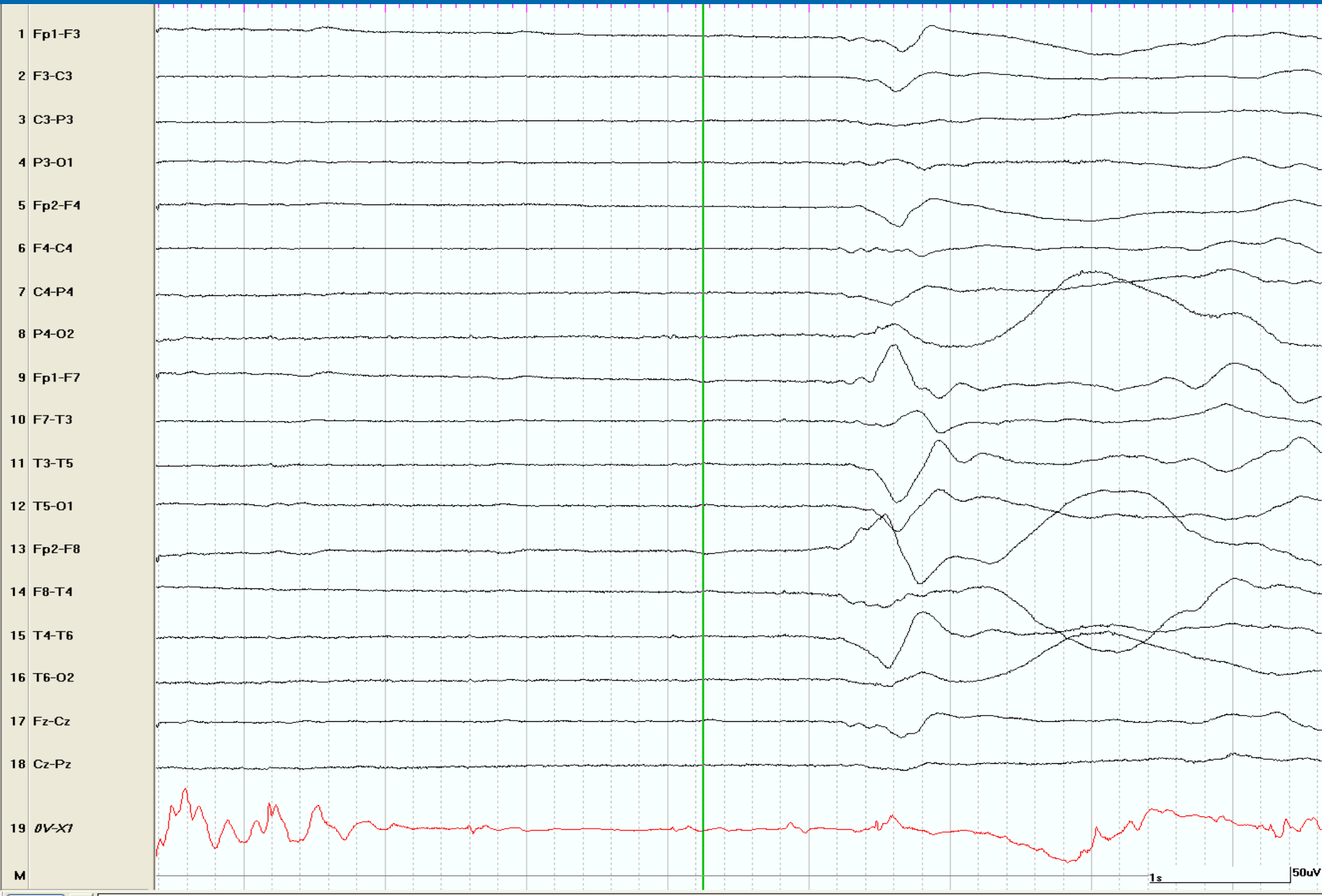
11 T3-T5
12 T5-O1
13 Fp2-F8
14 F8-T4
15 T4-T6
16 T6-O2
17 Fz-Cz
18 Cz-Pz
19 0V-X1
M
Processed wave
Continued flattening of the EEG
1s
50uV

