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คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี

Management of acute seizure and status epilepticus

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Outlines

- Seizure cluster/ Acute repetitive seizures

- Status epilepticus

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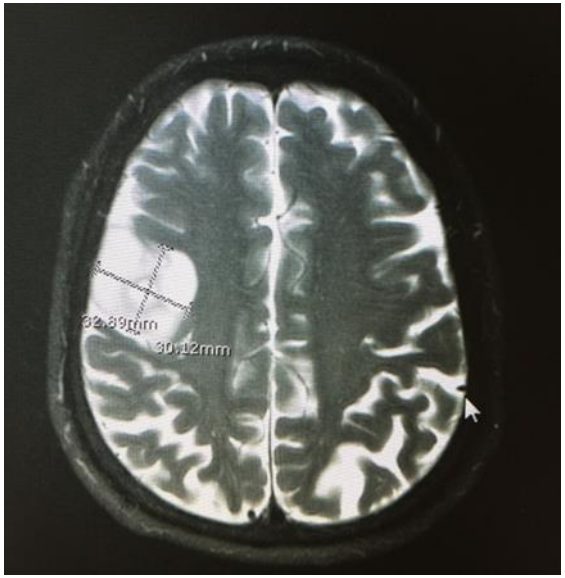
Seizure cluster

- A 45-yo male with past medical history of brain tumor s/p partial tumor removal presented to the outpatient clinic with chief complaint of frequent and repetitive focal seizures with preserved awareness for a day. Each seizure was characterized by left face clonic with preserved awareness, lasting for two hours. He had experienced seizure clusters, 4 times a day. He had one GTCs.



Definition of epileptic seizure by the International League Against Epilepsy (ILAE)

- An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Epilepsia, 46(4):470–472, 2005

Acute Repetitive Seizures (ARS)

- The practical definition of acute repetitive seizures has not been established.

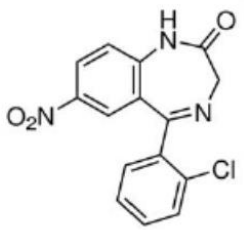
- Acute repetitive seizures is neurologic emergency and a common clinical phenomenon describing an increase in seizures occurring over a specific period of time (ranging from several minutes up to 24 hours).

- Acute repetitive seizures may include any type of seizure and may vary in severity, but by definition there is complete recovery in between seizures.

Curr Opin Neurol 2015;28(2):143Y150.

Oral tablet benzodiazepine

- Lorazepam
- Clonazepam
- Clobazam

Clonazepam 	Rivotril tab 0.5 mg	
	Rivotril tab 2 mg	
	Prenarpil tab 0.5 mg	
	Prenarpil tab 1 mg	
	Prenarpil tab 2 mg	
Clobazam 	Frisium 5 mg	

Outpatient acute benzodiazepine therapy

- Rectal diazepam is the only currently marketed treatment available for use by nonmedical caregivers in the USA, and buccal midazolam is approved in the European Union.

Outpatient acute benzodiazepine therapy

Medications	Formulation	Notes
Diazepam	oral tablet	
	rectal gel **(FDA approved)**	N Engl J Med 1998; 338:1869–1875. and Neurology 1998; 51:1274–1282.
	intramuscular	
Midazolam	buccal	
	intranasal	
	intramuscular	The Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART) in pre-hospital status epilepticus
Lorazepam	oral tablet	
	intranasal	
	sublingual	
Progesterone	cyclic natural progesterone	catamenial epilepsy Neurology 2014; 83:345–348.

CNS Drugs (2015) 29:55–70

Management of acute repetitive seizures (ARS)

- Diagnosis of seizure clusters
- Identify the etiology of ARS
- Benzodiazepines remain the mainstay of therapy in ARS. The treatment of ARS includes the usage of extra doses of usual antiepileptic medications and oral benzodiazepines (diazepam or lorazepam) for mild ARS.
- Educating the patient and families about seizure first aid and the use of rescued anti-seizure medications.

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Status epilepticus (SE)

Status epilepticus

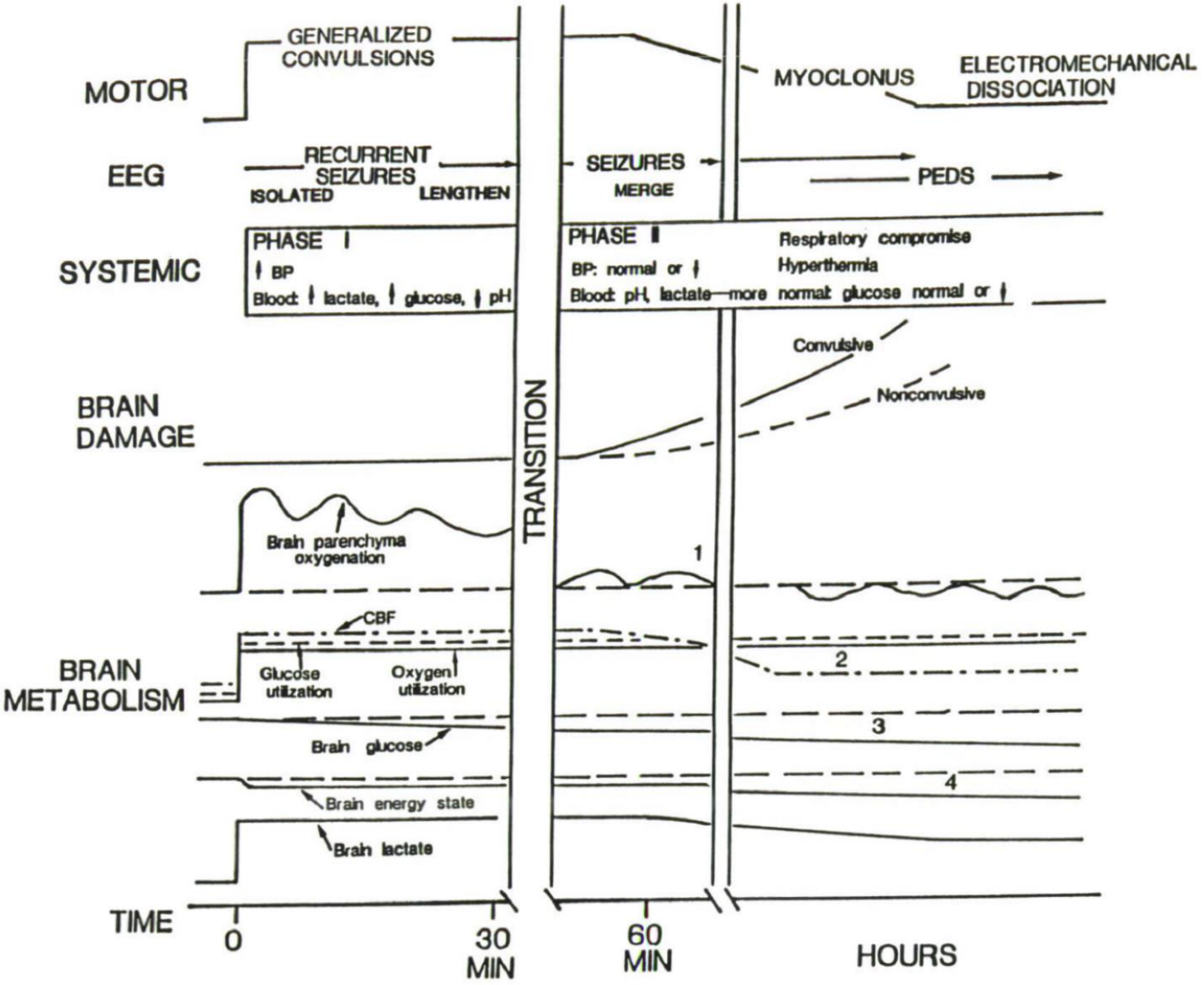
- Status epilepticus(SE) is a neurologic emergency with high morbidity and mortality. It represents the persistence of abnormal excitation and the ineffective recruitment of inhibition.

- The management of SE requires immediate action and diligence to avoid pharmacoresistance and brain injury.

Old definition of SE

- A definition of more than 30 minutes of continuous seizure activity or two or more sequential seizures without full recovery of consciousness between was widely adopted, citing neuronal damage in animal models beyond this timeframe.

Epilepsy Foundation, 1993



Lothman 1990

Phase 1: compensation

Cerebral changes	Systemic and metabolic changes	Autonomic and cardiovascular changes
increased cerebral blood flow	hyperglycemia	increased blood pressure
increased cerebral metabolism	lactic acidosis	increased cardiac output
increased lactate concentration		massive catecholamine release
increased glucose concentration		cardiac dysthymia
		urine incontinence

J Neurol Neurosurg Psychiatry 2001;70(suppl II):ii22–ii27

Phase 2: decompensation

Cerebral changes	Systemic and metabolic changes	Autonomic and cardiovascular changes
failure of cerebral autoregulation	hypoglycemia	hypoxia
hypoxia	hypokalemia/ hyperkalemia	falling blood pressure
hypoglycemia	metabolic and respiratory acidosis	falling cardiac output
increased intracranial pressure and cerebral oedema	hepatic and renal dysfunction	cardiac failure
	consumptive coagulopathy	respiratory failure
	DIC	hyperpyrexia
	rhabdomyolysis, myoglobinuria	

J Neurol Neurosurg Psychiatry 2001;70(suppl II):ii22–ii27

A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus

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Epilepsia, 56(10):1515–1523, 2015
doi: 10.1111/epi.13121

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Summary

The Commission on Classification and Terminology and the Commission on Epidemiology of the International League Against Epilepsy (ILAE) have charged a Task Force to revise concepts, definition, and classification of status epilepticus (SE). The proposed new definition of SE is as follows: *Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t_1). It is a condition, which can have long-term consequences (after time point t_2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.* This definition is conceptual, with two operational dimensions: the first is the length of the seizure and the time point (t_1) beyond which the seizure should be regarded as "continuous seizure activity." The second time point (t_2) is the time of ongoing seizure activity after which there is a risk of long-term consequences. In the case of convulsive (tonic–clonic) SE, both time points (t_1 at 5 min and t_2 at 30 min) are based on animal experiments and clinical research. This evidence is incomplete, and there is furthermore considerable variation, so these time points should be considered as the best estimates currently available. Data are not yet available for other forms of SE, but as knowledge and understanding increase, time points can be defined for specific forms of SE based on scientific evidence and incorporated into the definition, without changing the underlying concepts. A *new diagnostic classification system* of SE is proposed, which will provide a framework for clinical diagnosis, investigation, and therapeutic approaches for each patient. There are four axes: (1) semiology; (2) etiology; (3) electroencephalography (EEG) correlates; and (4) age. Axis 1 (semiology) lists different forms of SE divided into those with prominent motor systems, those without prominent motor systems, and currently indeterminate conditions (such as acute confusional states with epileptiform EEG patterns). Axis 2 (etiology) is divided into subcategories of known and unknown causes. Axis 3 (EEG correlates) adopts the latest recommendations by consensus panels to use the following descriptors for the EEG: name of pattern, morphology, location, time-related features, modulation, and effect of intervention. Finally, axis 4 divides age groups into neonatal, infancy, childhood, adolescent and adulthood, and elderly.

KEY WORDS: Status epilepticus, Seizure, Definition, Classification, Seizure duration.

Type of SE	Operational dimension 1 Time (t1), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)
Tonic- clonic SE	5 min	30 min
Focal SE with impaired consciousness	10 min	> 60 min
Absence status epilepticus	10-15 min[a]	unknown

a= Evidence for the time frame is currently limited and future data may lead to modifications

Epilepsia, 56(10):1515–1523, 2015

Classification of SE

- 1 Semiology
- 2 Etiology
- 3 EEG correlates
- 4 Age

Epilepsia, 56(10):1515–1523, 2015

Axis 1: Semiology

- The presence or absence of prominent motor symptoms
- The degree (qualitative or quantitative) of impaired consciousness

Epilepsia, 56(10):1515–1523, 2015

Axis 1: Semiology

A) With prominent motor symptoms

A.1 Convulsive SE (CSE, synonym: tonic–clonic SE)
- A.1.a. Generalized convulsive
- A.1.b. Focal onset evolving into bilateral convulsive SE
- A.1.c. Unknown whether focal or generalized

A.2 Myoclonic SE (prominent epileptic myoclonic jerks)
- A.2.a. With coma
- A.2.b. Without coma

A.3 Focal motor
- A.3.a. Repeated focal motor seizures (Jacksonian)
- A.3.b. Epilepsia partialis continua (EPC)
- A.3.c. Adversive status
- A.3.d. Oculoclonic status
- A.3.e. Ictal paresis (i.e., focal inhibitory SE)

A.4 Tonic status

A.5 Hyperkinetic SE

Epilepsia, 56(10):1515–1523, 2015

Axis 1: Semiology

(B) Without prominent motor symptoms (i.e., non- convulsive SE, NCSE)

B.1 NCSE with coma (including so-called “subtle” SE)

B.2 NCSE without coma

- B.2.a. Generalized
  - B.2.a.a Typical absence status
  - B.2.a.b Atypical absence status
  - B.2.a.c Myoclonic absence status
- B.2.b. Focal
  - B.2.b.a Without impairment of consciousness (aura continua, with autonomic, sensory,visual, olfactory, gustatory, emotional/ psychic/experiential, or auditory symptoms)
  - B.2.b.b Aphasic status
  - B.2.b.c With impaired consciousness

B.2.c Unknown whether focal or generalized

- B.2.c.a Autonomic SE

Epilepsia, 56(10):1515–1523, 2015

Axis 2: Etiology

- Known (i.e., symptomatic)

  - Acute (e.g., stroke, intoxication, malaria, encephalitis, etc.)

