

# A 10-year-old boy with sleep fragmentation



# A 10-year-old boy with sleep fragmentation

CC: Frequent night time awakening for 2 years

## **Present illness:**

5 years PTA: He did not have good sleep due to frequent brief nocturnal awakening compared to his twin A.

2 years PTA : He has had increased night time awakening that disturbs his mother's sleep. After falling asleep at 9.30 PM, he wakes up 1-2 times per night at 1-2 AM for 10-15 minutes and then returns back to his sleep. It occurs 4-5 nights per week. There is no sleep walking or other unusual behaviors noted.

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## **Sleep History**

Sleep time 9-10 PM, sleep onset latency: 15-20 min

Wake-up time 6-7 AM, difficulty to be awakened at times

(+) occasional snoring, denies symptoms of RLS

Brief nap 1-2 times per week

Denies daytime sleepiness, Epworth sleepiness scale = 0

## **Past History**

Twin B, multiple food allergy, underweight, slow learner

Fever provoked seizures x 6, onset 1 y/o, on VPA until aged 6 y/o

EEG at 4, 6 y/o: normal

# A 10-year-old boy with sleep fragmentation

## **Family History**

(+) Epilepsy and slow learner in Maternal aunt

(+) Febrile seizure in one male cousin

(-) Parasomnia, other sleep disorder

## **Physical and Neurological Examination**

BW 22 kg (< P3), Ht 133 cm (P25)

Mallampati class II

Otherwise normal

# A 10-year-old boy with sleep fragmentation

## Problem List

1. Sleep fragmentation with morning sleep inertia
2. Past history of epilepsy
3. Family history of epilepsy and febrile seizure
4. Multiple food allergy
5. Failure to gain weight

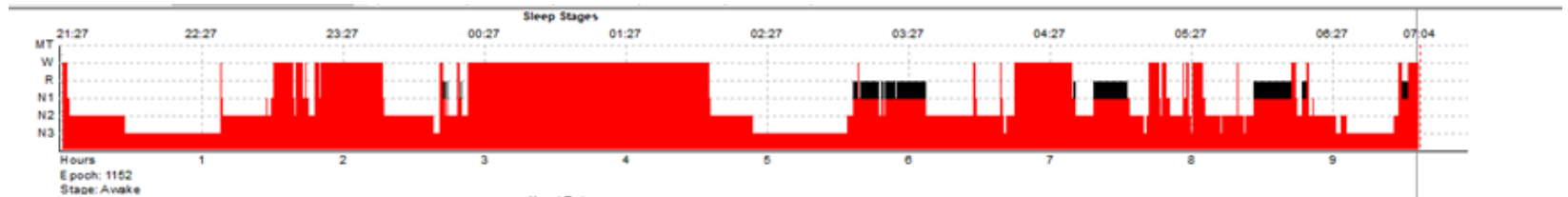


## Differential Diagnosis

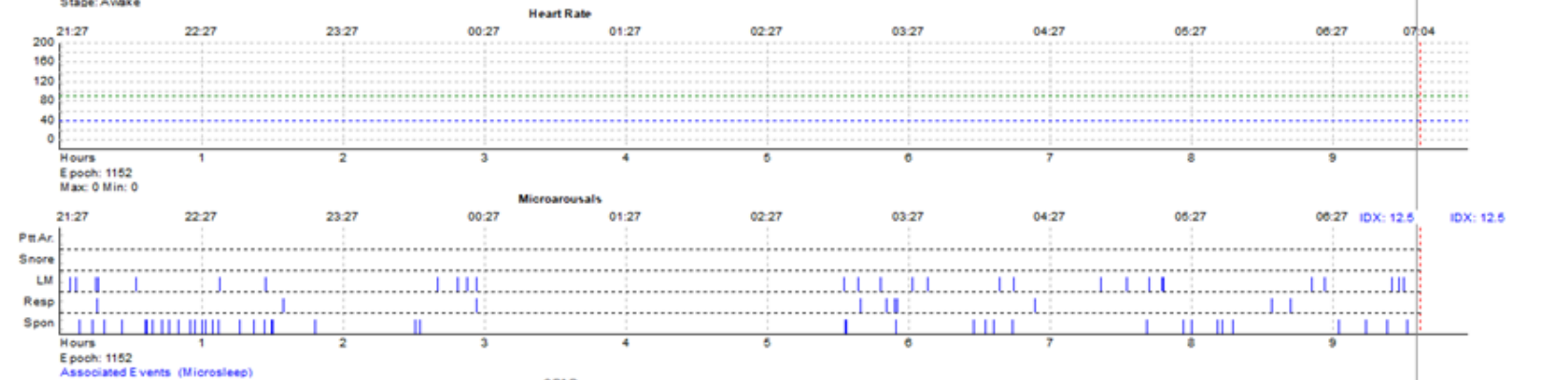
1. Sleep disordered breathing
2. Medical illness: allergic disease
3. Restless leg syndrome
4. Epilepsy

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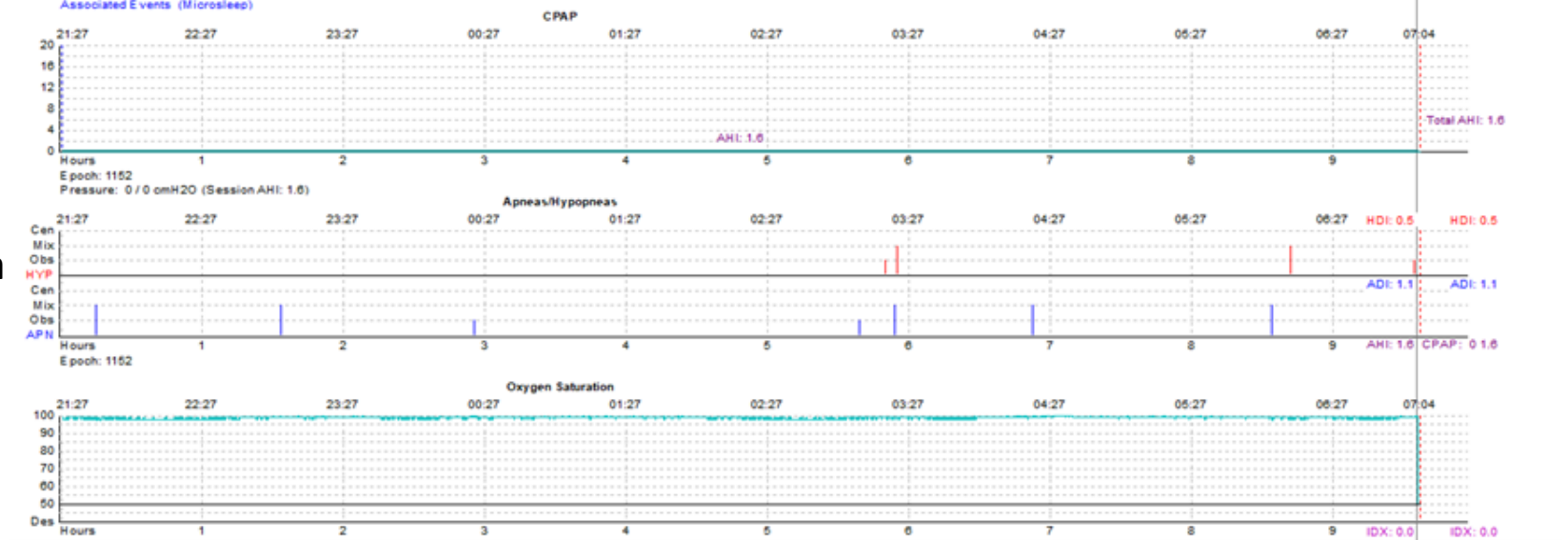
Sleep stage