EEG - Syncope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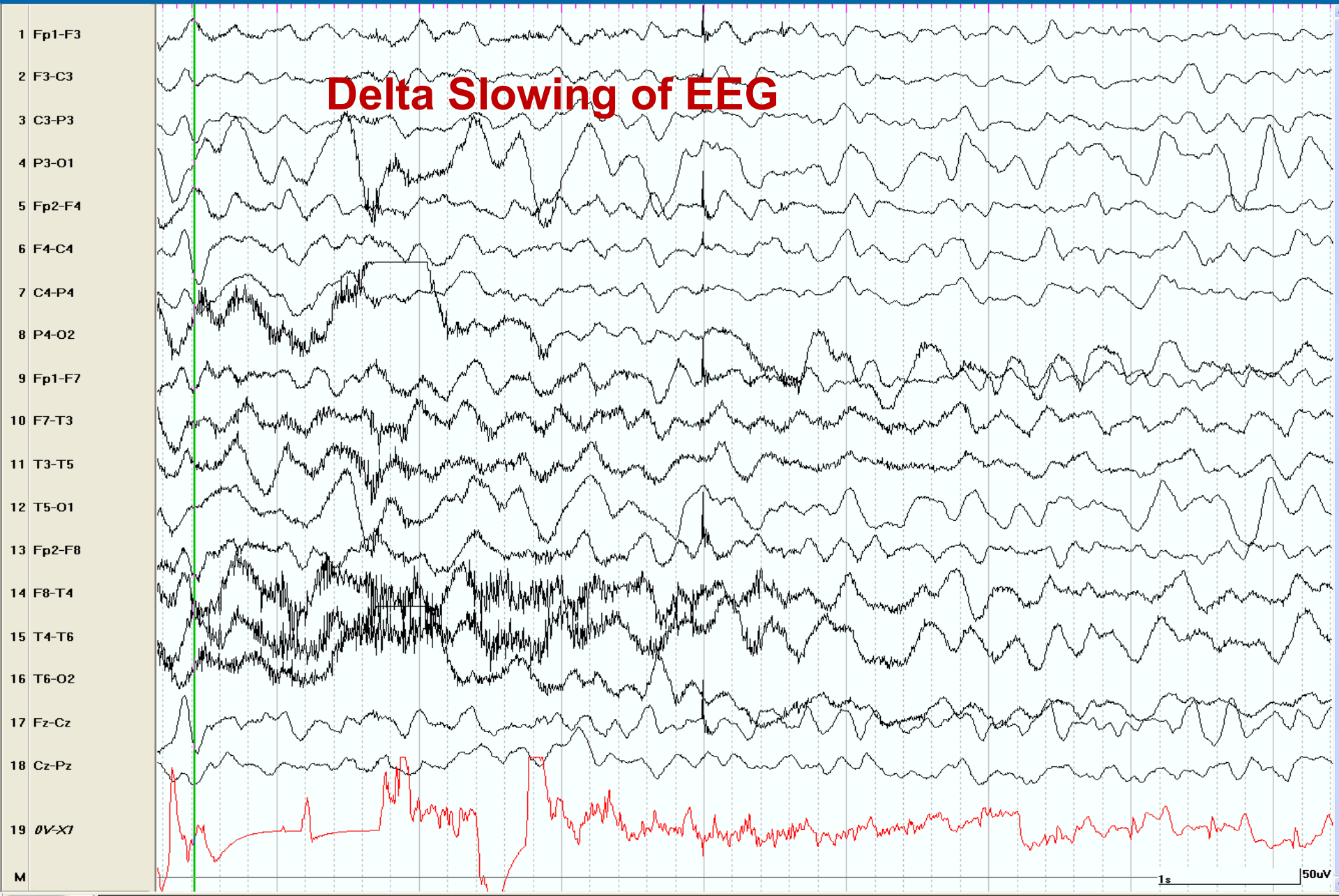
M
1s
50uV

EEG - Syncope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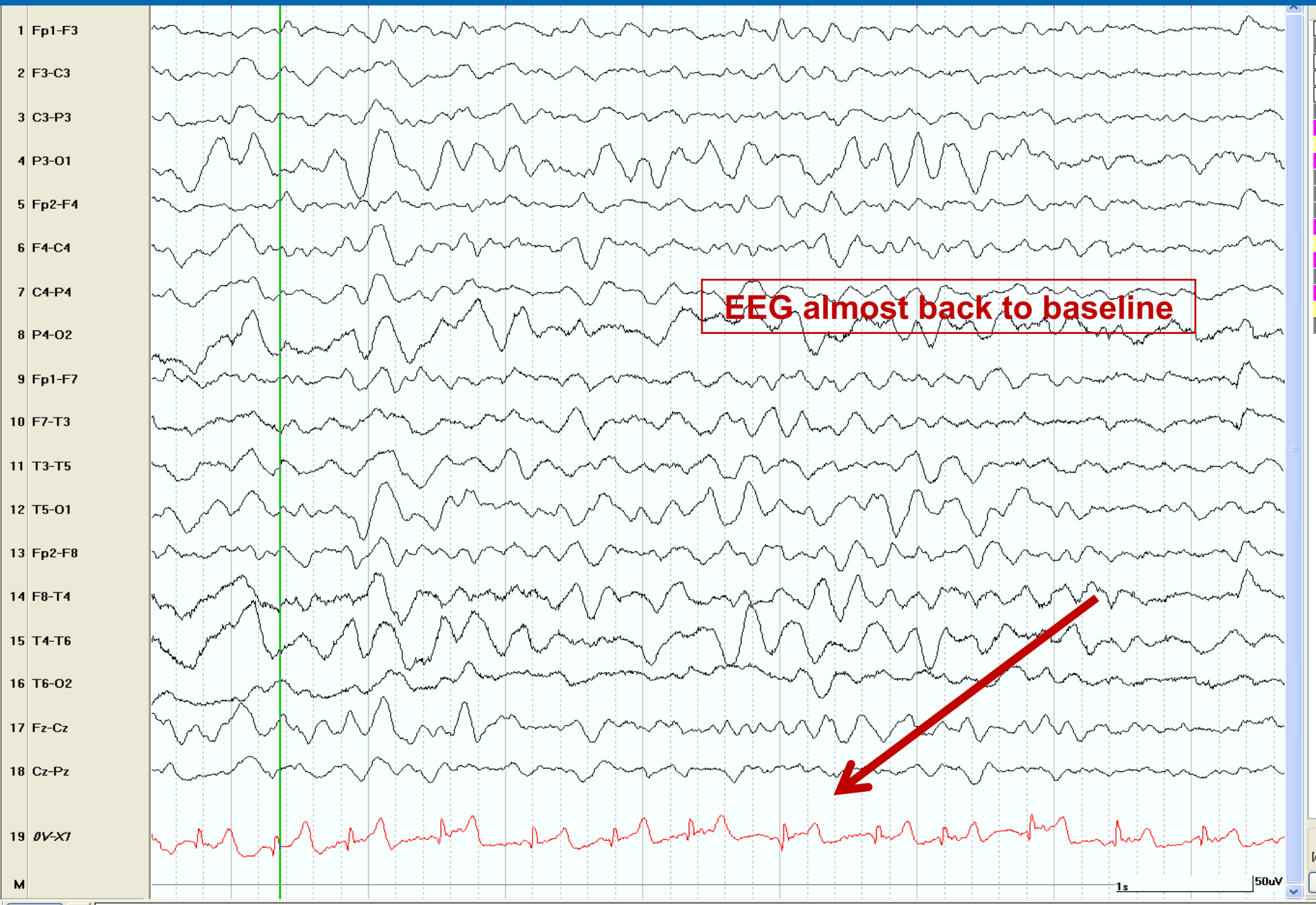
1s
50uV