  - Remote (e.g., posttraumatic, postencephalitic, poststroke, etc.)
  - Progressive (e.g., brain tumor, Lafora's disease and other PMEs, dementias)

  - SE in defined electroclinical syndromes

- Unknown (i.e., cryptogenic)

Epilepsia, 56(10):1515–1523, 2015

Axis 3: Electroencephalographic correlates

- Currently there are no evidence-based EEG criteria for SE.

Epilepsia, 56(10):1515–1523, 2015

EEG patterns in SE

1. Location: generalized (including bilateral synchronous patterns), lateralized, bilateral independent, multifocal.

2. Name of the pattern: Periodic discharges, rhythmic delta activity or spike-and-wave/sharp- and-wave plus subtypes.

3. Morphology: sharpness, number of phases (e.g., triphasic morphology), absolute and relative amplitude, polarity.

4. Time-related features: prevalence, frequency, duration, daily pattern duration and index, onset (sudden vs. gradual), and dynamics (evolving, fluctuating, or static).

5. Modulation: stimulus-induced vs. spontaneous.

6 Effect of intervention (medication) on EEG.

Epilepsia, 56(10):1515–1523, 2015

Axis 4: Age

1. Neonatal (0 to 30 days)

2. Infancy (1 month to 2 years)

3. Childhood (> 2 to 12 years)

4. Adolescence and adulthood (> 12 to 59 years)

5. Elderly (≥ 60 years)

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Management of status epilepticus

Principle of management in patients with SE

1. Stop both ongoing clinical and electrographic seizures

2. Identify and treat the etiology of SE

3. Identify and treat the complications of SE

Choosing the anti-seizure medications

- Age
- Clinical seizure type:
  - CSE and NCSE
- Comorbidities
  - cardiovascular disease
  - liver disease
  - kidney disease
- History of drug allergy
  - minor rash to SJSs

- Anti-seizure medications
  - administration
  - mechanism of action
  - pharmacodynamics
  - pharmacokinetics
  - efficacy for seizure type
  - recommended doses
  - adverse effects
  - drug interactions

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Convulsive status epilepticus (CSE)

Definition of CSE

- CSE is a convulsive seizure lasting more than 5 min or consecutive seizures without recovery of consciousness.

- In the case of convulsive SE, both time points (t1 at 5 min and t2 at 30 min) are based on animal experiments and clinical research.

Epilepsia, 56(10):1515–1523, 2015

Type of SE	Operational dimension 1 Time (t1), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)
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Epilepsia, 56(10):1515–1523, 2015

Time is the brain!

- The response to AEDs treatment is decreasing with time and ongoing seizures probably due to the following reasons;

  - Functional GABA receptors are decreased due to internalization of GABA receptors.

  - NMDA receptors are up-regulated. This can resulted in calcium influx intracellularly which makes seizure control more difficult and may causes cellular damage and secondary brain injury.

  - There is the upregulation of drug-efflux transporters such as P- glycoprotein.

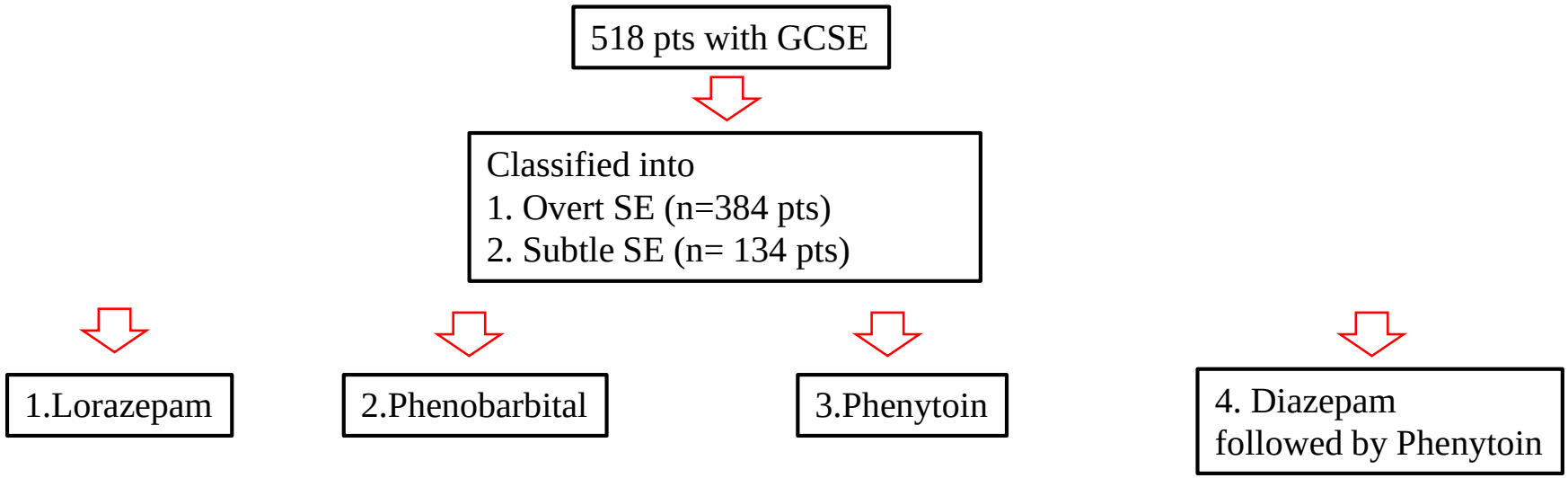
  - Ongoing status can resulted in an increment of pro-inflammatory agents.

Epilepsia 2009;50(Suppl. 8):19–21.

Ann N Y Acad Sci 2016;1378:166–73.

The US Department of Veterans Affairs (VA) Cooperative Study randomized controlled clinical trial

Five-year randomized, double blind, multicenter trial of four intravenous regimens



Conclusions

As initial intravenous treatment for overt generalized convulsive status epilepticus, lorazepam is more effective than phenytoin. Although lorazepam is no more efficacious than phenobarbital or diazepam and phenytoin, it is easier to use.

N Engl J Med 1998;339(12):792Y798

Established Status Epilepticus Treatment Trial (ESETT)

- **Full title:** A Multicenter, Randomized, Blinded, Comparative Effectiveness Study of Fosphenytoin, Valproic Acid, or Levetiracetam in the Emergency Department Treatment of Patients With Benzodiazepine-refractory Status Epilepticus

- Estimated study completion date: in July 2020

Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society

Epilepsy Currents, Vol. 16, No. 1 (January/February) 2016 pp. 48–61

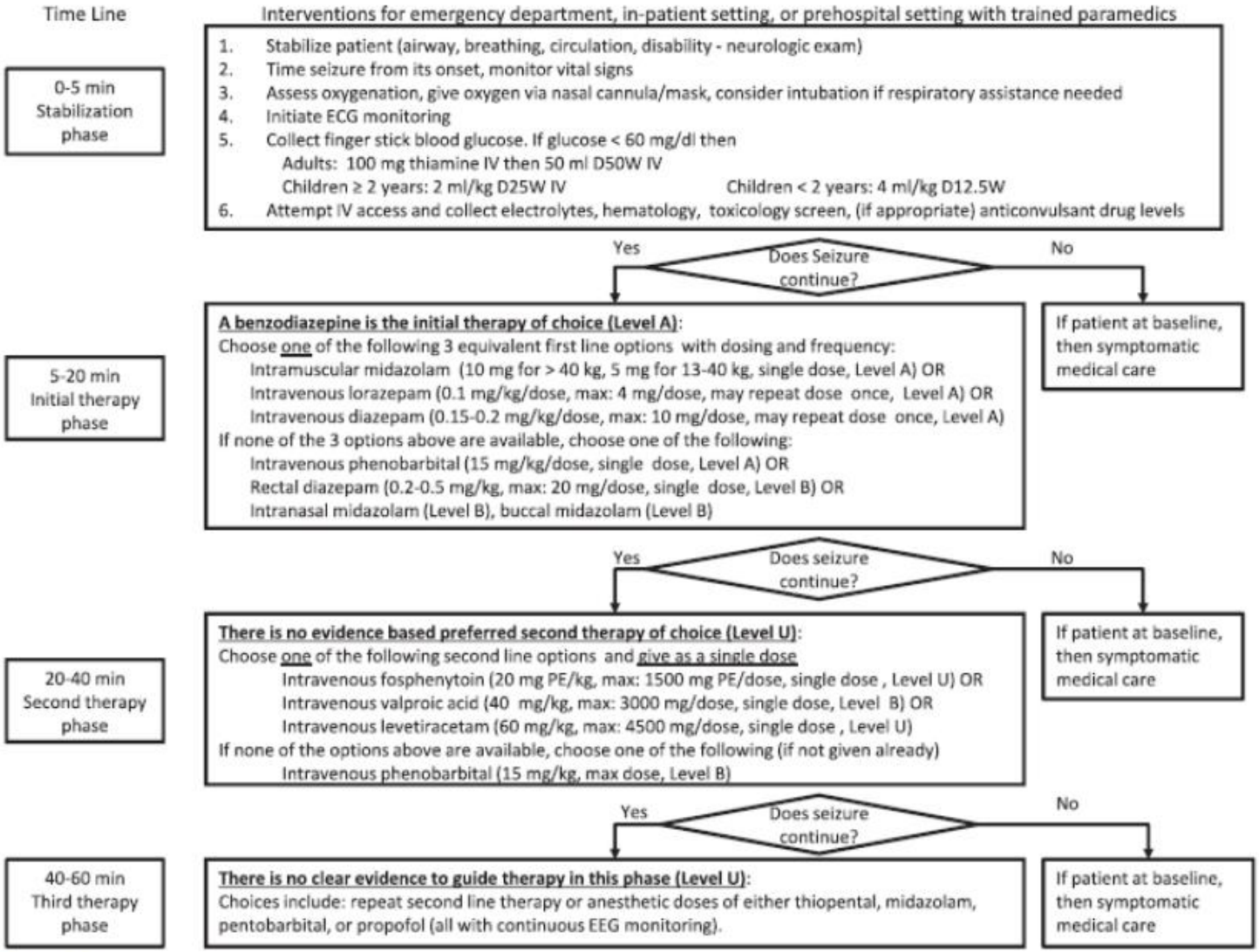


FIGURE 1. Proposed treatment algorithm for status epilepticus.

Disclaimer: This clinical algorithm/guideline is designed to assist clinicians by providing an analytical framework for evaluating and treating patients with status epilepticus. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this algorithm/guideline will not fit or work with all patients. Approaches not covered in this algorithm/guideline may be appropriate.

Treatment phases of CSE

- **Stage 1 (early or impending CSE)**

  - Benzodiazepines are the drugs of choice.

  - RAMPART (Rapid Anticonvulsant Medication Prior to Arrival Trial) IV lorazepam vs IM midazolam*

  - AES guideline state that IM midazolam has a superior effectiveness compared to intravenous lorazepam in adults with CSE without established intravenous access (Level A)**

*N Engl J Med 2012; 366:591-600

**Epilepsy Curr 2016;16:48–61.

Treatment phases of CSE

- **Stage 2 (Established SE)**: CSE persisting after first-line treatments

  - phenytoin (fosphenytoin)
  - phenobarbital
  - valproic acid
  - levetiracetam
  - lacosamide

Treatment phases of CSE

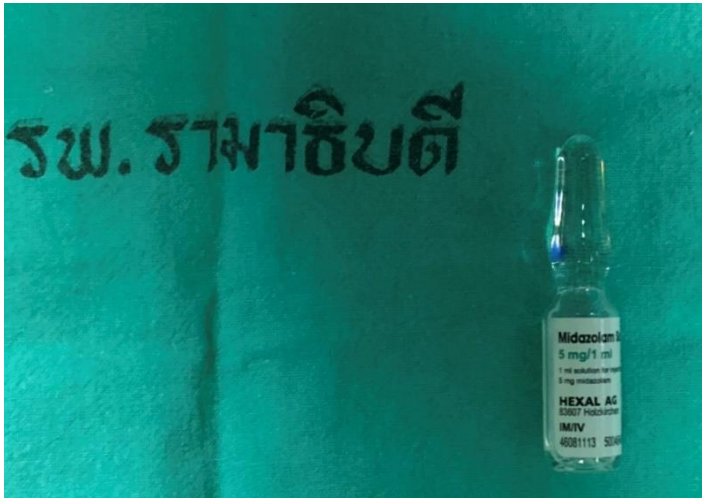
- **Stage 3 (refractory CSE):** CSE persisting > 60 minutes after second-line treatments

  - Anesthetic agents are the drugs of choice for the treatment of refractory CSE.