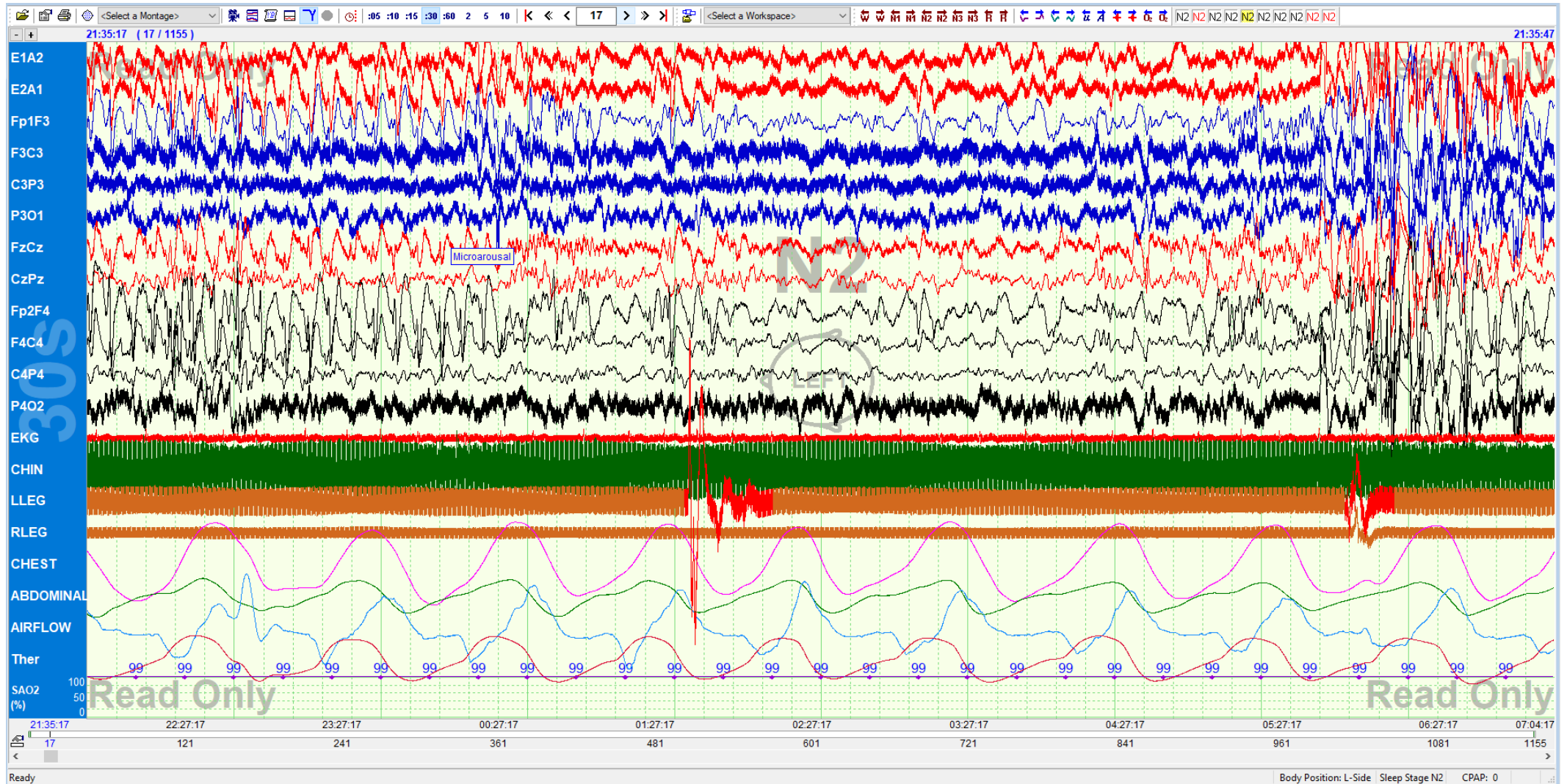
Arousal



Apnea-hypopnea

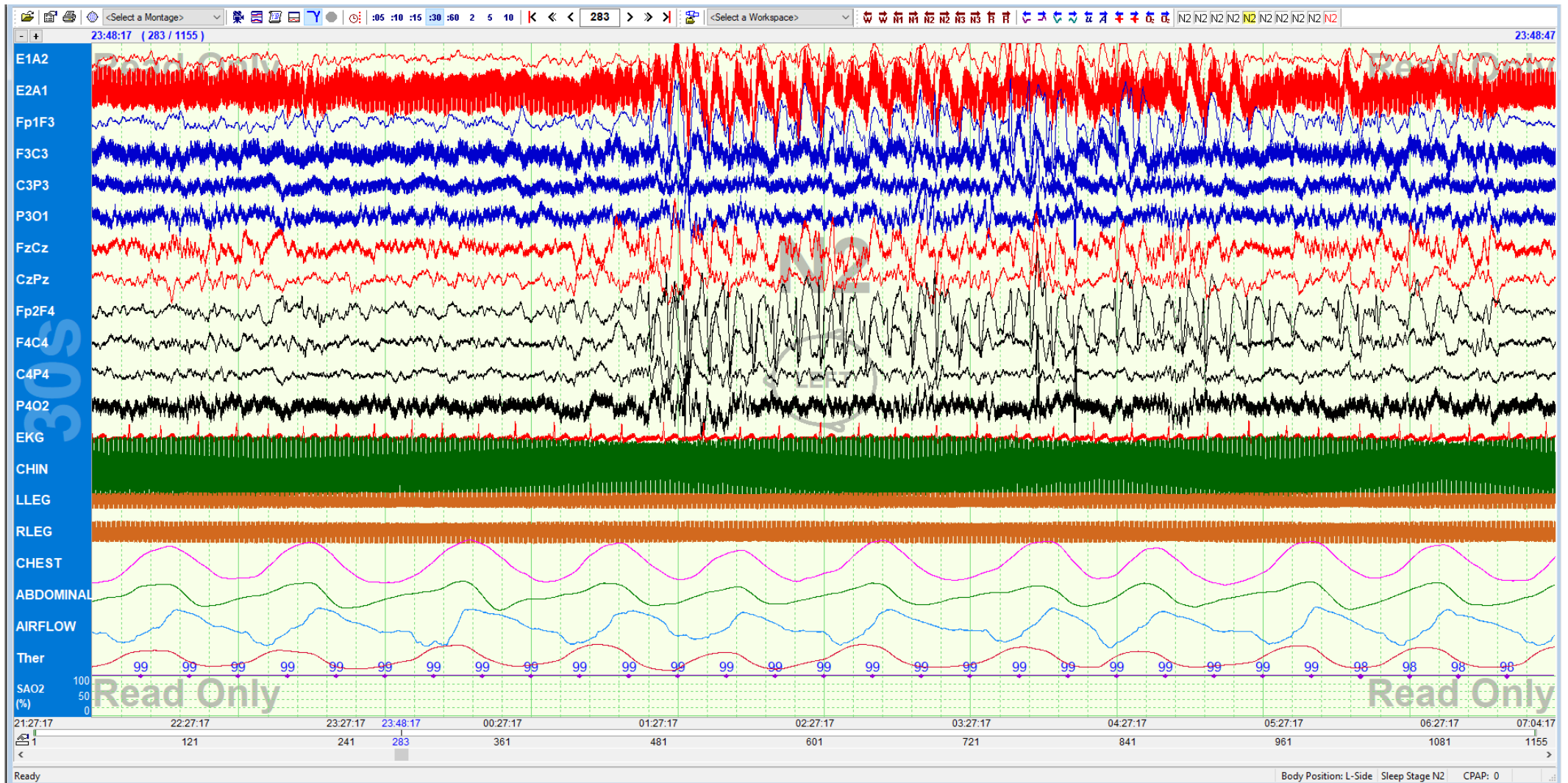


# A 10-year-old boy with sleep fragmentation



30 seconds/epoch

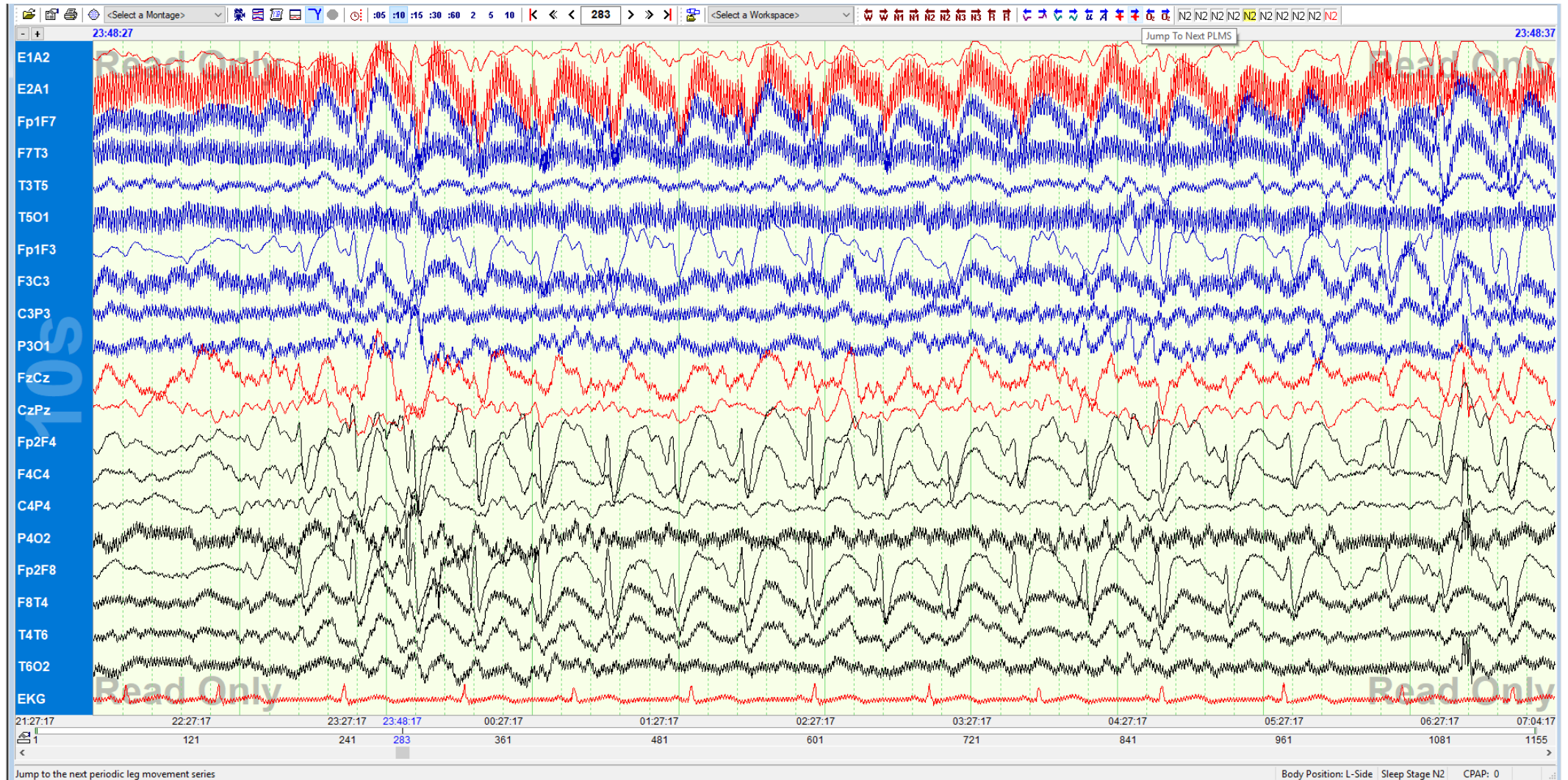
# A 10-year-old boy with sleep fragmentation