EEG - Syncope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11 T3-T5
12 T5-O1
13 Fp2-F8
14 F8-T4
15 T4-T6
16 T6-O2
17 Fz-Cz
18 Cz-Pz
19 0V-X1
M
EEG almost back to baseline
1s
50uV

Syncope

Neurocardiogenic syncope

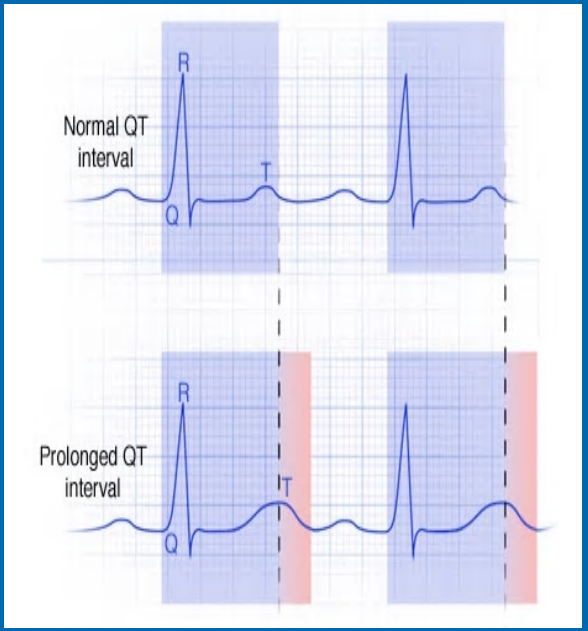
- **Reflex syncope**
  - transient disturbance autonomic control of HR and BP.
  - common triggers: coughing, micturition, swallowing

***Autonomic activation -- → parasympathetic cardioinhibitory response --→ vasodepression.*

Syncope

- Dx: check orthostatic blood pressure
  Tilt table test (if recurrent)
  EEG: diffuse slowing and flattening
- Tx: reassurance
  avoidance of precipitating factor
  increase H20 and salt intake
  if recurrent : beta blockers, alpha adrenergic agonists, mineralocorticoids,

Syncope



Cardiogenic syncope

- Rare; life threatening
- Usually without warning
- Secondary to electrophysiological conduction defect:

  - prolonged QT syndrome may predispose to malignant ventricular arrhythmias and cardiac arrest *(Compton and Berkovic Lancet Neurol 2009)*.
- Exercise is a known precipitant.

Breath holding spells

- 6 mos to 6 years (peak 2-3 years)
- cyanotic and pallid

Cyanotic

- Provocation → cries → then holds breath in expiration → cyanosis → LOC/ loss of tone

- precipitating event: mild injury/upset.
- if apnea prolonged → opisthotonus or clonic jerks.

- Treatment: behavioral modification of parents response
  Iron deficiency screening (if recurrent)

(McVivar and Adam 2006; Engel and Pedley 2008; Macakay 2005)

Breath holding spells

Pallid breath holding

- induced by minor trauma → stops breathing, pale, +/- brief cry → then followed by loss of consciousness
- bradycardia or asystole may occur

- Tx – most no treatment;
  some studies: atropine

Breath holding spells

Compulsive Valsalva

- Common in autistic spectrum disorder.
- Compulsive behavior.
- "fainting lark syndrome" – Bends knees, several breaths, then suddenly stands up while performing a forced expiration against a closed glottis (Valsalva maneuver).
- Technique causes effects of acute orthostatic stress, straining and hyperventilation -→ acute cerebral hypoxia-> syncope.

(*Kuiper et al J Clin Mov Disorder 2016; Martin et al, Arch Disc Child Educ 2009*)