Midazolam

	Loading dose	Initial rate	Maintenance dose
Midazolam	0.2 mg/kg IV over 2 to 5 minutes; repeat 0.2 to 0.4 mg/kg boluses every 5 minutes until seizures stop, up to a maximum loading dose of 2 mg/kg	0.1mg/kg/hr	0.05 to 2.9 mg/kg/hour

Mechanism of action of midazolam	GABA-A agonists
Onset of action	3-5 minutes
Half-life elimination	3 hours
Metabolism	hepatic CYP3A4
Excretion	urine
Dosing: hepatic impairment	no data; use with caution
Dosing: renal impairment	no data; use with caution
Adverse effects	respiratory and cardiovascular depression development of tachyphylaxis with prolonged infusions



Propofol

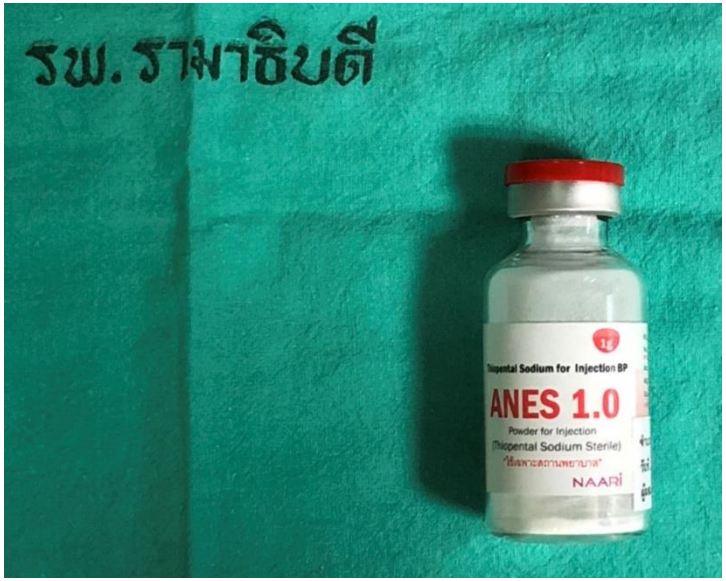
	Loading dose	Initial rate	Maintenance dose
Propofol	1 to 2 mg/kg IV over 3 to 5 minutes; repeat boluses every 3 to 5 minutes until seizures stop, up to maximum total loading dose of 10mg/kg	20 microgram/kg/min; bolus and increase rate until seizure control	30 to 200 microgram/kg/min titrated to EEG with 5 to 10 microgram/kg/min every 5 minutes or 1 mg/kg bolus for breakthrough status epilepticus

Mechanism of action of propofol	GABA-A agonists, N-methyl-D-aspartate (NMDA) antagonist
Onset of action	30 seconds
Half-life elimination	40 minutes- 7 hours
Metabolism	hepatic
Excretion	urine
Dosing: hepatic impairment	no dosage adjustment necessary
Dosing: renal impairment	no dosage adjustment necessary
Adverse effects	respiratory and cardiovascular depression, ‘‘propofol infusion syndrome,’’ which includes potentially fatal myocardial failure with lactic acidosis, hypertriglyceridemia, and rhabdomyolysis

Thiopental

	Loading dose	Maintenance dose
Thiopental	100-250 mg IV drip > 20 seconds then 50 mg IV every 2- 3minutes until seizure was stopped.	3-5 mg/kg/hour

Mechanism of action of thiopental	GABA-A agonists
Onset of action	30 seconds
Half-life elimination	5-22 hours
Metabolism	hepatic, primary to inactive metabolites
Excretion	urine, primary to inactive metabolites
Dosing: hepatic impairment	no data
Dosing: renal impairment	no data
Adverse effects	dose-dependent respiratory and cardiovascular depression, long recovery time, immunosuppression



Ketamine

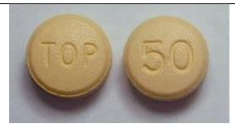
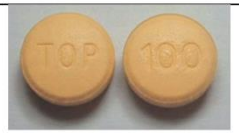
	Loading dose	Initial rate	Maintenance dose
Ketamine	1 to 4.5 mg/kg with supplements of 0.5-2.5 mg/kg every 30-45 minutes or 10 to 50 microgram/kg/min	1.5 mg/kg every 3 to 5 minutes until seizures stops, up to a maximum of 4.5 mg/kg	5 to 125 microgram/kg/min (0.3-7.5 mg/kg/hr)

Mechanism of action of ketamine	N-methyl D-aspartate (NMDA) receptor antagonists
Onset of action	30 seconds
Half-life elimination	2.5 hours
Metabolism	hepatic via CYP3A4
Excretion	urine
Dosing: hepatic impairment	no data
Dosing: renal impairment	no data
Adverse effects	elevation of blood pressure, increased intracranial pressure

Topiramate

	Loading dose	Maintenance dose	Side effects
Topiramate	100 mg PO q 12 hours	400-800 mg/day q 12 hours	metabolic acidosis topiramate+propofol→ refractory acidosis topiramate+ sodium valproate→ hyperammonemia

Mechanism of action of topiramate	Blockade of the ionotropic glutamatergic AMPA/kainate receptors Blocks neuronal voltage-dependent sodium channels Enhancement of GABAergic activity
Onset of action	2-4 hours
Half-life elimination	20 hours
Metabolism	Minor amounts metabolized in liver
Excretion	Urine 70%
Dosing: hepatic impairment	no data; use with caution in patient with severe hepatic impairment
Dosing: renal impairment	reduce dose to 50% if CrCl < 70
Adverse effects	drowsiness, metabolic acidosis, hyperammonemia

Topamax tab 25 mg (film-coated)	
Topamax tab 50 mg (film-coated)	 0.7 cm เหลือง
Topamax tab 100 mg (film-coated)	 0.9 cm ส้ม

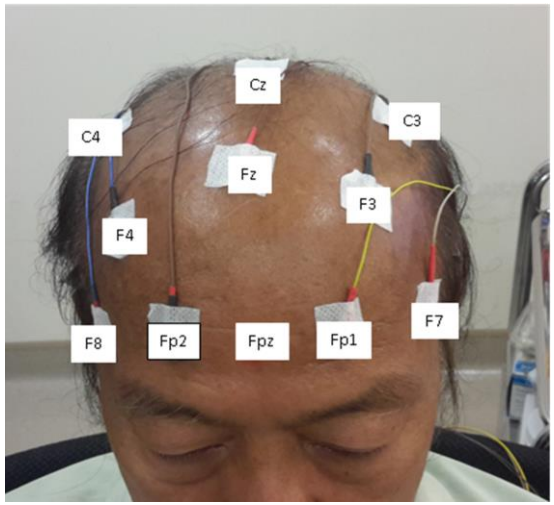
Refractory status epilepticus (RSE)

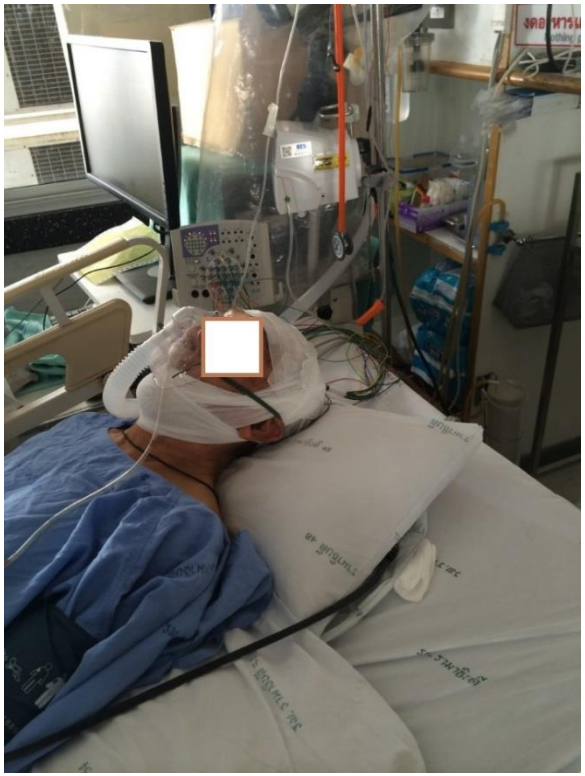
- Quick check lists

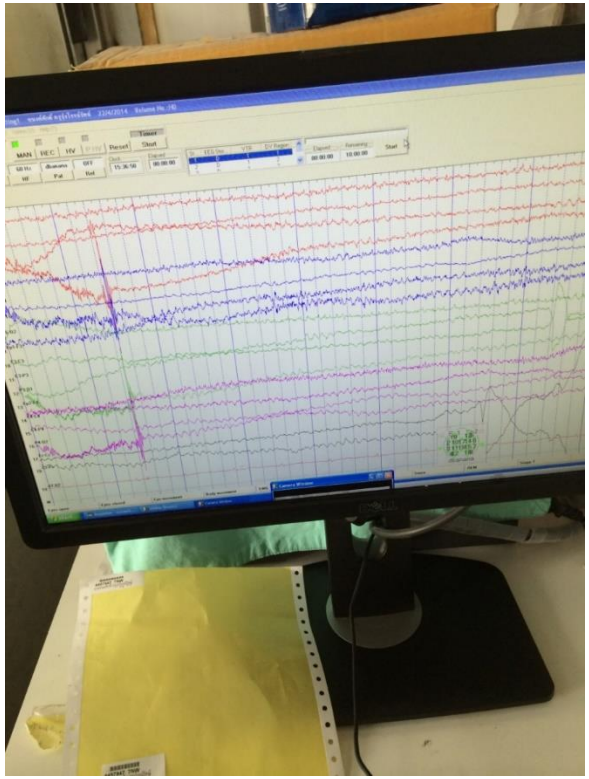
  - The patient must be intubated and should be admitted in the intensive care unit for respiratory monitoring, and hemodynamic monitoring.

  - Continuous electroencephalography(cEEG) monitoring is critical during the treatment of RSE and should be performed in every patient with RSE (if possible).

cEEG monitoring







The usefulness of cEEG monitoring

- cEEG monitoring is necessary to confirm that ongoing seizures have been completely stopped and under controlled after the treatment of RSE.

- Ongoing electrographic seizures may be masked when using paralytics for intubation; therefore patients may continue to seize without any clinical manifestations.

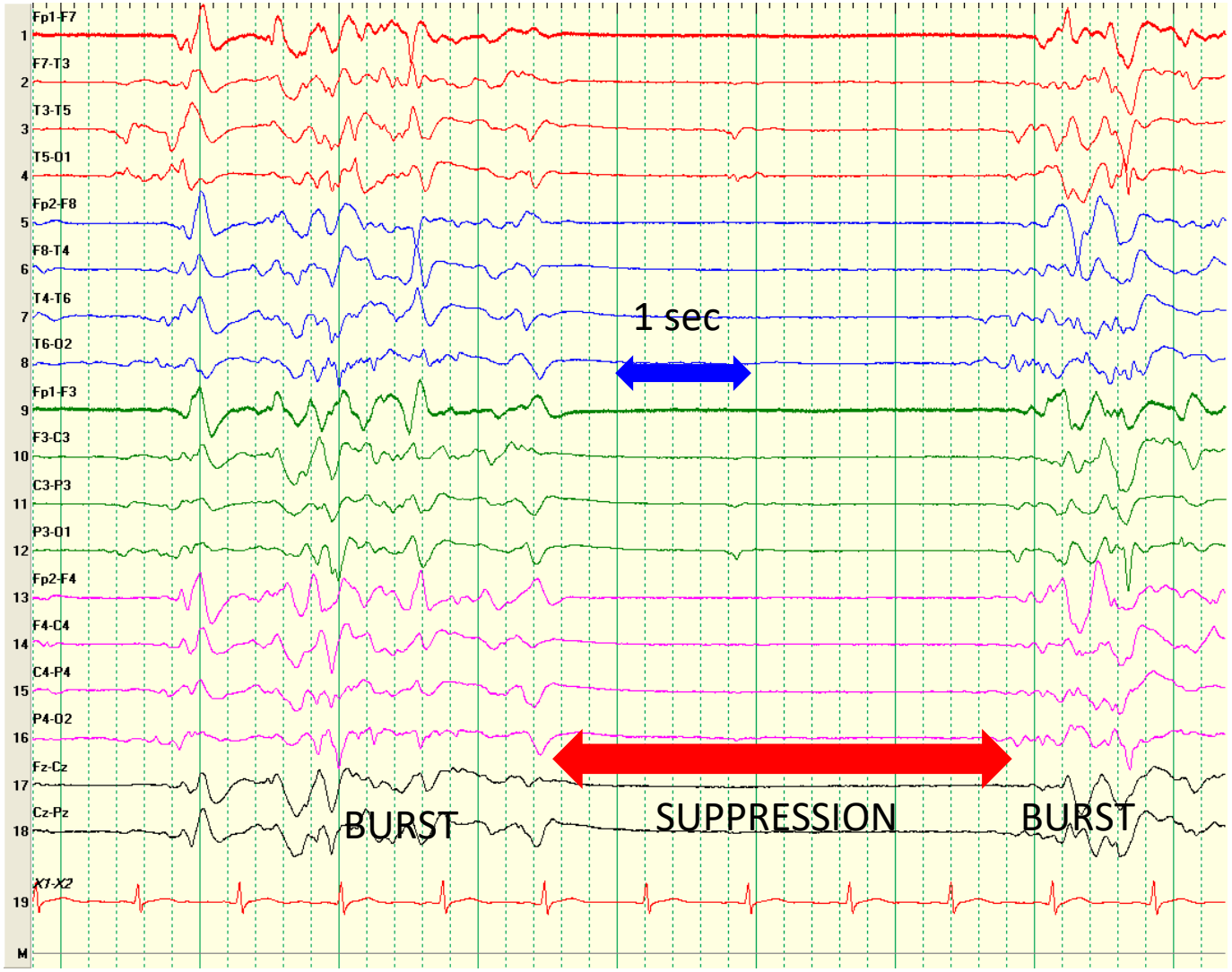
- The depth of anesthesia, the level of CNS suppression, degree of encephalopathy, ongoing electrographic seizures can be assessed by using the cEEG monitoring. Thus, the information from cEEG monitoring is very useful for the treatment of RSE including the adjustment of anti-seizure medications.