30 seconds/epoch

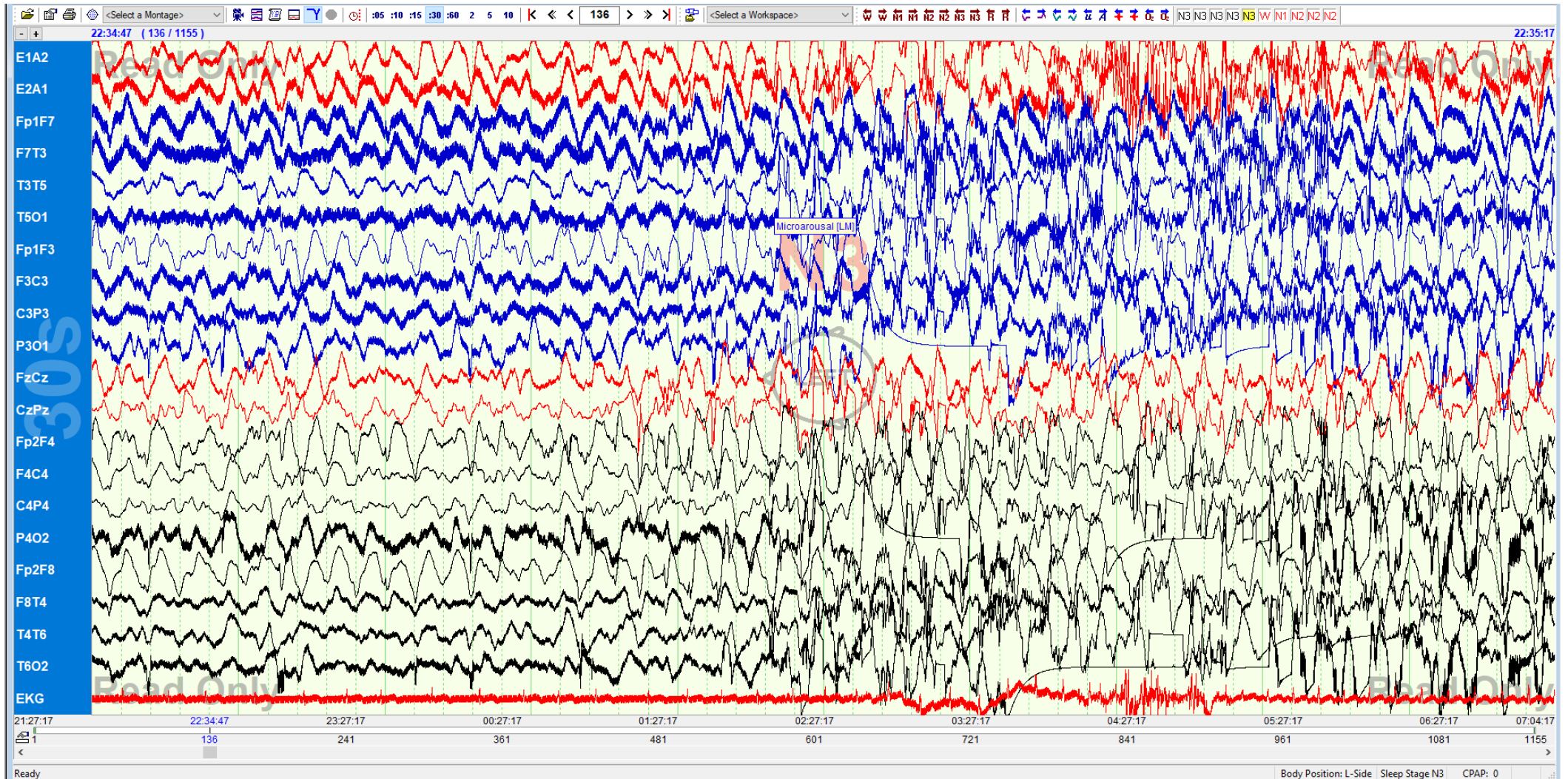


# A 10-year-old boy with sleep fragmentation



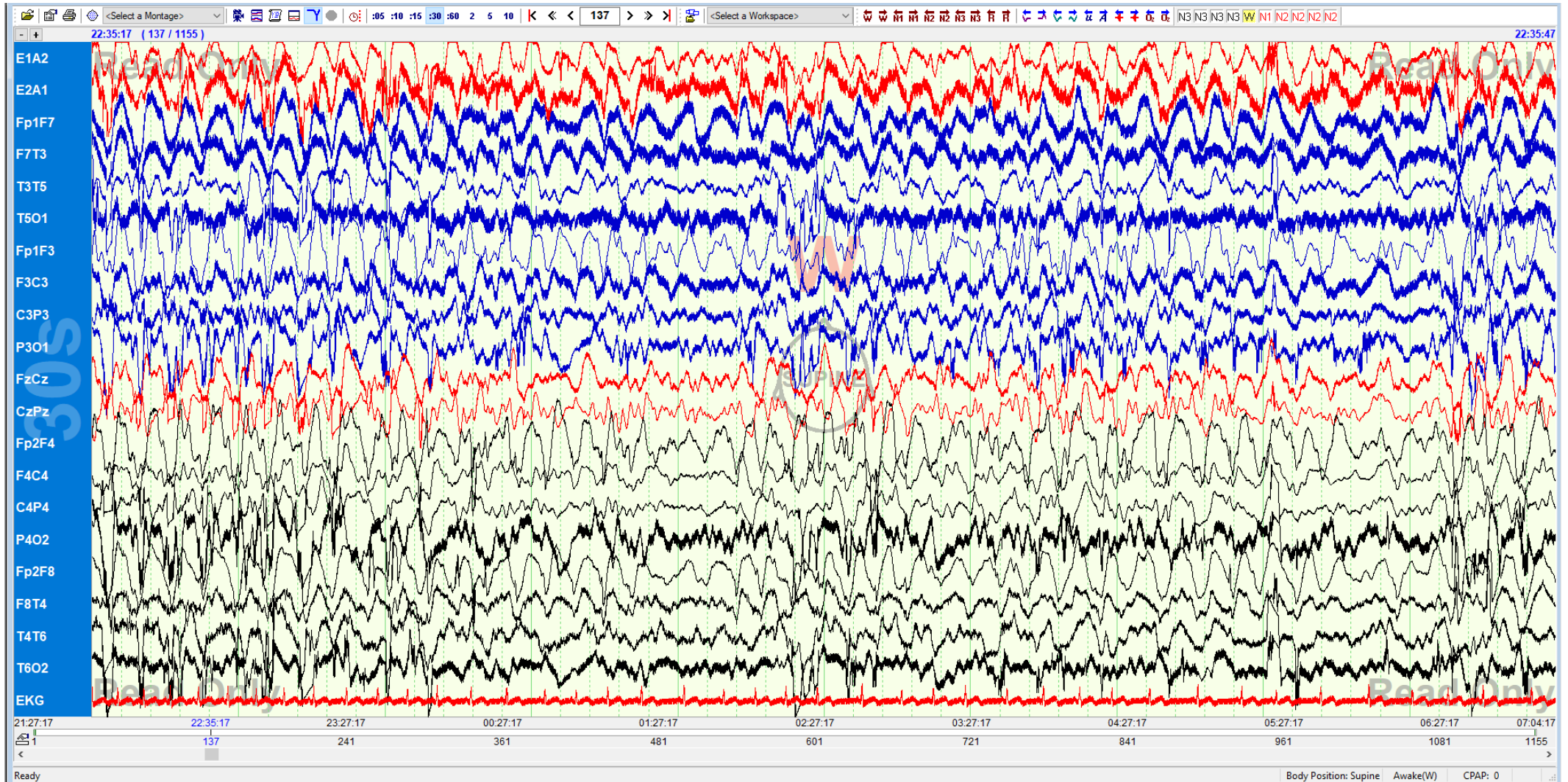
10 seconds/epoch

# Habitual event: N3



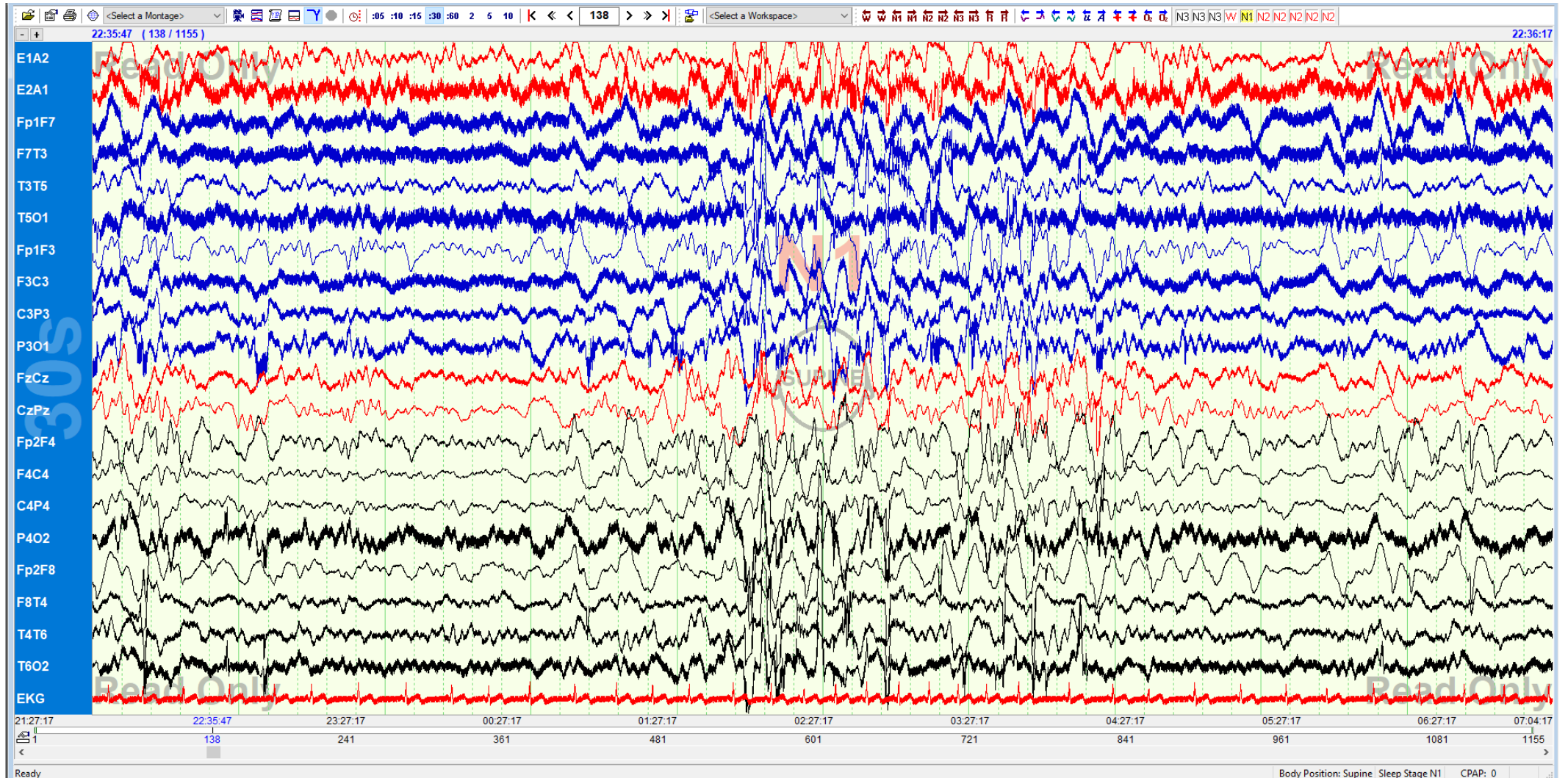
30 seconds/epoch

# Habitual event: W



30 seconds/epoch

# Habitual event: N1



30 seconds/epoch

# A 10-year-old boy with sleep fragmentation

## **Problem List**

- 1. Sleep fragmentation with morning sleep inertia**
- 2. Past history of epilepsy**
- 3. Family history of epilepsy and febrile seizure**
- 4. Multiple food allergy**
- 5. Failure to gain weight**

**Frontal lobe epilepsy**  
**Sleep Related Hypermotor Epilepsy**

# Sleep Related Hypermotor Epilepsy

**Lunliya Thampratankul**

**Apisit Boongird**

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**Mahidol University**

1977: Pedley & Guilleminault  
Screaming, vocalization, complex  
automatism, ambulation  
Ceased with AEDs (CBZ, PHT)

Complex motor attacks  
Twisting of the trunk and violent  
hyperkinetic movements  
Tonic/dystonic posturing

**Paroxysmal arousal**

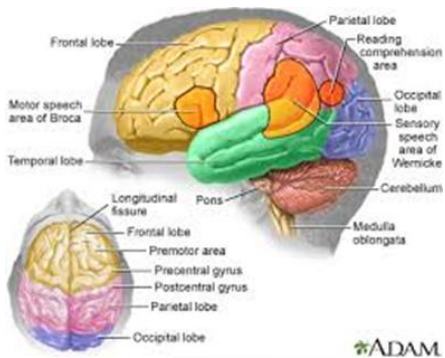
**Nocturnal wandering**



**Hypnogenic paroxysmal dystonia**



**Nocturnal paroxysmal dystonia (NPD)**



**Nocturnal frontal lobe epilepsy (NFLE)**



**Sleep related hypermotor epilepsy (SHE)**



# Diagnosis of SHE

- 1. Possible: witnessed based on the description of the core clinical features**
- 2. Clinical: video documented**
- 3. Confirmed: video-EEG documented**

## NREM parasomnia

- **Disorders of arousal**
- Tend to disappear throughout life
- Triggering factors
- First third of the night
- Constant amnesia

## REM Parasomnia

- **RBD**
- Late onset
- No Fm Hx
- Often in neurodegen dis
- **Nightmare**
- Last third of the night
- Mild autonomic activation
- Memory of dream mentation

## SHE

- Any age
- Any time during the night
- Several per night
- Brief duration
- Stereotype

**Diagnostic delay of  
12.8 ± 10.1 y in  
53.7% of SHE**

# Sleep Quality in Patients with SHE

	NFLE 33	Control 27	
ESS			
Mean score (S.D.)	5.6 (3.2)	5.7 (3.0)	0.57*
BQS			
Mean score (S.D.)	3.6 (2.6)	2.8 (2.2)	0.30*
Tiredness at least almost daily	18.2%	3.7%	0.12
Resistible sleepiness at least almost daily	21.2%	3.7%	0.06
Excessive daytime sleepiness#	12.1%	7.4%	0.68
Tiredness after awakening at least almost all mornings	36.4%	11.1%	0.04
Falling asleep in more than 30 minutes	10.3%	4.3%	0.62
Difficulties in falling asleep at least almost all nights	9.1%	0	0.25
Spontaneous midsleep awakenings at least almost all nights	50.0%	22.2%	0.03
Spontaneous early morning awakenings at least almost all nights	12.1%	0	0.12
Snoring	51.5%	51.9%	1.00
OSAS risk	12.1%	3.7%	0.37

ESS: Epworth sleepiness scale

BQS: Bologna questionnaire on sleepiness-related symptoms Vignatelli L, et al. Epilepsia. 2006.