Non-epileptic paroxysmal disorders

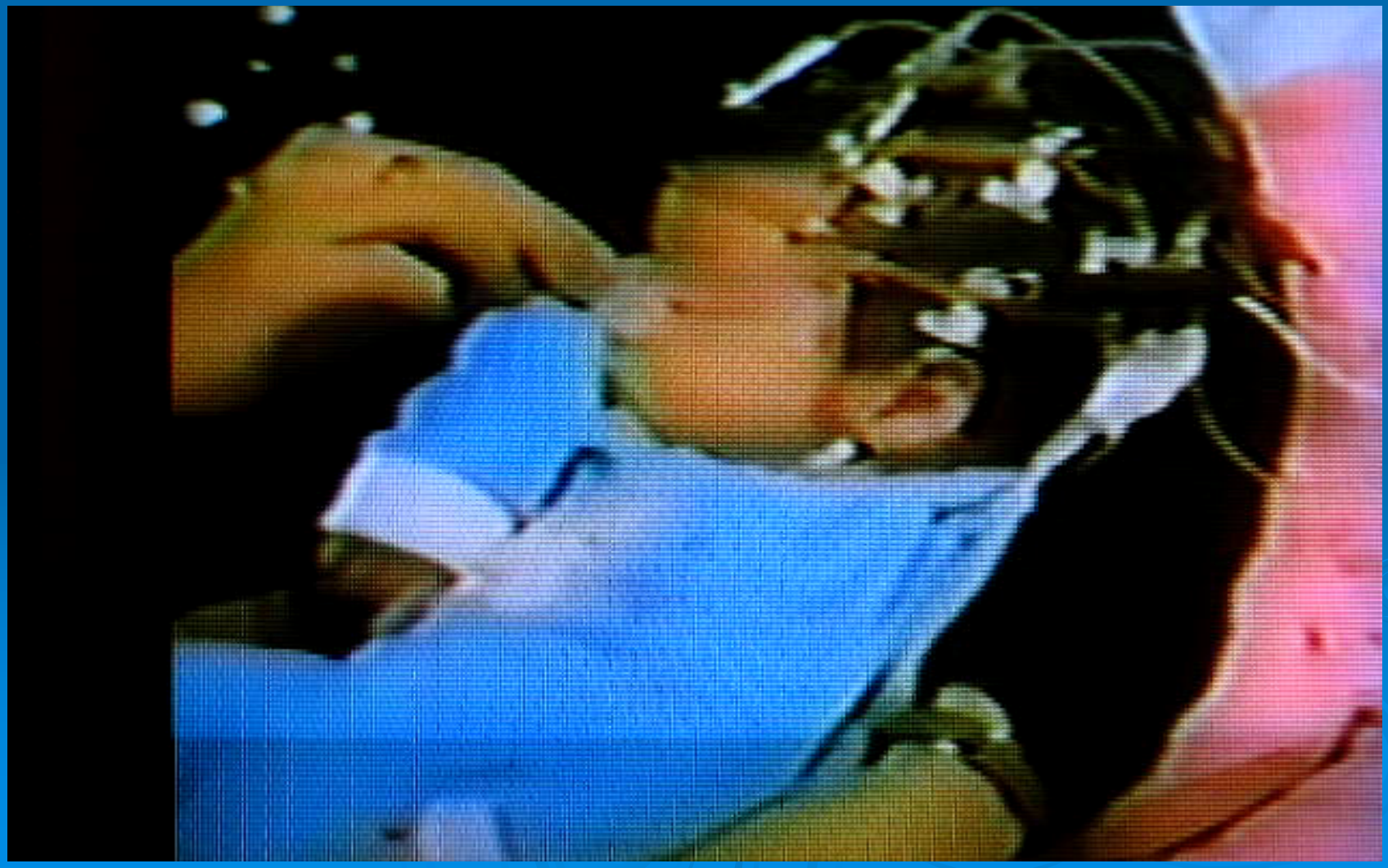
- **Sleep related conditions**

- Sleep related rhythmic movement disorders
- Hypnogogic jerks
- Parasomnias
- REM sleep disorders
- Benign neonatal sleep myoclonic
- Periodic leg movements
- Narcolepsy-cataplexy

Benign neonatal sleep myoclonus

- Healthy newborns
- Onset within 15 days of life
- repetitive myoclonic jerks of the extremities during non-REM sleep
- occur q2-3 secs and may last as long as 60 mins (Daoust-Roy and Seshia 1992).
- bilateral, asynchronous and asymmetric movements (migrate from one muscle group to another and occur bilaterally)
- EEG: normal
- Spontaneously resolves before 6 mos. of age

Benign neonatal sleep myoclonus



Parasomnias and Sleep Disorders

- **Night terrors** – usual onset: 4 years old

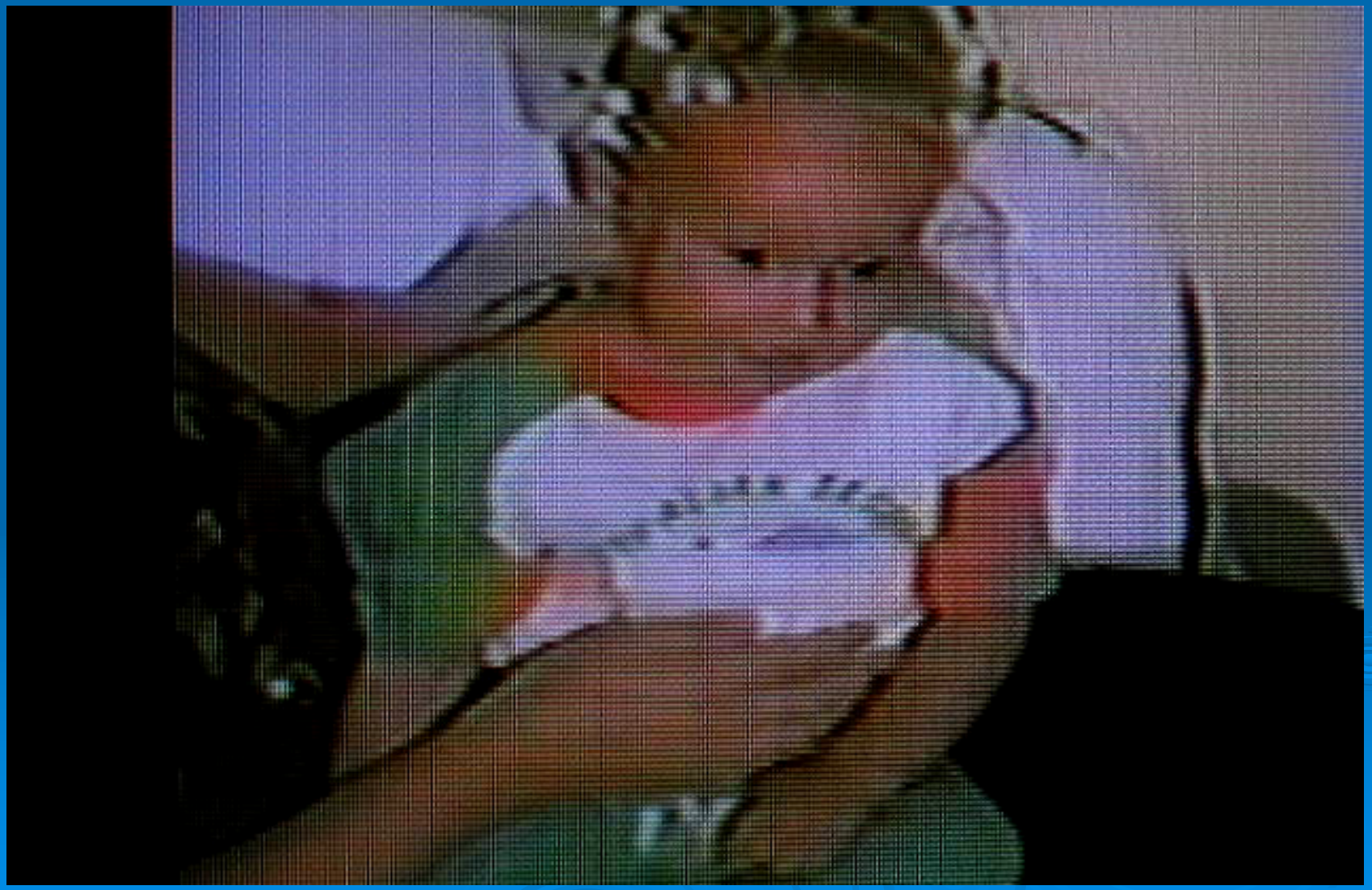
  wakes up from sleep, agitated, inconsolable; no recollection of event; r/o frontal lobe seizures