Optimal electroclinical endpoint of treatment

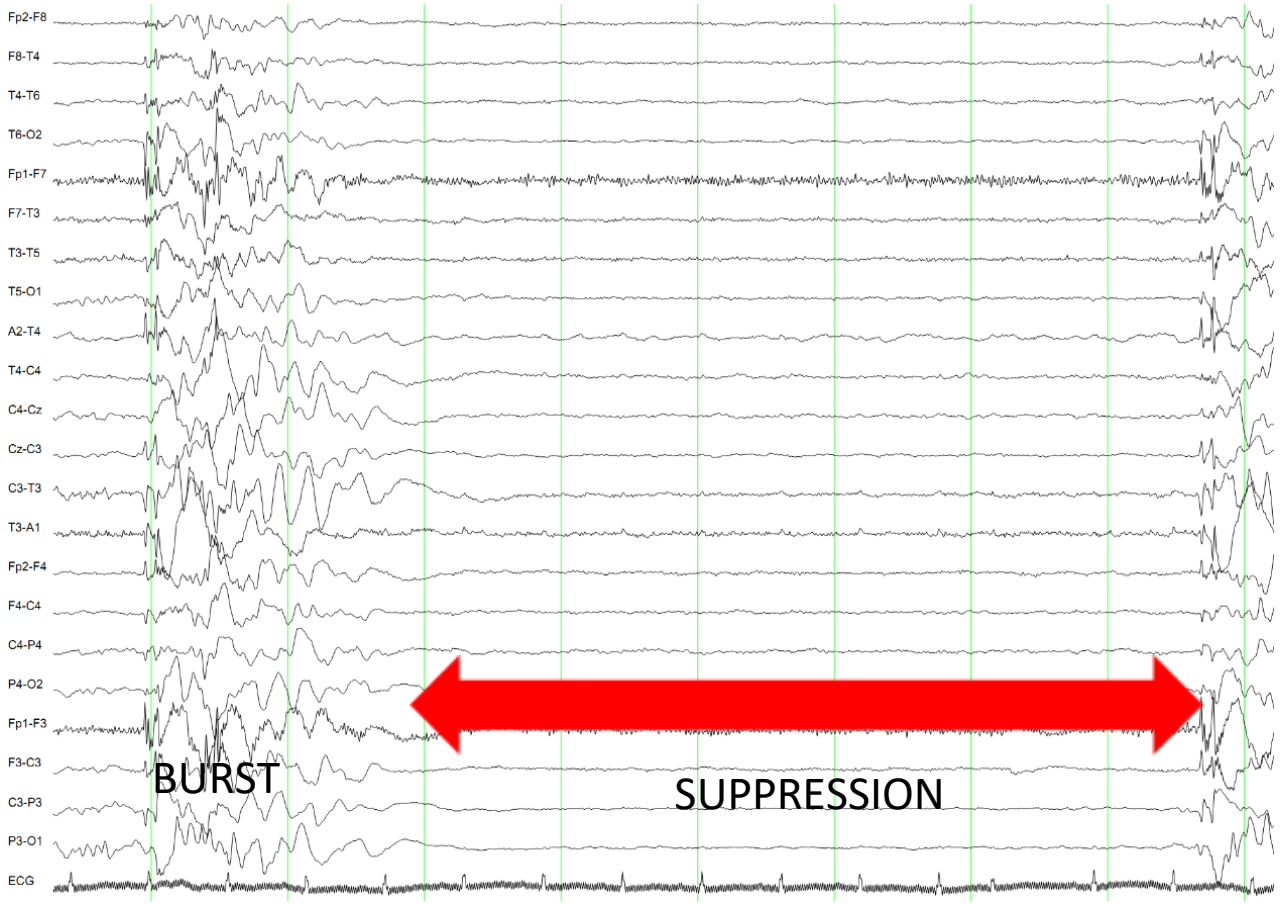
- To best of our knowledge, the optimal electroclinical endpoint of treatment has not been studied in a well-designed clinical trials. Therefore, it is uncertain whether the goal should be simple cessation of both clinical and electrographic seizures, or some degree of suppression of cerebral activity.

- **Thai clinical practice guideline:** no clinical and electrographic seizures plus burst suppression with interburst interval of 5-15 seconds for 24 hours.

Burst suppression with interburst intervals of 3 seconds



Burst suppression with interburst intervals of 5 seconds



Tapering off anesthetic agents in patient with RSE

- **Thai clinical practice guideline:** no clinical and electrographic seizures for 24-48 hours.

- Before tapering off anesthetic agent, it is critical that high therapeutic levels of at least one longer-acting anti-seizure medication be maintained before tapering continuous infusions.

  - avoid anti-seizure medications with a primarily GABAergic mechanism

  - avoid > 2 anti-seizure medications

  - try anti-seizure medications with multiple mechanisms of action and low drug interactions

http://thaiepilepsysociety.com/

Tapering off anesthetic agents in patient with RSE

- When electrographic seizures re-appear during tapering off anesthetic agent, most experts recommend to re-treat with higher doses of the anesthetic agent, or for longer at doses that were successful earlier. Additional anti-seizure medications should be immediately prescribed before considering the next attempt.

Treatment phases of CSE

- **Stage 4 (super-refractory CSE)*:** CSE persisting for more than 24 hours after administration of third-line treatments

  - anesthetic agents
  - ketamine
  - immunomodulatory therapy
  - hypothermia
  - new anti-seizure medications
  - ketogenic diet*

*Brain 2011;134:2802–18.

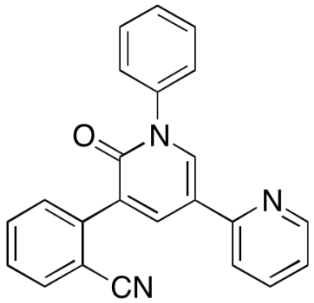
**Neurology. 2017 Mar 7;88(10):938-943.

Perampanel (PER)

- PER has a novel mechanism of action. It is a first in class orally active, selective, non-competitive alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor agonist.

- PER
  - initial dose in case small case series: 2-32 mg
  - adult patients with refractory and super-refractory status epilepticus in a neurological intensive care unit

Epilepsy Behav. 2015 Aug;49:354-8.

Perampanel 	Fycompa tab 2 mg (film-coated)		ฯ	72
	Fycompa tab 4 mg (film-coated)		ฯ	114.25
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มหาวิทยาลัยมหิดล
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Focal motor status epilepticus

Epilepsia partialis continua (EPC)

- Treatment

  - identify and treat causal or precipitating factors

  - anti-seizure medications

    - first-generation: carbamazepine, valproate, clonazepam

    - second-generation: topiramate, levetiracetam

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Non-convulsive status

Non-convulsive status epilepticus (NCSE)

- Positive symptoms
  - agitation, aggression, delirium, psychosis
  - facial twitching, automatisms
  - sustained eye deviation, nystagmus

- Negative symptoms
  - aphasia
  - mutism
  - eye staring
  - confusion, lethargy, coma

Non-convulsive status epilepticus (NCSE)

- Patients with NCSE may have no clinical signs or develop only subtle jerks of the face, eyes, and extremities.

- NCSE is diagnosed only by electroencephalography(EEG).

Salzburg EEG consensus criteria for non-convulsive status epilepticus (SCNC)

Patients without known epileptic encephalopathy
• EDs > 2.5 Hz, or
• EDs ≤ 2.5 Hz or rhythmic delta/theta activity (> 0.5Hz) AND one of the following: - EEG and clinical improvement after IV AED*, or - Subtle clinical ictal phenomena, or - Typical spatiotemporal evolution**

Patients with known epileptic encephalopathy
• Increase in prominence or frequency when compared to baseline with observable change in clinical state
• Improvement of clinical and EEG* features with IV AEDs
* If EEG improvement without clinical improvement, or if fluctuation without definite evolution, this should be considered possible NCSE.
** Increment onset(increase in voltage and change in frequency), or evolution in pattern(change in frequency > 1Hz or change in location), or decrementing termination(voltage and frequency).
EDs: epileptiform discharges(spikes, polyspikes, sharp-waves, sharp-and-wave complexes) IV AED: intravenous antiepileptic drugs

Epilepsy Behav: E&B 2015;49(August)158–63 Lancet Neurol 2016;15(September (10)) 1054–62

Management of NCSE

- The aggressiveness of anti-seizure medication treatment should be individualized on each patient with NCSE. The following variables should be considered;

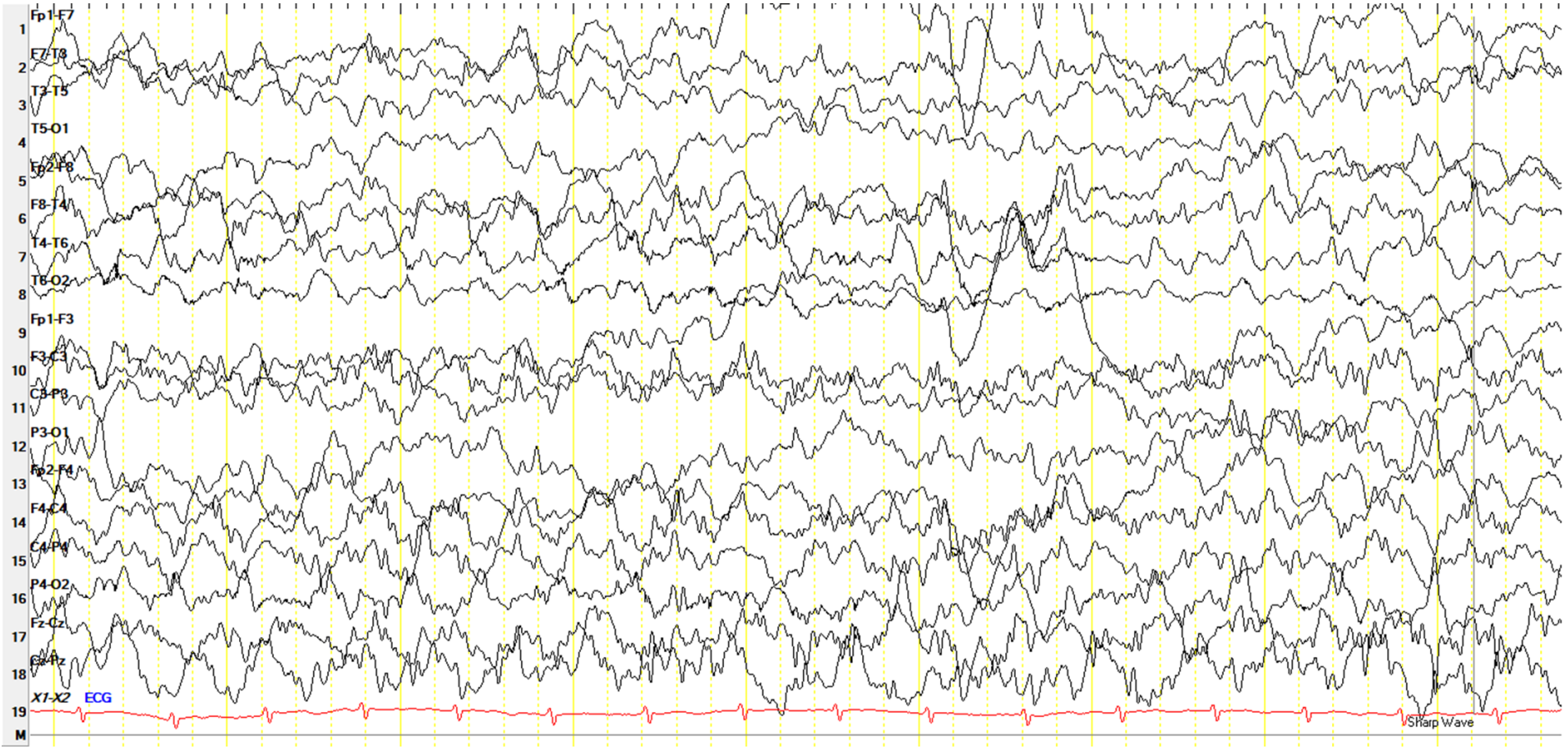
  - degree of impairment of consciousness

  - etiology

NCSE without coma

- For NCSE patients without coma, we suggest treatment with an IV benzodiazepine combined with an IV noncoma-inducing anti-seizure medications(AEDs).