# Sleep Quality in SHE vs Healthy Controls

TABLE 2. Daytime sleepiness-related symptoms and subjective sleep quality in patients with NFLE and controls

N	Patients with NFLE 33	Controls 27	p§
ESS			
Mean score (S.D.)	5.6 (3.2)	5.7 (3.0)	0.57*
Median score (range)	5 (1–14)	6 (0–12)	
BQS			
Mean score (S.D.)	3.6 (2.6)	2.8 (2.2)	0.30*
Median score (range)	3 (0–10)	3 (0–9)	
Tiredness at least almost daily	18.2%	3.7%	0.12
Resistible sleepiness at least almost daily	21.2%	3.7%	0.06
Excessive daytime sleepiness#	12.1%	7.4%	0.68
Tiredness after awakening at least almost all mornings	36.4%	11.1%	0.04
Falling asleep in more than 30 minutes	10.3%	4.3%	0.62
Difficulties in falling asleep at least almost all nights	9.1%	0	0.25
Spontaneous midsleep awakenings at least almost all nights	50.0%	22.2%	0.03
Spontaneous early morning awakenings at least almost all nights	12.1%	0	0.12
Snoring	51.5%	51.9%	1.00
OSAS risk	12.1%	3.7%	0.37

ESS: Epworth sleepiness scale

BQS: Bologna questionnaire on sleepiness-related symptoms

# Sleep Quality in SHE with different seizure frequency

TABLE 3. Subjective daytime sleepiness and sleep quality in patients with NFLE by perceived frequency of seizures

N	Seizures at least 2–3 nights per week 18	Seizures fewer than 2–3 nights per week 8	Seizure-free 5
ESS			
Mean score (S.D.)	6.0 (3.2)	5.3 (4.1)	5.0 (1.9)
Median score (range)	5 (2–14)	3.5 (1–13)	4 (3–7)
BQS			
Mean score (S.D.)	4.1 (2.8)	3.3 (2.7)	2.4 (1.9)
Median score (range)	4 (0–10)	2 (1–8)	3 (0–5)
Tiredness at least almost daily	20.0%	12.5%	20.0%
Resistible sleepiness at least almost daily	30.0%	12.5%	0
Excessive daytime sleepiness#	15.0%	12.5%	0
Tiredness after awakening at least almost all mornings	40.0%	50.0%	0
Falling asleep in more than 30 minutes	5.9%	25.0%	0
Difficulties in falling asleep at least almost all nights	10.0%	12.5%	0
Spontaneous midsleep awakenings at least almost all nights	57.9%	37.5%	40.0%
Spontaneous early morning awakenings at least almost all nights	20.0%	0	0
Snoring	40.0%	75.0%	60.0%
OSAS risk	10.0%	12.5%	20.0%

**Clinical Feature**
**Score**
**Age at onset**

At what age did the patient have their first clinical event?

&lt;55 y

≥55 y

**Duration**

What is the duration of a typical event?

&lt;2 min

2-10 min

&gt;10 min

**Clustering**

What is the typical number of events to occur in a single night?

1 or 2

3-5

&gt;5

**Timing**

At what time of night do the events most commonly occur?

Within 30 min of sleep onset

Other times (including if no clear pattern identified)

**Symptoms**

Are the events associated with a definite aura?

Yes

No

Does the patient ever wander outside the bedroom during the events?

Yes

No (or certain)

Does the patient perform complex, directed behaviors (eg, picking up objects, dressing) during events?