- **Cataplexy** *- sudden loss of muscle tone precipitated by a stimuli; r/o atonic seizures

- **Narcolepsy** * - excessive daytime sleepiness, sudden sleep attacks; hypnagogic hallucinations; sleep paralysis.

** Multiple sleep latency (short latency from sleep onset to REM); video EEG

Cataplexy



Video courtesy of Dr. Bhagwan Moorjani

Sleep related disorders

- Hypnagogic jerks –

  - brief, bilateral body jerks

  - a physiologic motor phenomenon (Matagna 2004, Fusco and Specchio 2005)

- Rhythmic movement disorders

  - occur at sleep onset and brief arousals.

  - head banging or rolling or body rocking.

  - occur 1 to 4 years old.

Non-epileptic paroxysmal disorders

- **Miscellaneous events**

- Benign myoclonus of infancy and shuddering attacks
- Jitteriness
- Sandifer syndrome
- Non-epileptic head drops
- Spasmus nutans
- Raised intracranial pressure

Sandifer syndrome

- Intermittent abnormal posturing such as stiffening and opisthotonic posturing.
- Gastroesophageal reflux
- associated with feedings
- Tx : Anti-reflux medications

Shuddering attacks

- Spells of tremor of head, arms, trunk with adduction and flexion of elbows.
- last a few seconds
- starts at 4 months; most improve by 10 years of age.
- precipitated by anger, fear, frustration
- Family hx of essential tremor (Holmes et.al. Am J Dis Child 1986)
- EEG: normal
- No treatment, reassurance

Spasmus nutans

- Triad: head nodding, head tilt (torticollis), nystagmus
- 4 – 12 months of age
- Pathophysiology: unknown
- MRI: r/o mass lesion of optic chiasm or 3rd ventricle
- Usually remits spontaneously within 1-2 years at onset.

Spasmus nutans

Benign myoclonus of infancy

- First year of life (3 to 8 months)
- Brief tonic or myoclonic contractions involving the axial muscles
- Spasms occur in cluster, usually mealtime
- Resolves by 2 years old
- EEG: normal
- Tx: reassurance

Non-epileptic head drops

- Can occur in normal developing child.
- Not associated with limb movements or change in facial expression.
- EEG: no epileptiform activity
- Video-EEG monitoring
  - head drops –recovery and drop phases similar in velocity.
  - seizure: rapid drop/descent followed by slow recovery; with ictal changes plus subtle myoclonic movements. *(Brunquell et al, Epilepsia 1990)*