- Noncoma-inducing AEDs
  - phenytoin
  - sodium valproate
  - levetiracetam
  - lacosamide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P3-O1
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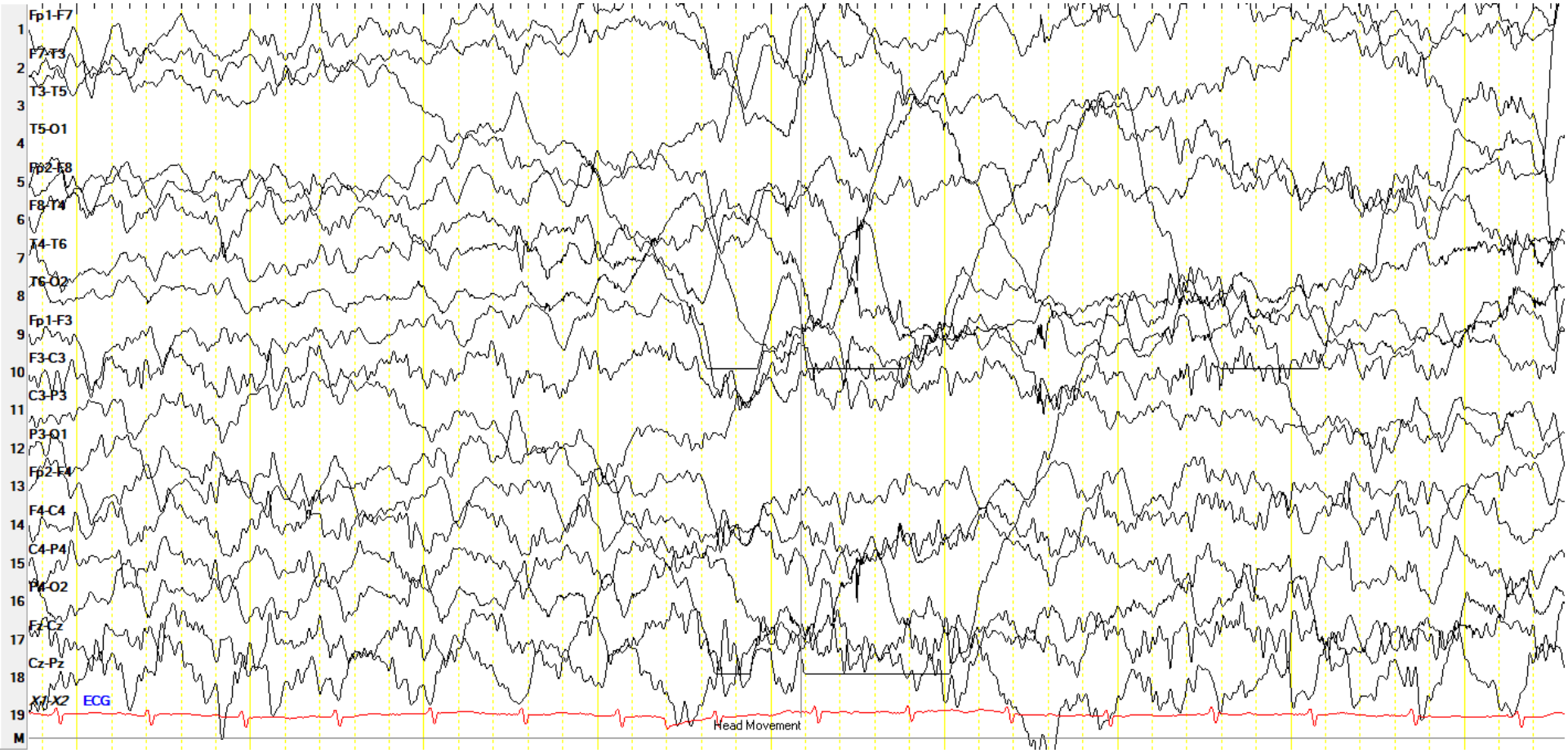
P4-O2
Fz-Cz
Cz-Pz
X1-X2 ECG
Sharp Wave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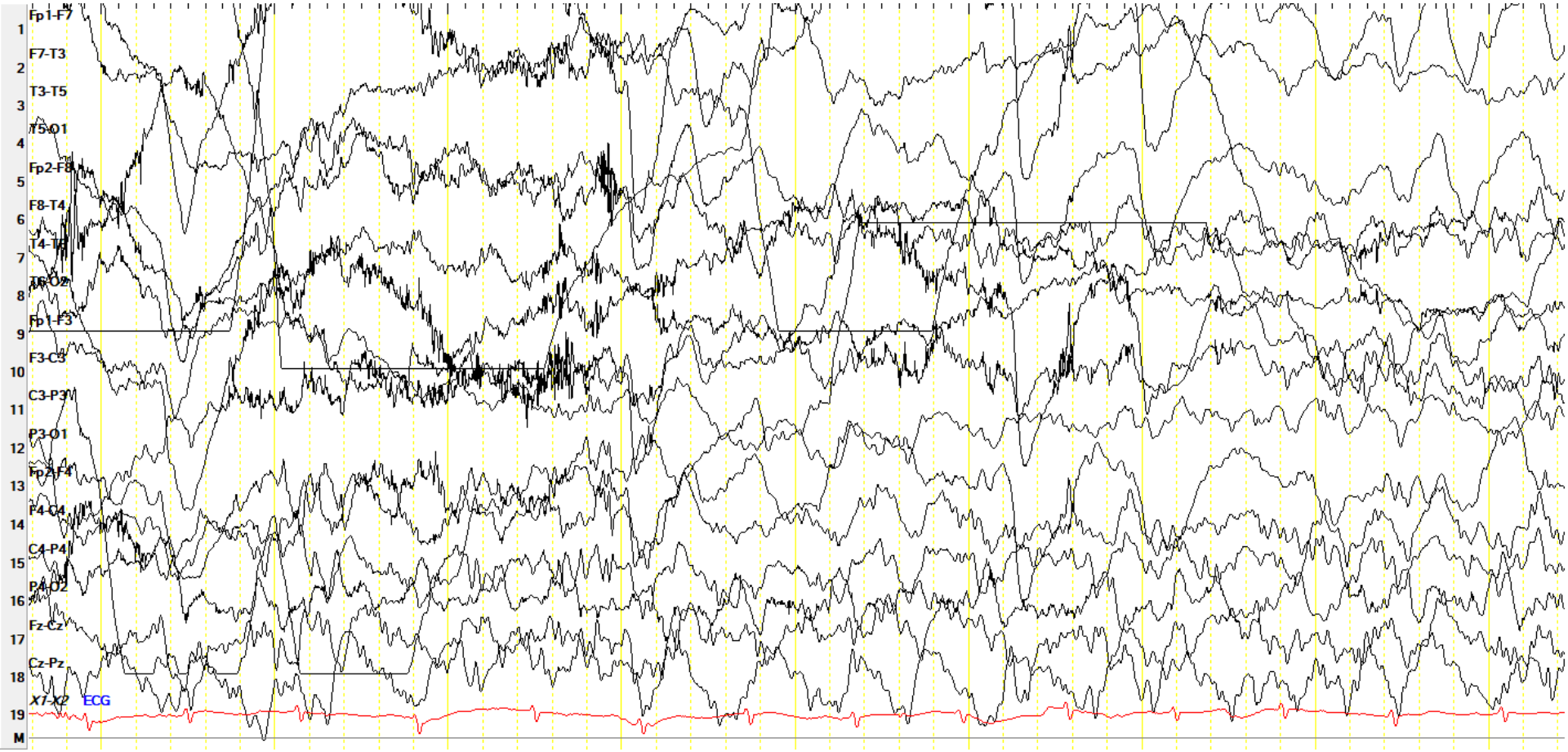
Head Movement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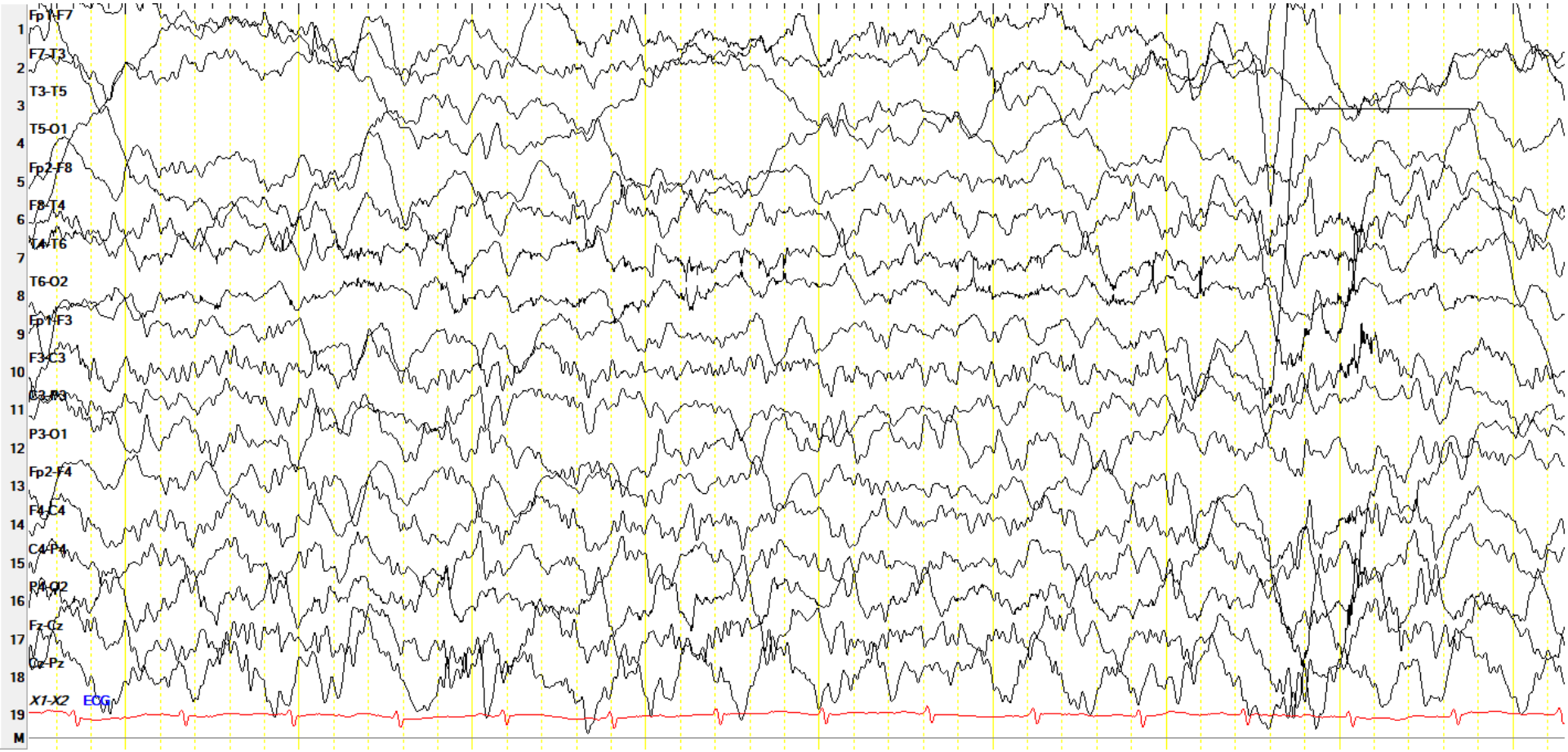