Yes

No (or uncertain)

Is there a clear history of prominent dystonic posturing, tonic limb extension, or cramping during events?

Yes

No (or uncertain)

**Stereotypy**

Are the events highly stereotyped or variable in nature?

Highly stereotyped

Some variability/uncertain

Highly variable

**Recall**

Does the patient recall the events?

Yes, lucid recall

No or vague recollection only

**Vocalization**

Does the patient speak during the events and, if so, is there subsequent recollection of this speech?

No

Yes, sounds only or single words

Yes, coherent speech with incomplete or no recall

Yes, coherent speech with recall

**Total score**
**Frontal lobe  
epilepsy and  
parasomnia  
(FLEP) scale**

0

-1

+1

0

-2

0

+1

+2

+1

0

+2

0

-2

0

-2

0

+1

0

+1

0

-1

+1

0

0

0

-2

+2

# Sleep Related Hypermotor Epilpesy (SHE)

- Different intensity and durations ranging from paroxysmal arousals to nocturnal wandering that could occur in a single patient, during a single night
- Brief (< 2min)
- Abrupt onset and offset
- > 90% sleep (NREM) related
- Several episodes per night
- Level of awareness; not a crucial clinical signs

# Sleep Related Hypermotor Epilepsy (SHE)

- Hypermotor seizures occurring predominantly in clusters during **non-REM sleep**
- Asymmetric tonic/dystonic posturing and/or complex hyperkinetic seizures
- No differences in clinical features: genetic vs structural cause
  - Genetic: ADSHE; autosomal dominant nocturnal frontal lobe epilepsy
- Estimated minimum prevalence of 1.8/100,000 individuals
- 10% of drug-resistant surgical cases.



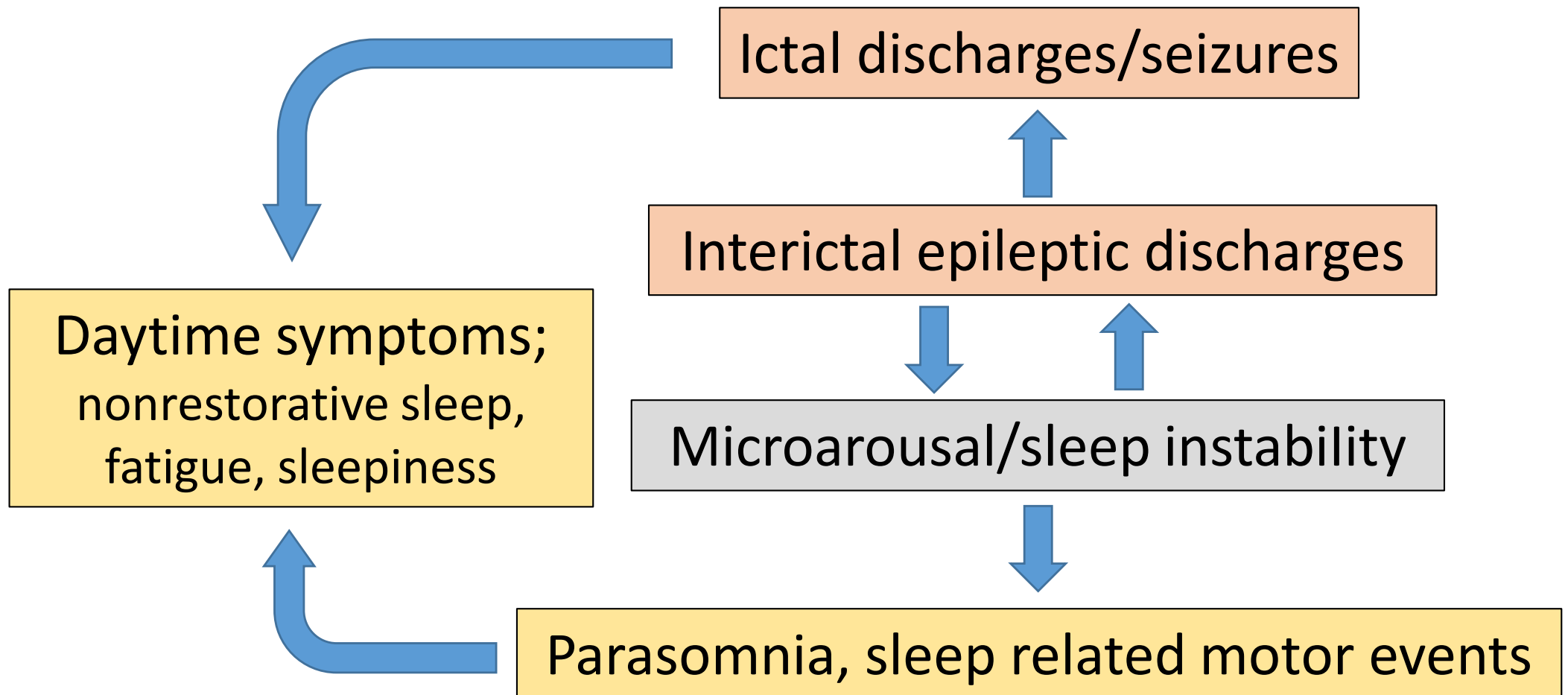
# Genetic background of SHE

- Autosomal-dominant ADNFLE/ADSHE
- **CHRNA4**; alpha-4 subunit of the neuronal nicotinic acetyl choline receptor (nAChR)
- **CHRNA2, CHRNB4**
- Corticotropin-releasing hormone gene promoter
- **KCNT1**: a sodium-gated potassium channel
  - Severe phenotype, frequent seizures, psychiatric symptoms, intellectual disabilities
- **DEPDC5, NPRL2 and 3**
- **CABP4** (neuronal Ca<sup>2+</sup> binding protein4)
- *Lack of data for genotype-phenotype correlation*

# Mechanism of SHE

- Cholinergic hyperactivation
- Enhanced GABAergic function
- Cortical and subcortical networks involved in the mechanism of arousal → epileptogenesis of ADSHE
- Defects in CLOCK expression → preferential occurrences of seizures during sleep
  - Circadian Locomotor Output Cycles Kaput
  - a transcription factor that regulated the circadian rhythm and the mTOR pathway

# Vicious loop of sleep-related epileptic discharges



# Impact of SHE: Cognitive function

- Neuropsychological function
  - deficits in memory, executive functions and visuo-spatial abilities in almost half of SHE patients.
  - Intellectual disabilities and psychiatric disorders
  - Boderline IQ 12%, psychiatric disorder 24%<sup>a</sup>
- Sleep deprivation
  - Vigilance, memory retention, sensory perception, executive function
- Sleep discontinuity, non-restorative sleep
  - Excessive sleep inertia in the morning, daytime tiredness

**Direct negative effect of interictal and ictal epileptic activity, sleep related encoding memory process**

# Management of SHE

- Injury prevention
- Bed and side pillow
- AEDs: carbamazepine, topiramate, acetazolamide
- Nicotine transdermal patch
- These may be not helpful for sleep instability
- Rx associated sleep disorder: OSA, parasomnia
- Epilepsy surgery: for seizure & sleep alteration
- SUDEP: autonomic alteration from insular involvement

# A 17-year-old male

**Chief Complaint:** Unusual behavior during sleep for 3 months

## **Present Illness:**

Known case hypoplastic left heart with pulmonary atresia s/p Fontan operation

**17 years PTA:** He had history of fever with seizure at age of one month. He was diagnosed with meningitis and was put on phenobarbital.

# Present Illness (cont.)

His seizures were very well controlled and the medication was discontinued at aged of 3 years.

**10 years PTA** (after 6+ years of no medication): He had recurrent seizures, characterized by clonic movement of left side of face and left arm. Sodium valproate was given.

**3 years PTA:** He has had no seizure for 7 years. The EEG was normal. VPA was slowly tapered off and eventually discontinued.

# Present Illness (cont.)

**6 months PTA:** He had loud snoring and occasional grasping without any witnessed apnea. His weight increased 14 kg in 2 years.

**3 months PTA:** He has had nocturnal spells which were not similar to his previous seizures.

“restlessness, body turning lasting 10-30 seconds”

They occurred 1-3 times every night. After the episode, he might wake up or return back to his sleep without any recall.



# Sleep History

- Sleep time: 8 PM
- Wake up time: 5.30-6 AM
- Denies daytime nap, daytime somnolence
- Denies morning headache
- Bedroom: sleep in the same room with parents

# Past History

- Congenital heart disease s/p surgery at age of 2 and 7 mo, currently on warfarin and captopril
- Intellectual disability, IQ = 76
- Otherwise are unremarkable

# Family History

- (-) epilepsy, parasomnia
- Unremarkable

# Physical Examination

- Alert, well cooperative, follow simple command appropriately, **obese**
- BT 37 °C, BP 128/64 mmHg, HR 86/min, RR 20/min
- BW 66 Kg, Height 156 cm, **BMI 27.1 kg/m<sup>2</sup>**
- HEENT: Not pale, anicteric, **short neck**,  
acantosis nigricans, tonsils 1+ both sides,  
**Mallampati class IV**
- No focal neurological deficit



# Problem List

Hypoplastic left heart syndrome with PA s/p surgery

Post-meningitis with recurrent epilepsy, off AED

Obesity and snoring R/O OSA

Nocturnal spells

# Diagnosis of Nocturnal Spells

- Brief spells, stereotyped
- Variable time across the night
- Snoring and obesity R/O OSA