Non-epileptic paroxysmal disorders

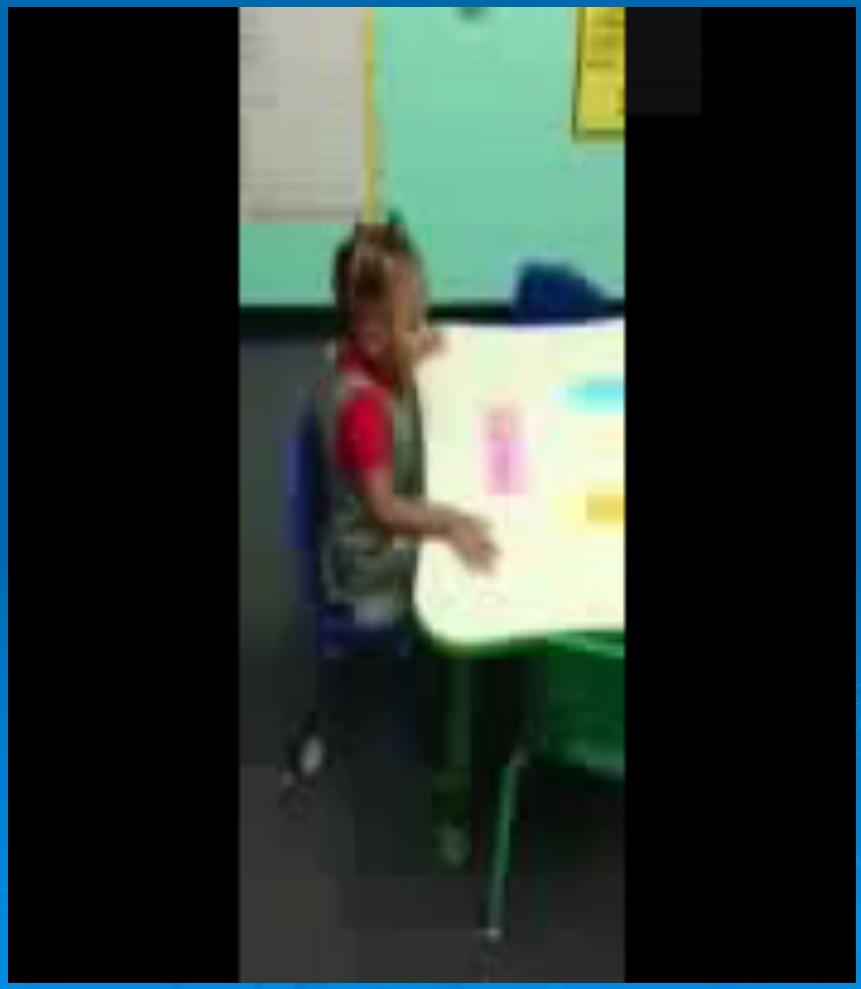
- **Behavioral, psychological and psychiatric disorders**
  - Daydreaming/inattention
  - Self gratification
  - Eidetic imagery
  - Tantrums and rage reactions
  - Out of body experience
  - Panic attacks
  - Dissociative states
  - Nonepileptic seizures
  - Hallucinations in psychiatric disorders

Self gratification behavior

- Infantile masturbation
- variant of normal behavior
- Rubbing of thighs together, rocking of the pelvis against hard surface
- Associated with sweating or flushing of face
- Distracting stimuli – stop these movements
- Tx: reassurance

Yang M L et al. Pediatrics 2005;116:1427-1432

Self gratification behavior



Video courtesy of Dr. Bhagwan Moorjani

Panic disorders, Dissociative phenomenon, Hallucinations

Non-epileptic event	Characteristic of non-epileptic event	Seizure characteristics	EEG
Panic disorder	Fear is in context to situation 5-20 minutes	Fear not in context to situation	No change
Dissociative phenomena	Fugue states Lack of memory for the event > 2 minute duration	No loss of awareness No memory loss < 2 minutes	No change
Hallucinations	In psychiatric conditions associated with speech instruction in the third person. Prolonged duration, persistent	Brief (less than a few seconds) No third person instructions	No change

Schachter SC. Atalas of Epilepsies 2010

Psychogenic nonepileptic seizures (PNES)

- Events that resemble an epileptic seizure but unaccompanied by EEG abnormalities .

  (Wichaidit BT et.al., 2015; Bhatia MS, 2005).

- Based on several poplation studies, the estimated incidence are at ranges from 1.5 to 5 per 100,000 persons per year.

  (Szaflarski JP et al, Neurology 2000; Reuber et al. Epilepsy and Behav. 2003; Duncan R et al. Epilepsy and Behav 2011)

- Related to a psychological process (Crompton and Berkovic 2009; Patel H, et al Epilepsia 2007; Kutluav E et al Epilepsy Behav 2010).

- Video EEG is the gold standard for diagnosis

Psychogenic nonepileptic seizures (PNES)

- Video EEG is the gold standard for diagnosis

- Yield of monitoring is high; 73 to 96 percent of patients will have typical PNES within the first 48 hours of recording

  (Woollacott IO, et al Epilepsy Behav. 2010; Perrin MW, et al.Epilepsy Behav. 2010; Parra J, et al. Epilepsia. 1998.)

Psychogenic nonepileptic seizures (PNES)

Danish hospital national survey (n=64)

- 5 historical characteristics
  - psychosocial stressors/trauma
  - sexual abuse
  - paroxysmal events occur in stressful situations.
  - no effect of antiepileptic meds
  - physical abuse

Wachaidit BT et al. Diagnostic practice of psychogenic nonepileptic seizures (PNES) in the Pediatric setting. Epilepsia. 2015; 56 (1):58-65.

Psychogenic nonepileptic seizures (PNES)

- 6 paroxysmal event characteristics
  - resistance to eyelid opening.
  - avoidance/guarding behavior
  - paroxysmal events occurring in the presence of others
  - closed eyes
  - rarely injury related to paroxysmal event.
  - absence of postictal change (Freeman 2005)

Wachaidit BT et al. Diagnostic practice of psychogenic nonepileptic seizures (PNES) in the Pediatric setting. Epilepsia. 2015; 56 (1):58-65.