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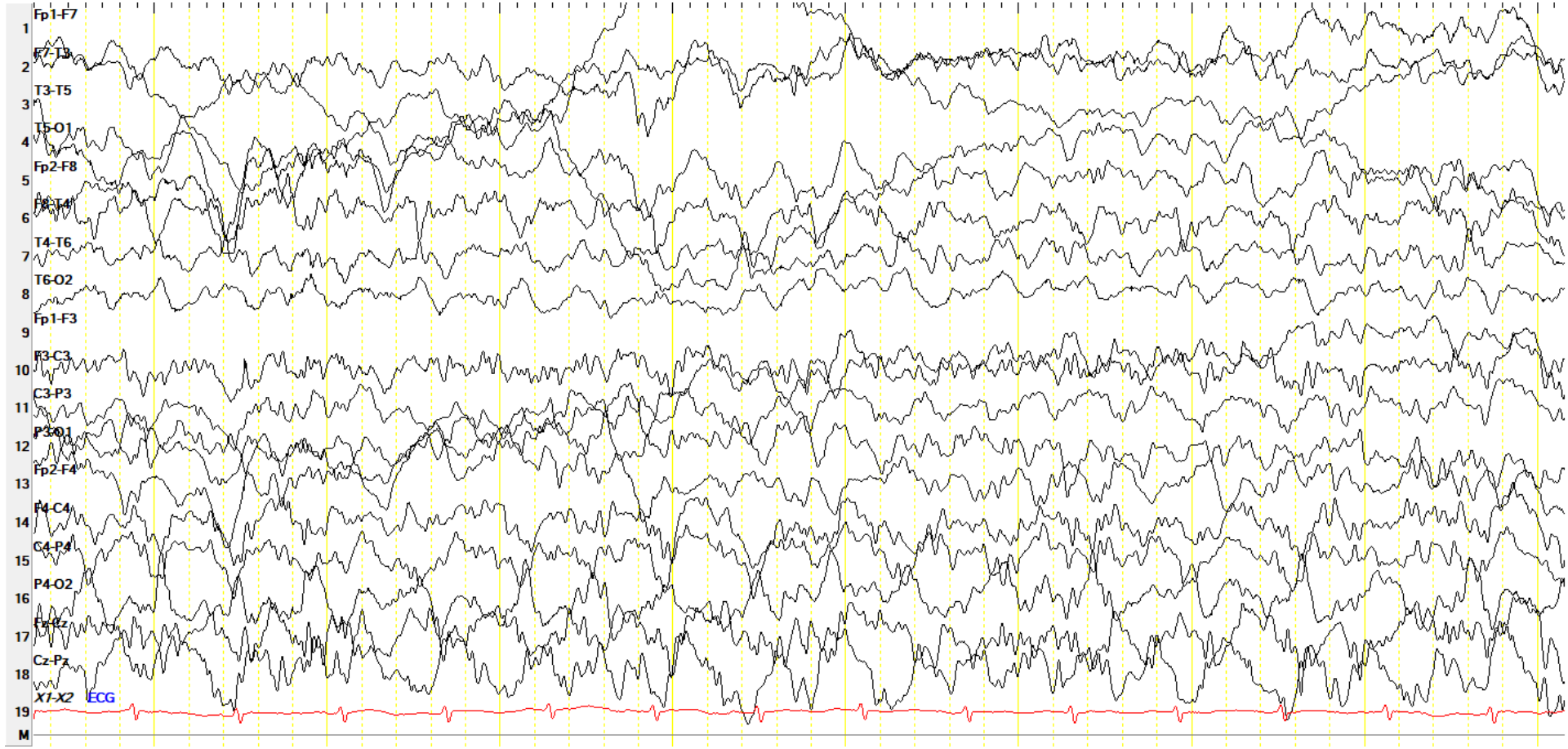
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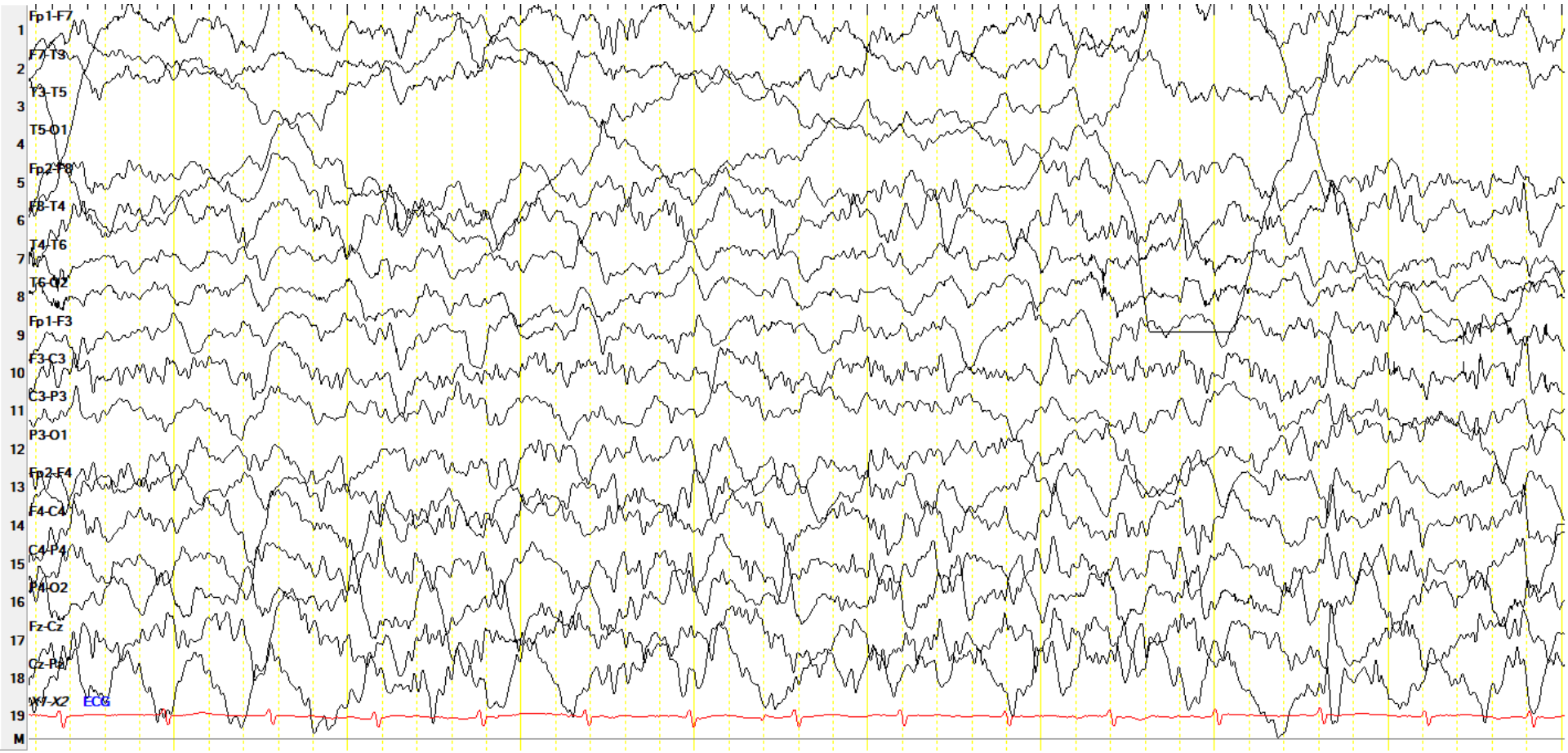
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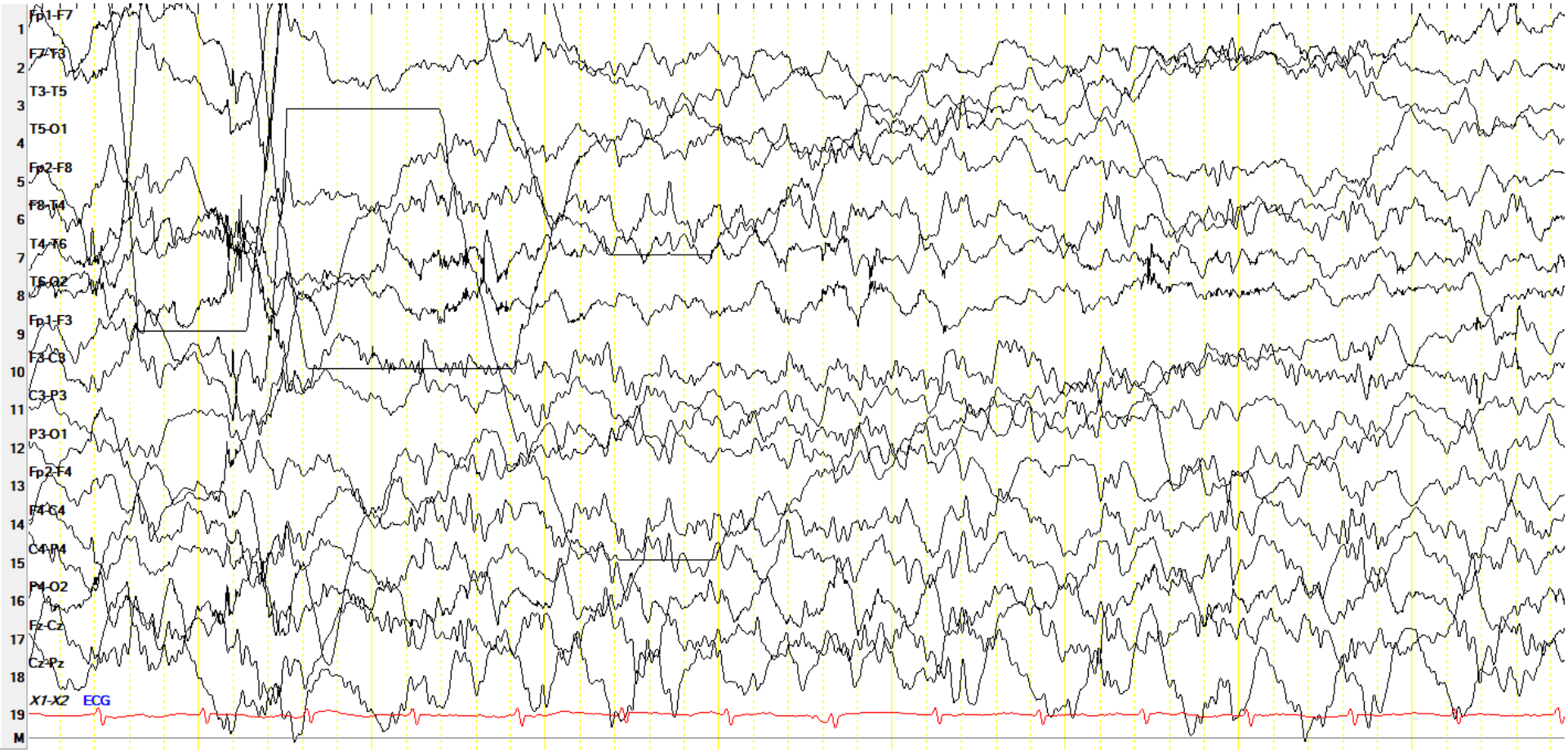
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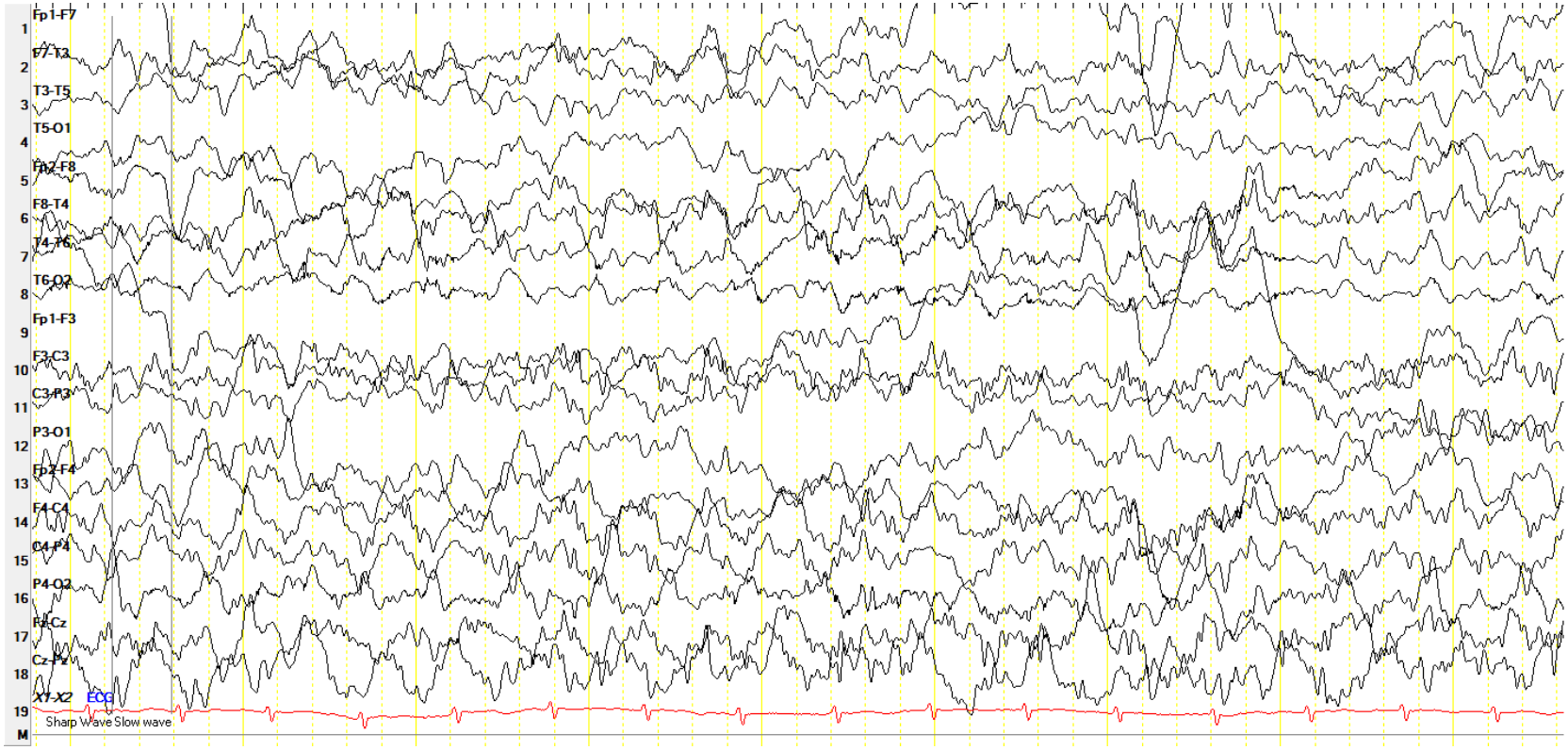
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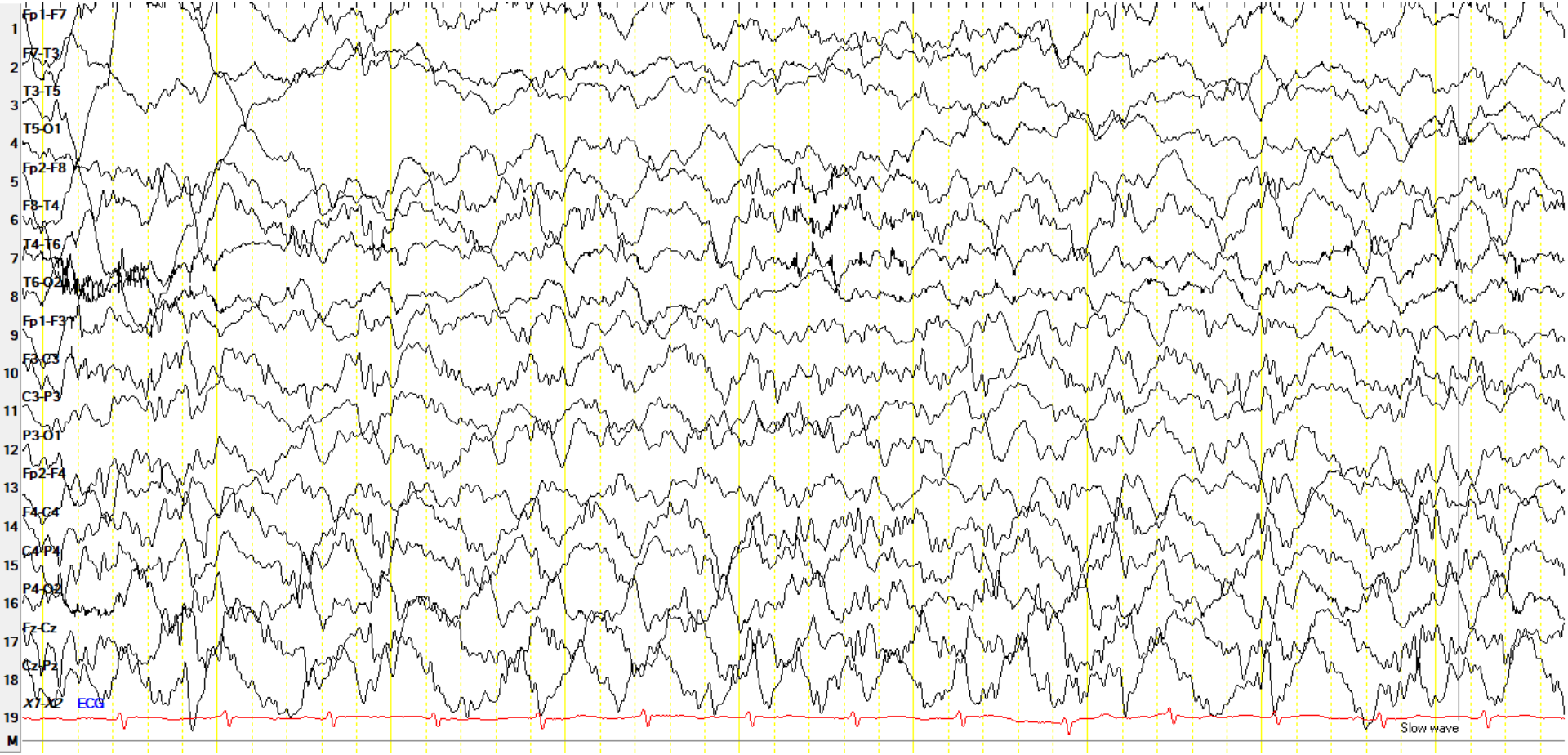