## Differential diagnosis

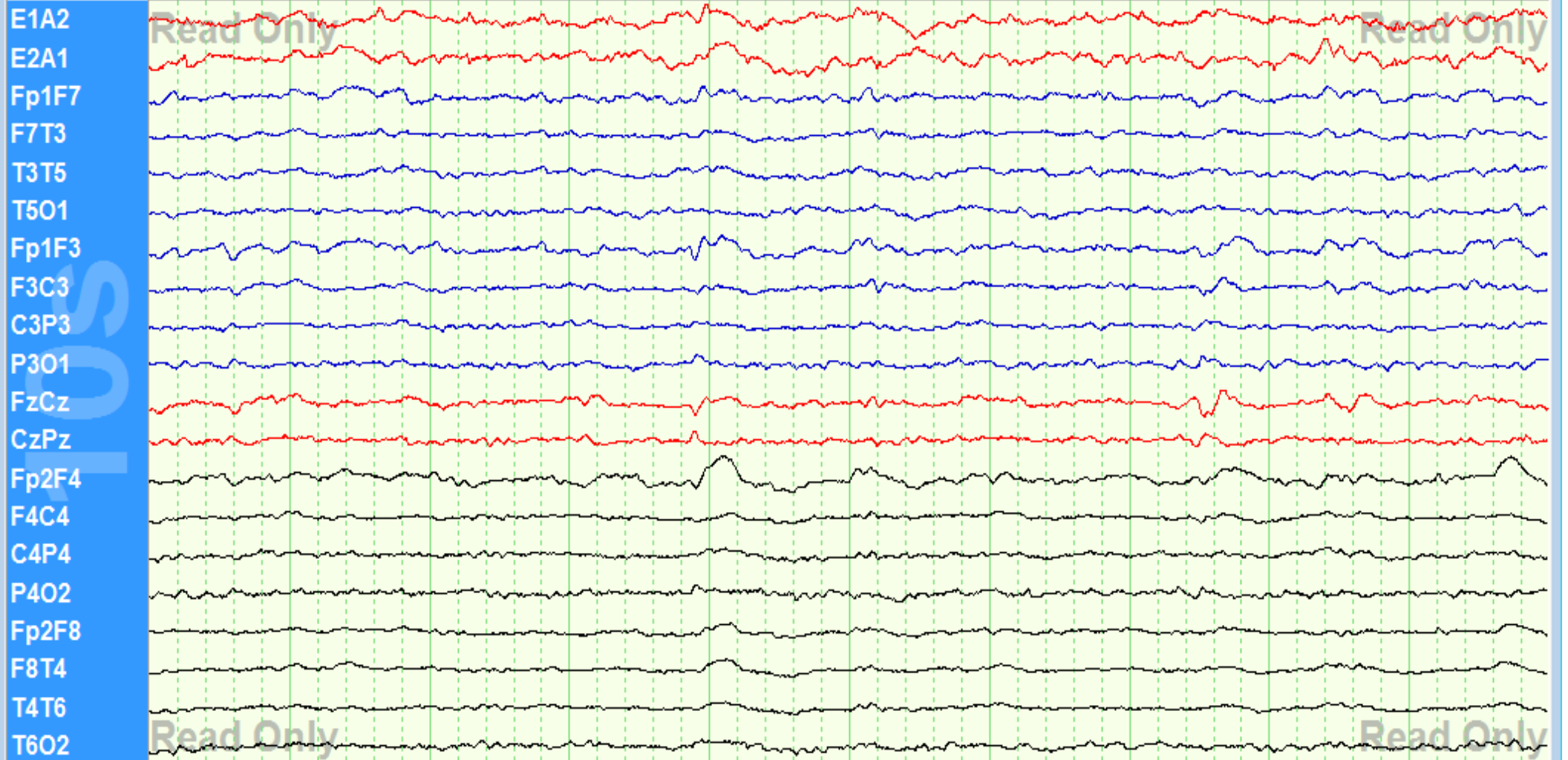
Secondary parasomnia  
(confusional arousal from OSA )  
Nocturnal seizure

# What would you like to do?

Overnight polysomnography  
with full lead EEG

21:07:00

21:07:10



Read Only

Read Only

Read Only

Read Only

20:22:40 21:06:40 22:22:40 23:22:40 00:22:40 01:22:40 02:22:40 03:22:40 04:22:40 05:22:40 06:22:40 07:09:10

1 89 241 361 481 601 721 841 961 1081 1201 1294

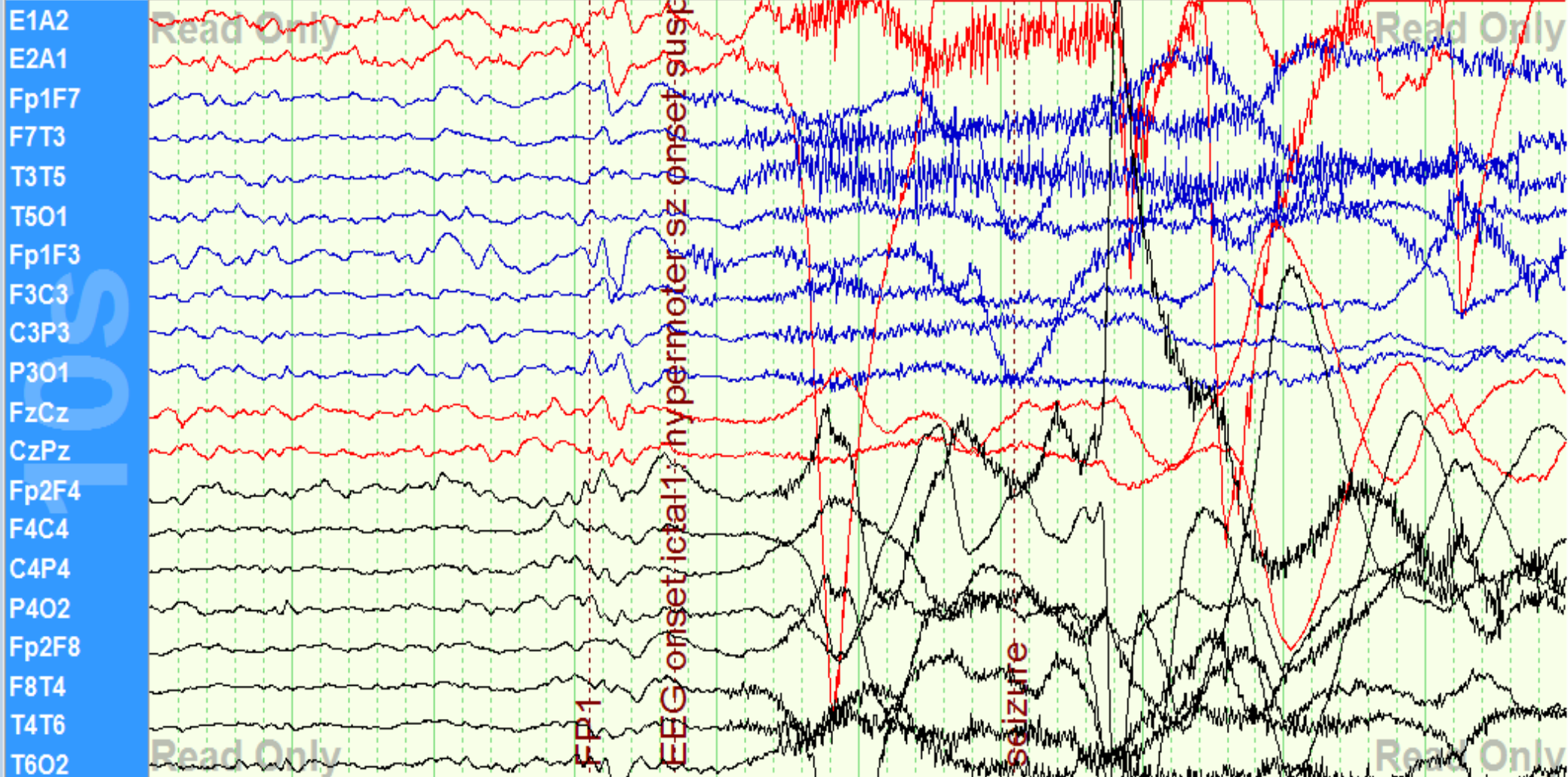
Ready

Body Position: Sitting

CPAP: 0

21:07:10

21:07:20



20:22:40 21:07:10 22:22:40 23:22:40 00:22:40 01:22:40 02:22:40 03:22:40 04:22:40 05:22:40 06:22:40 07:09:10