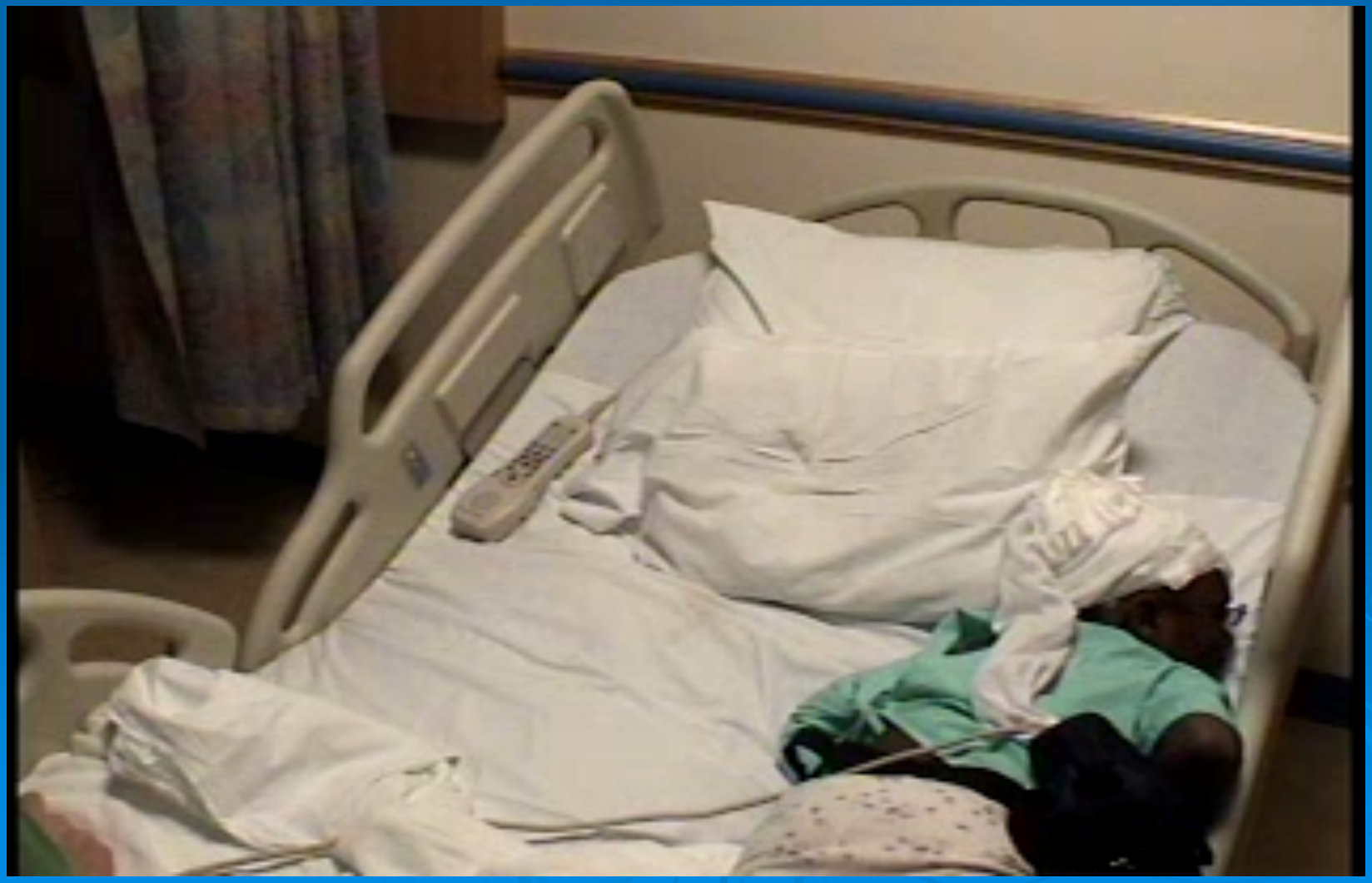
Psychogenic nonepileptic seizures (PNES)

- **Treatment**: cognitive behavioral therapy
- **Prognosis**:

  - In general, only a minority (25 to 38%) of patients achieve “seizure freedom”.
  - Children with better prognosis than adults, 70 to 80% achieve “seizure remission” [n= 18 pediatric, n=20 adult]

  (Wylie R et al, Neurology 1991).