X1-X2
ECG
Sharp Wave Slow wave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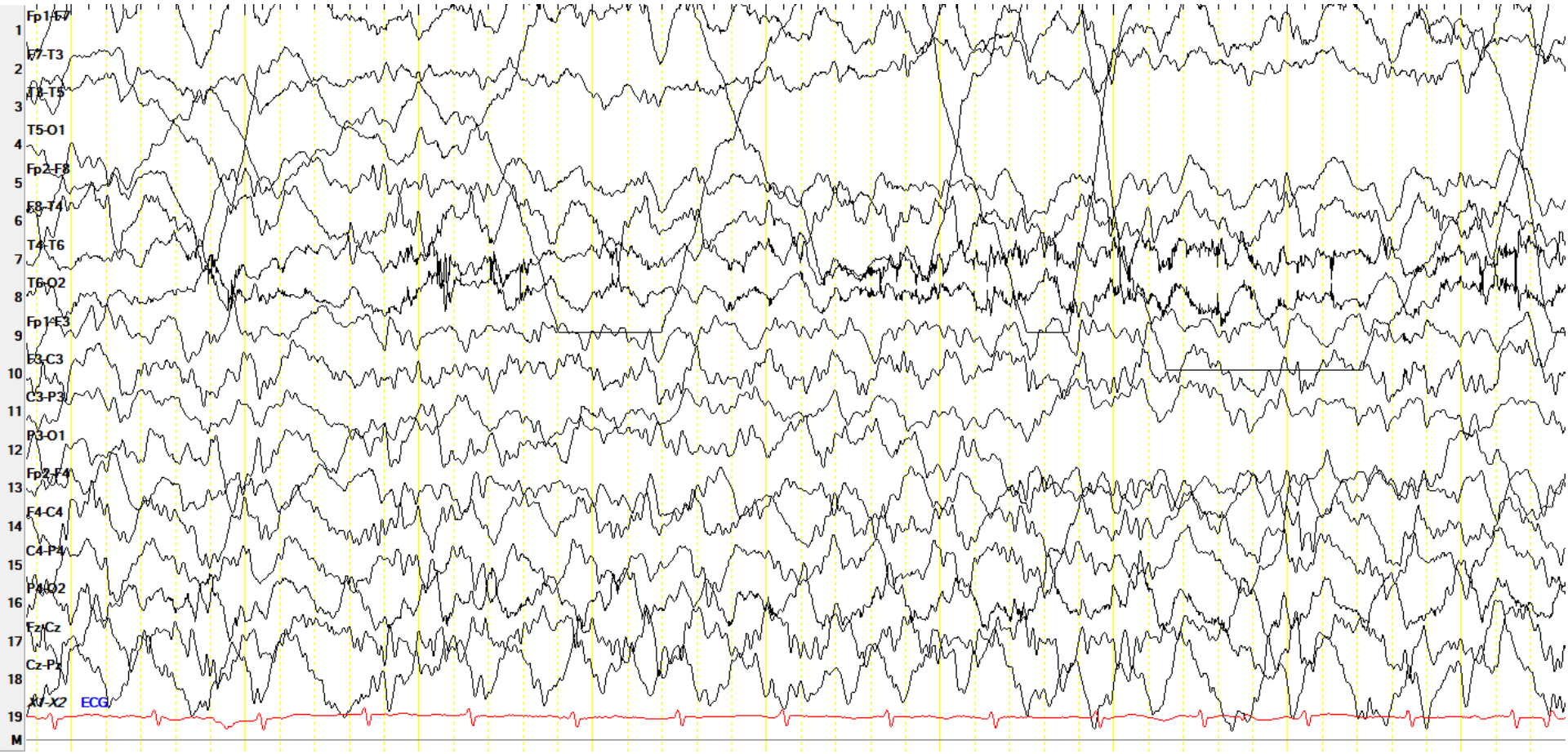
Cz-Pz
X1-X2
ECG
Slow wave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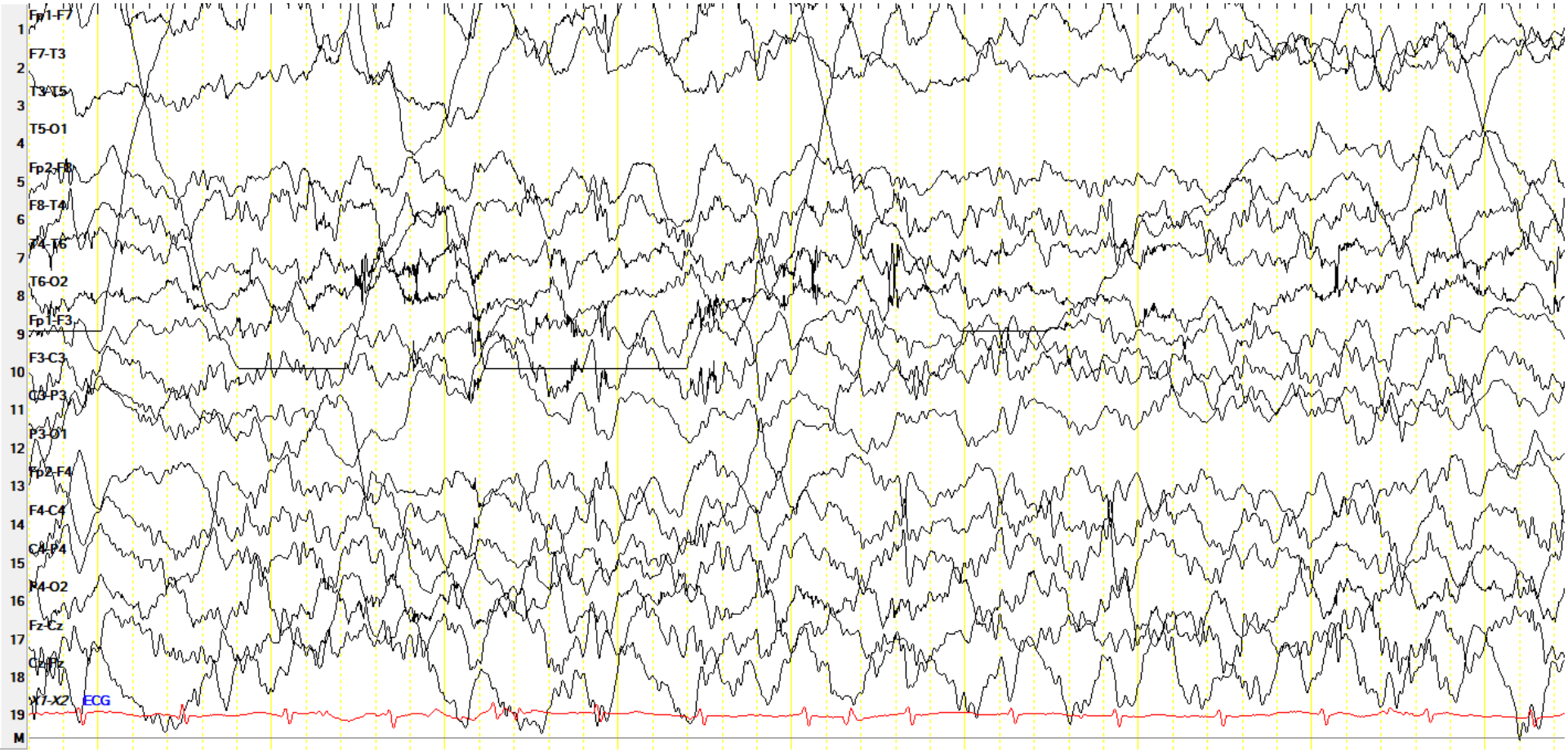
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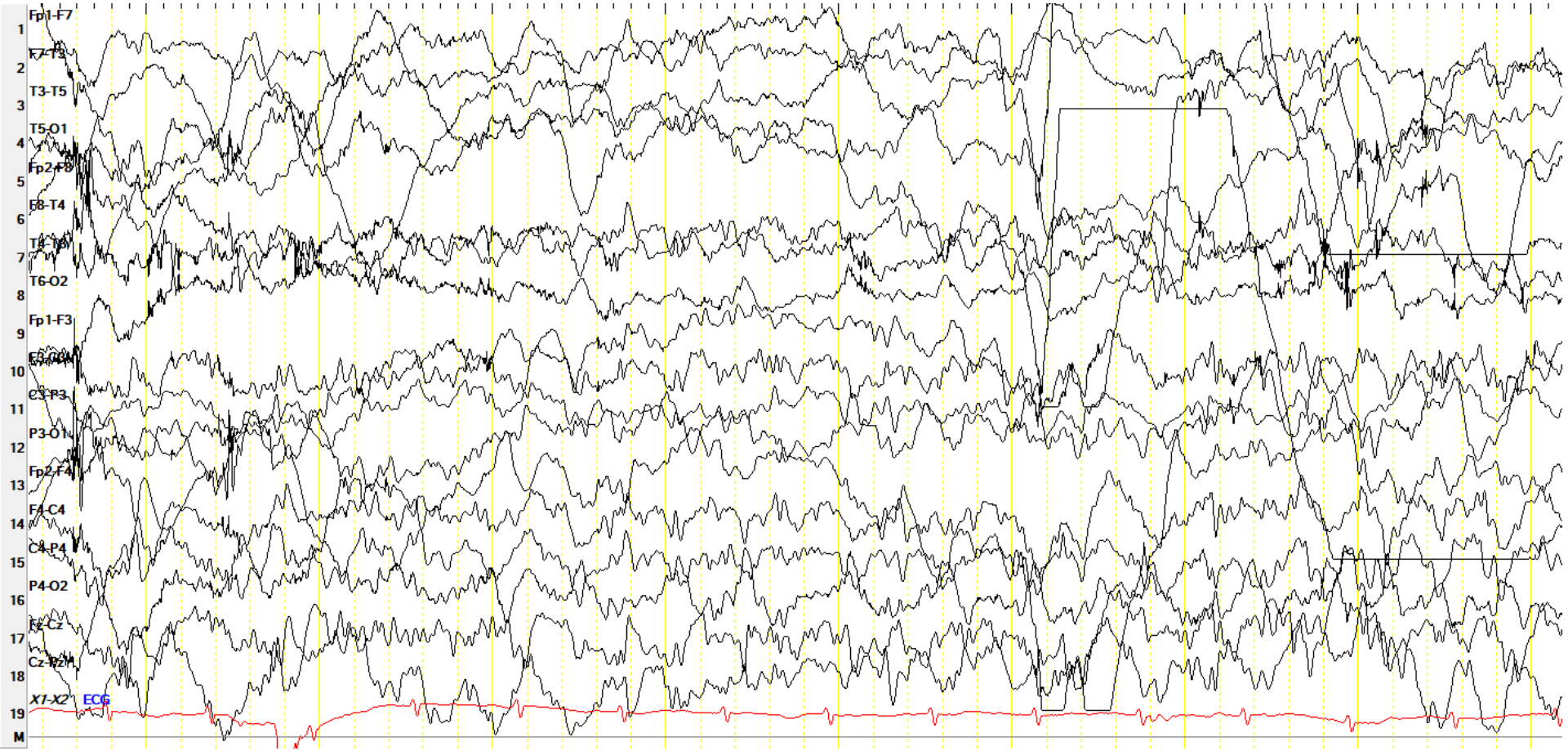
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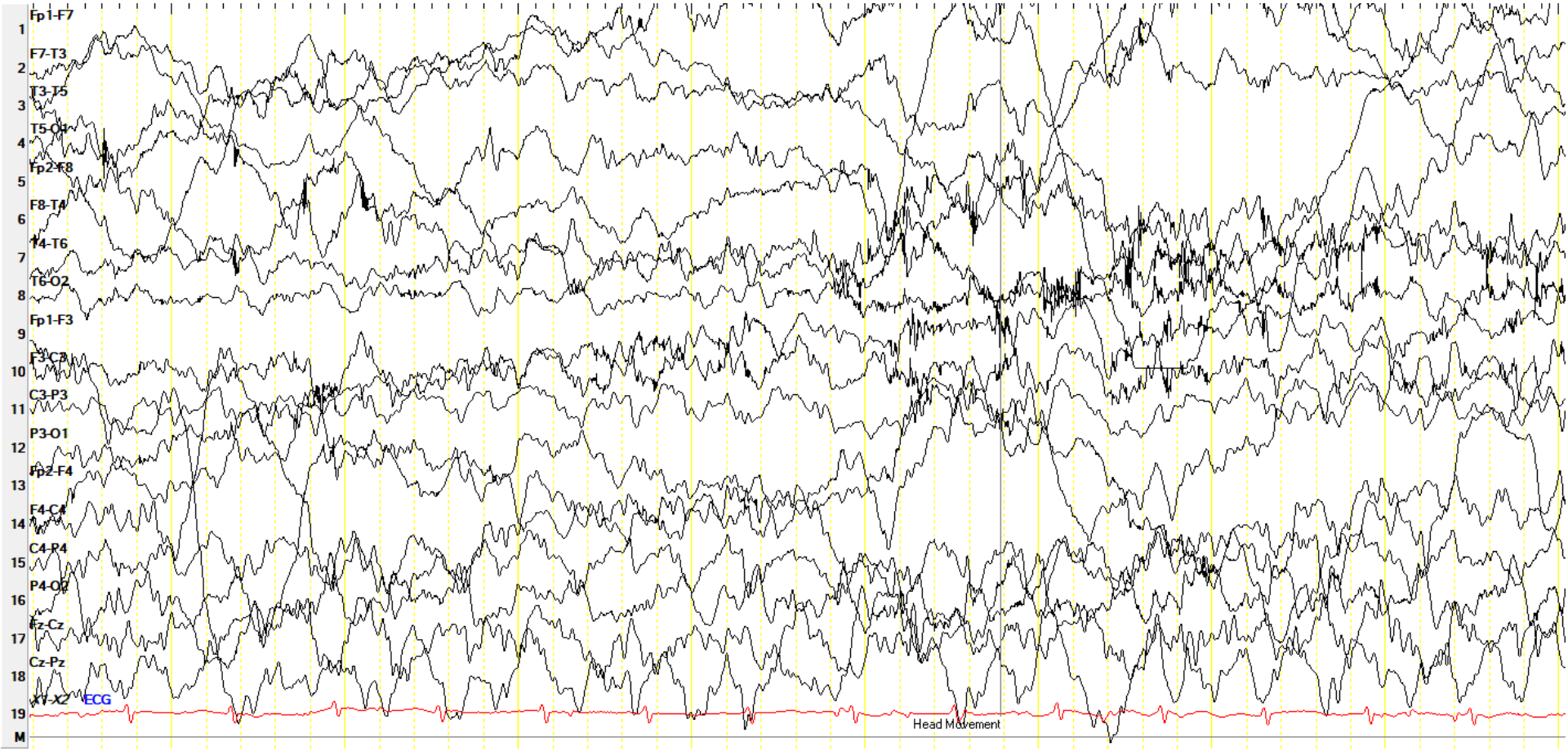