1 90 241 361 481 601 721 841 961 1081 1201 1294

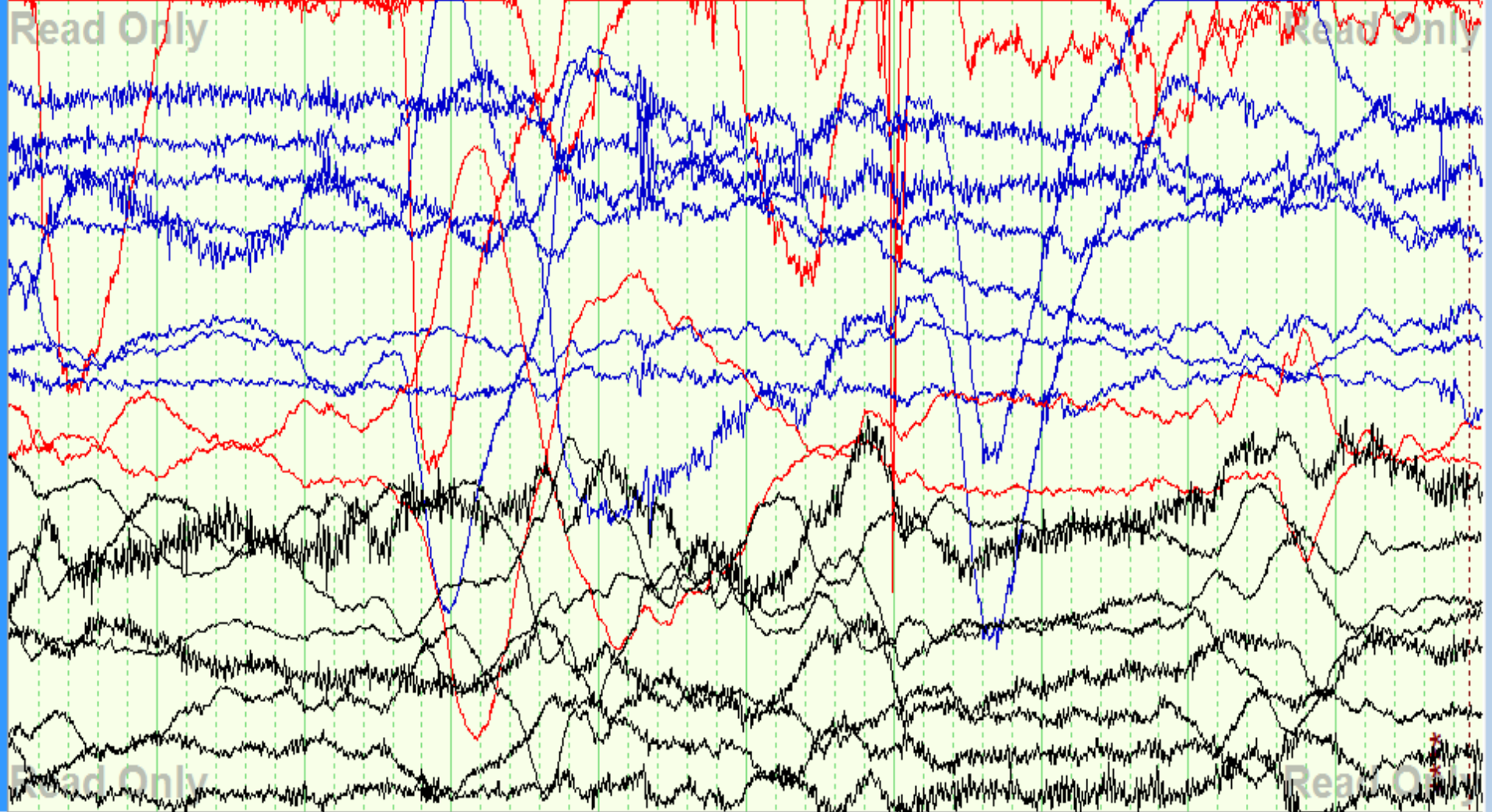




21:07:20

21:07:30

- E1A2
- E2A1
- Fp1F7
- F7T3
- T3T5
- T5O1
- Fp1F3
- F3C3
- C3P3
- P3O1
- FzCz
- CzPz
- Fp2F4
- F4C4
- C4P4
- P4O2
- Fp2F8
- F8T4
- T4T6
- T6O2



20:22:40 21:07:10 22:22:40 23:22:40 00:22:40 01:22:40 02:22:40 03:22:40 04:22:40 05:22:40 06:22:40 07:09:10

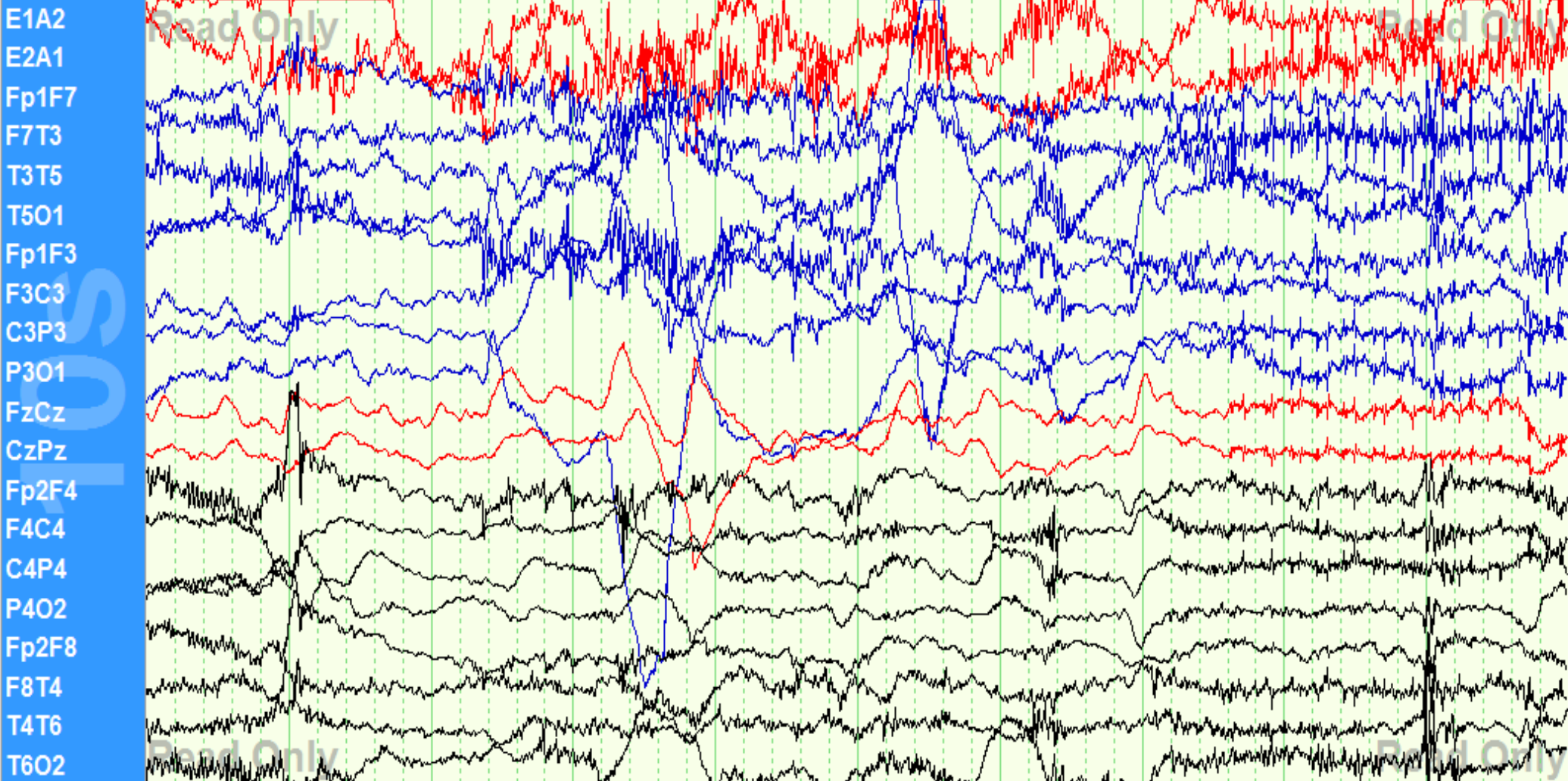
1 90 241 361 481 601 721 841 961 1081 1201 1294

Ready

Body Position: Sitting

CPAP: 0

21:07:30 21:07:40



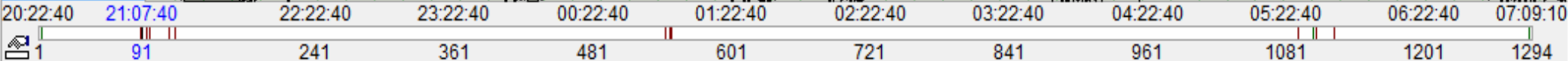
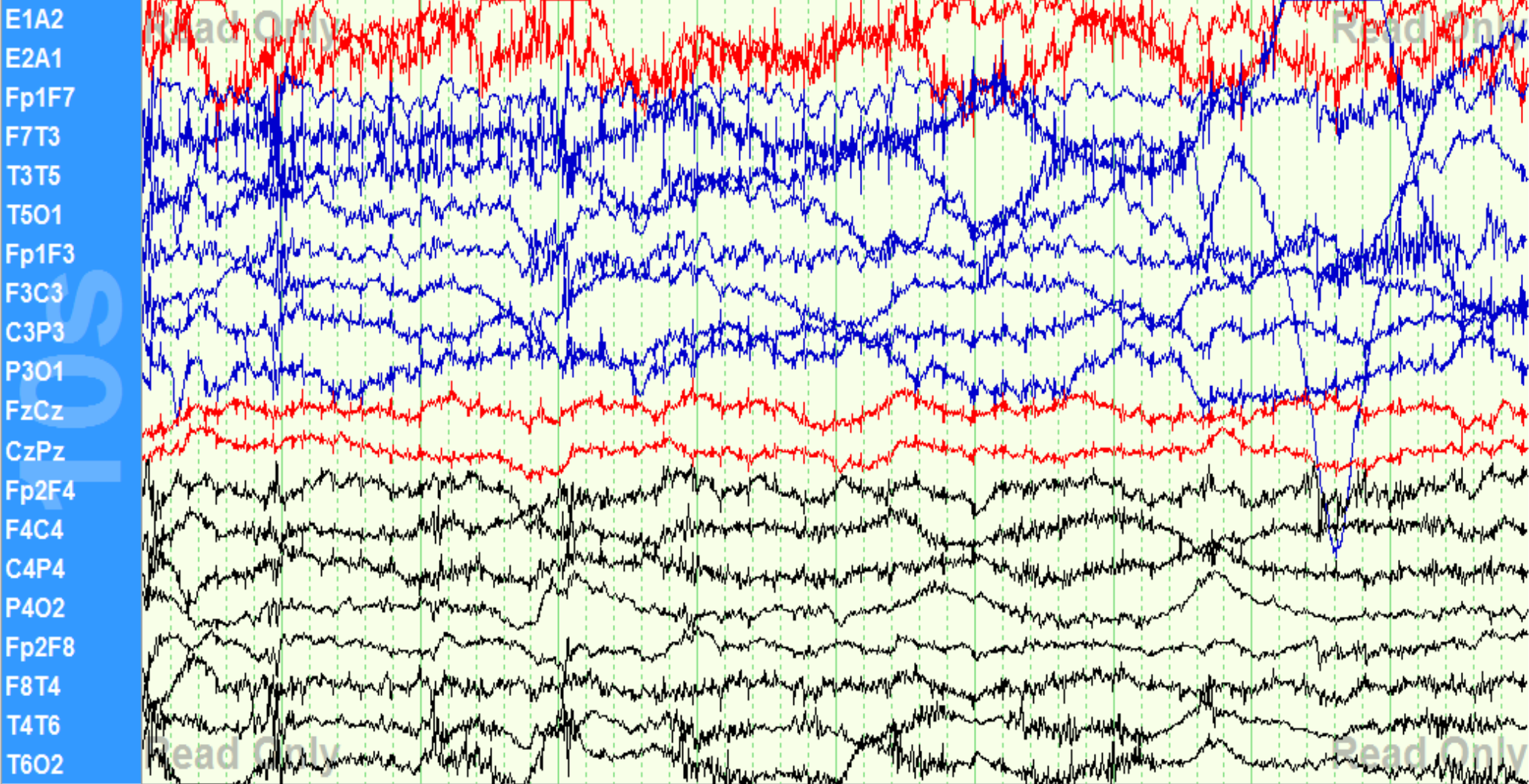
20:22:40 21:07:10 22:22:40 23:22:40 00:22:40 01:22:40 02:22:40 03:22:40 04:22:40 05:22:40 06:22:40 07:09:10