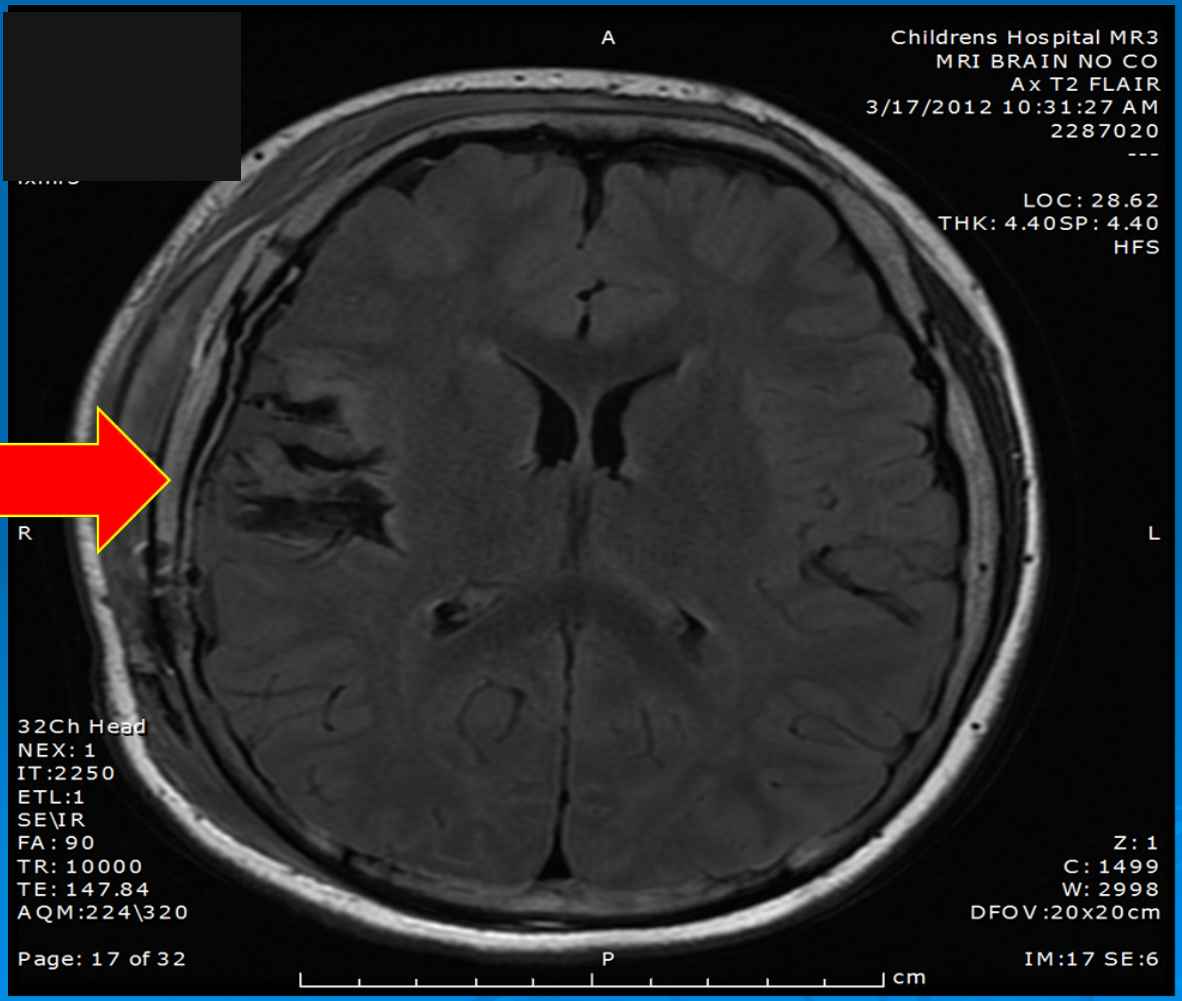
Psychogenic nonepileptic seizures



Psychogenic nonepileptic seizures

But……

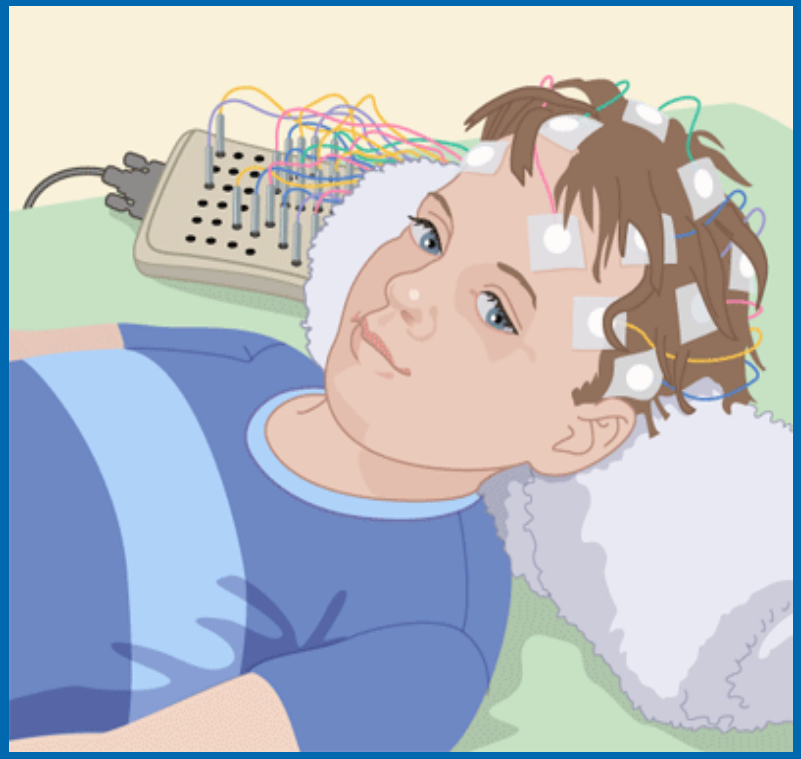
MRI


A
Childrens Hospital MR3
MRI BRAIN NO CO
Ax T2 FLAIR
3/17/2012 10:31:27 AM
2287020

LOC: 28.62
THK: 4.40SP: 4.40
HFS
R
L
32Ch Head
NEX: 1
IT:2250
ETL:1
SE\IR
FA: 90
TR: 10000
TE: 147.84
AQM:224\320
Page: 17 of 32
P
cm
Z: 1
C: 1499
W: 2998
DFOV:20x20cm
IM:17 SE:6

Conclusion

"The differential diagnosis of epileptic seizures includes a variety of benign, physiologic phenomena as well as pathologic conditions."



- thorough clinical history and examination
  - patient's age
  - description of event
  - time of occurrence

- Video EEG helpful
- *** dual diagnosis is possible

Board Questions

Question 1

- A 2 year old girl has been having spells consisting of rubbing of the thighs together, thrusting of the pelvis with sweating, grunting and flushing of the face. The child goes back to baseline after the event. Which work up is warranted?

a. electroencephalogram
b. Magnetic resonance imaging
c. No work up needed
d. Sleep study

Question 2

- These are spells of intermittent abnormal posturing such as stiffening associated after feeding.

a. Infantile spasms
b. Paroxysmal dystonia
c. Tonic seizures
d. Sandifer syndrome
e. Stereotypy

Question 3

- Which is a common finding in an EEG of a patient having syncope?

a. Spike waves

b. High voltage delta and flattening of the EEG

c. Preservation of the alpha rhythm

d. Beta activity

Question 4

- A 10 year old girl has been having spells of confusion, disorientation, lethargy, vomiting lasting for 3 hours and usually resolves following sleep. Which is the likely diagnosis?

a. Focal seizures

b. Confusional migraines

c. Psychogenic nonepileptic seizure

d. Neurocardiogenic syncope

Question 5

Which is not a typical characteristic of PNES?

a. resistance to eyelid opening.

b. paroxysmal events occurring in the presence of others

c. psychosocial stressors/trauma.

d. Some postictal change.

e. lack of response to antiepileptic meds.

Thank you