1 90 241 361 481 601 721 841 961 1081 1201 1294

- +

21:07:40

21:07:50



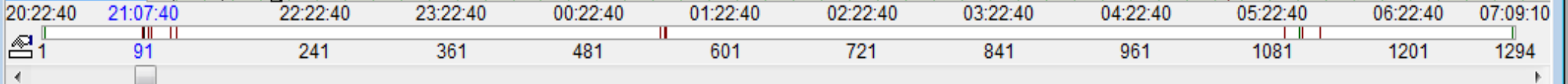
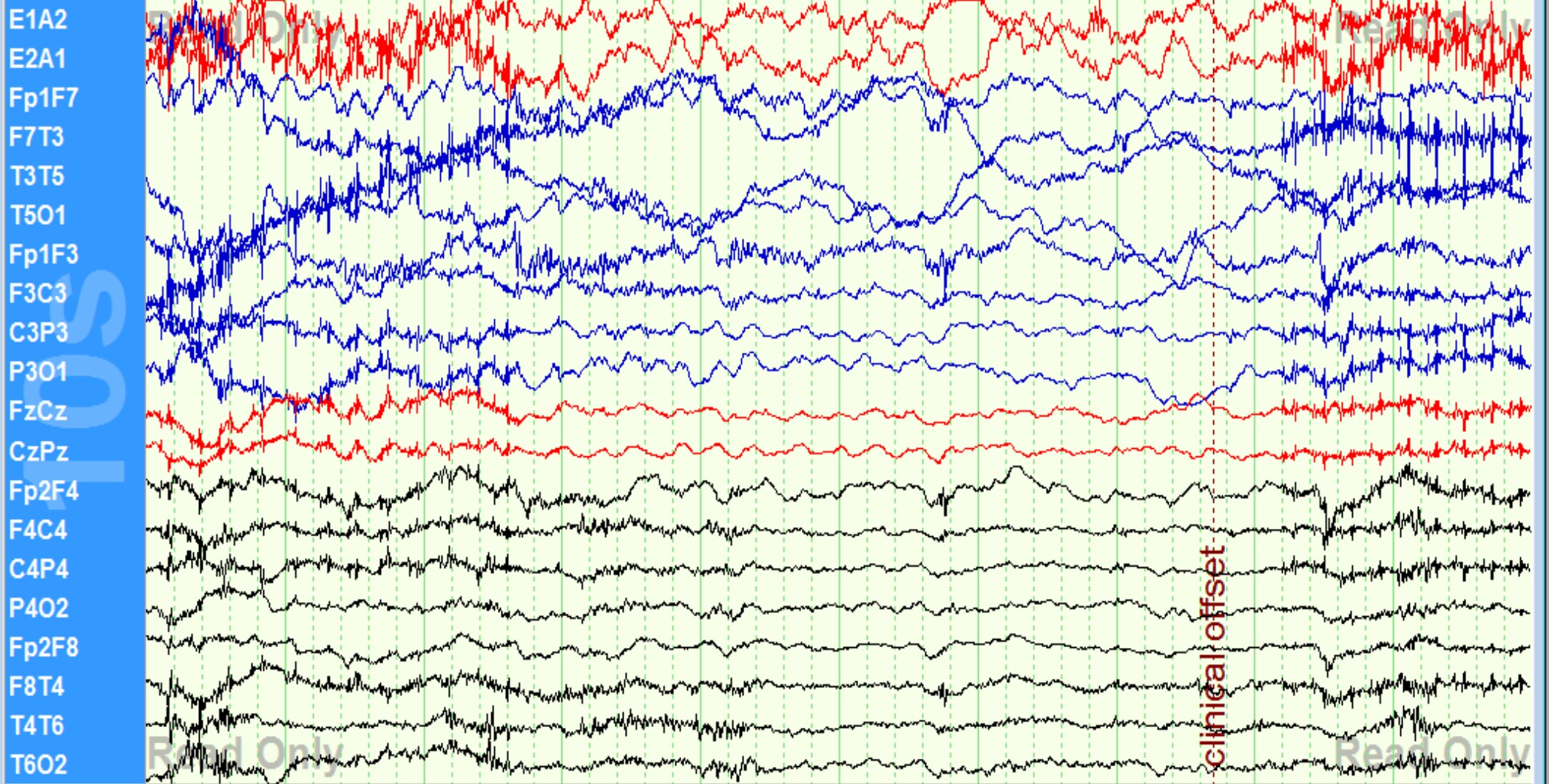
Ready

Body Position: Sitting

CPAP: 0

21:07:50

21:08:00



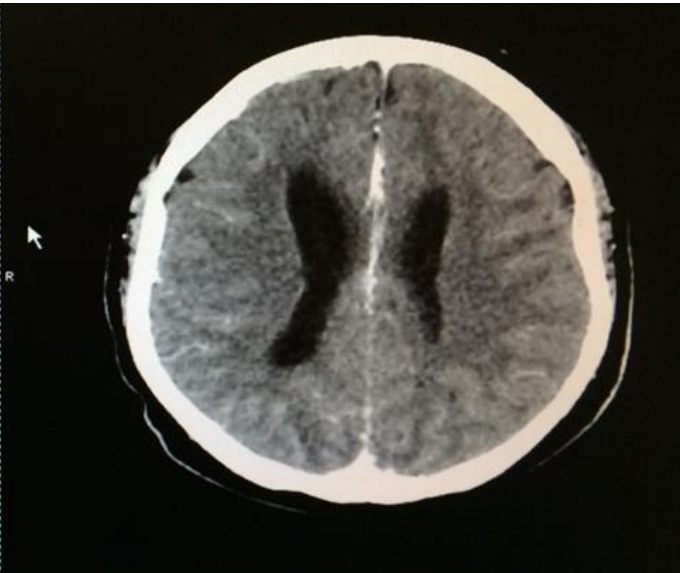
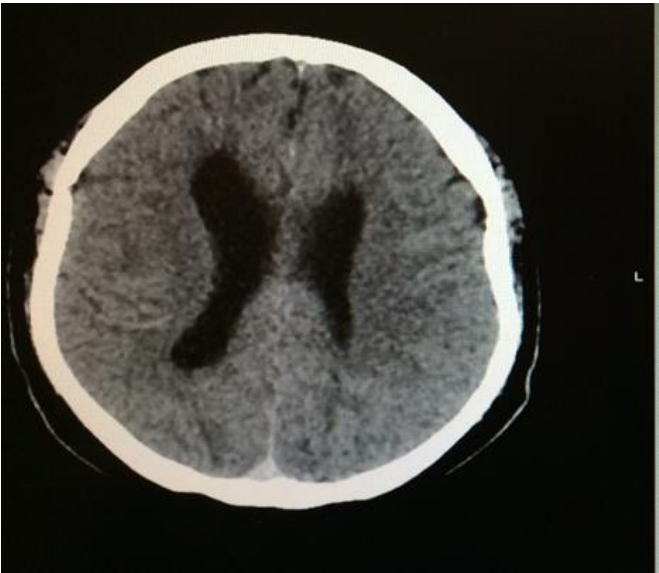
# Overnight Video-EEG/PSG

## EEG:

- Interictal: few spikes over left and right frontal regions (Fp1, Fp2).
- Ictal: 3 habitual spells captured, consistent with frontal lobe seizure

## PSG:

- Cannot performed respiratory monitor due to non-cooperation



# Final Diagnosis: Nocturnal frontal lobe epilepsy

## **Management**

- Control seizure with topiramate
- Diet control and weight reduction