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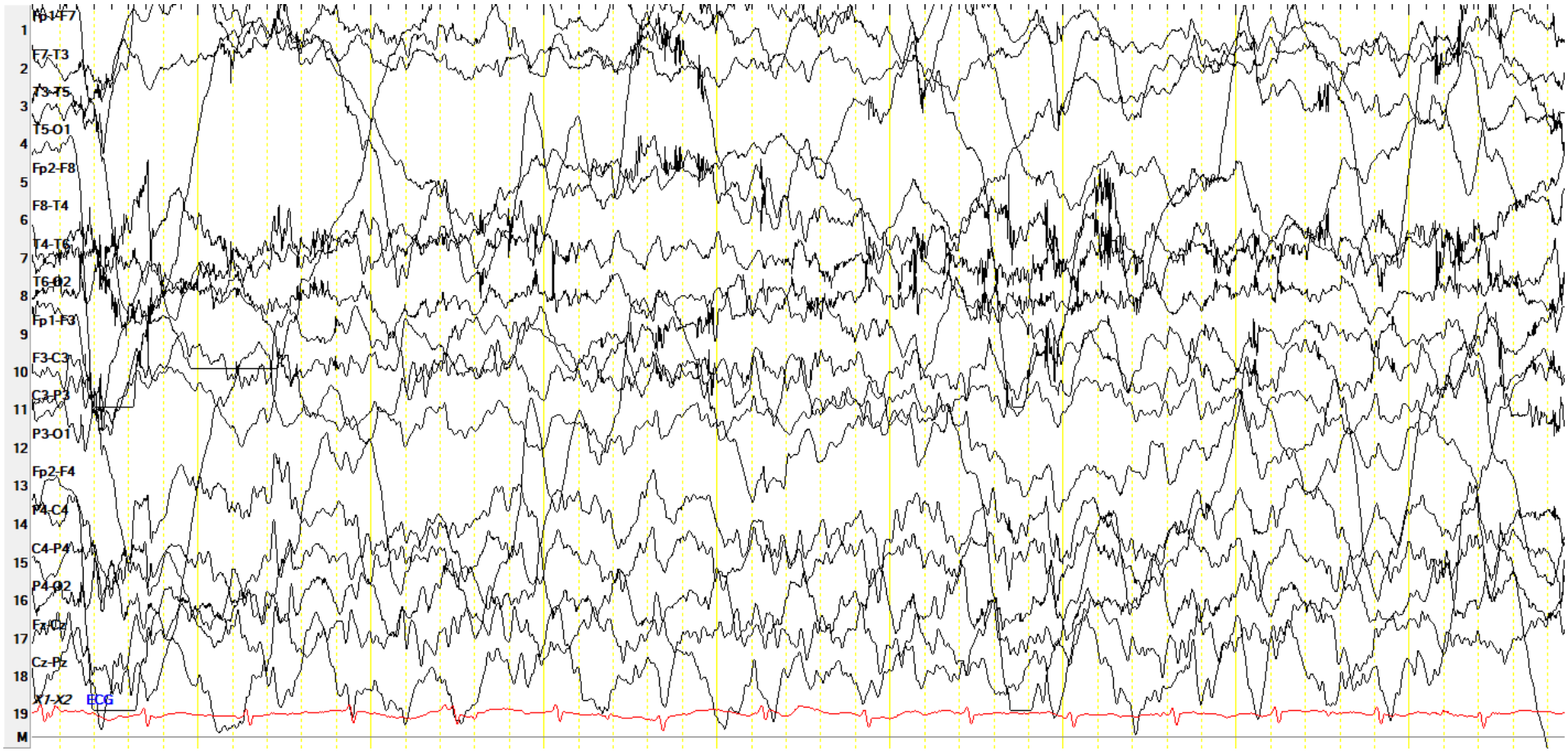
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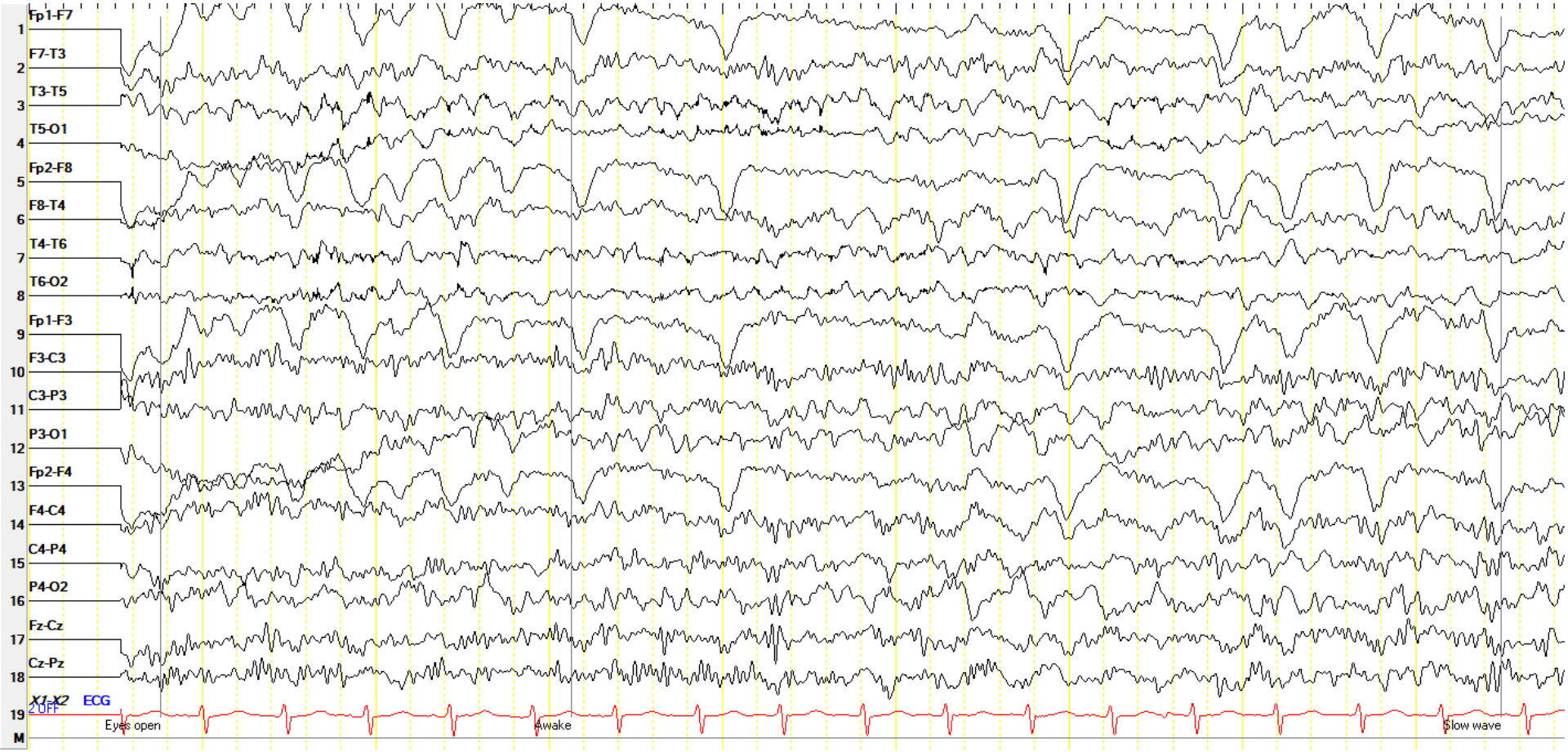
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P4-O2
Fz-Cz
Cz-Pz
X1-X2 ECG
2 OFF
Eyes open
Awake
Slow wave

NCSE with coma

- In the critically ill coma population, there is considerable controversy about whether to treat NCSE as aggressively as convulsive status epilepticus.

Refractory nonconvulsive status epilepticus

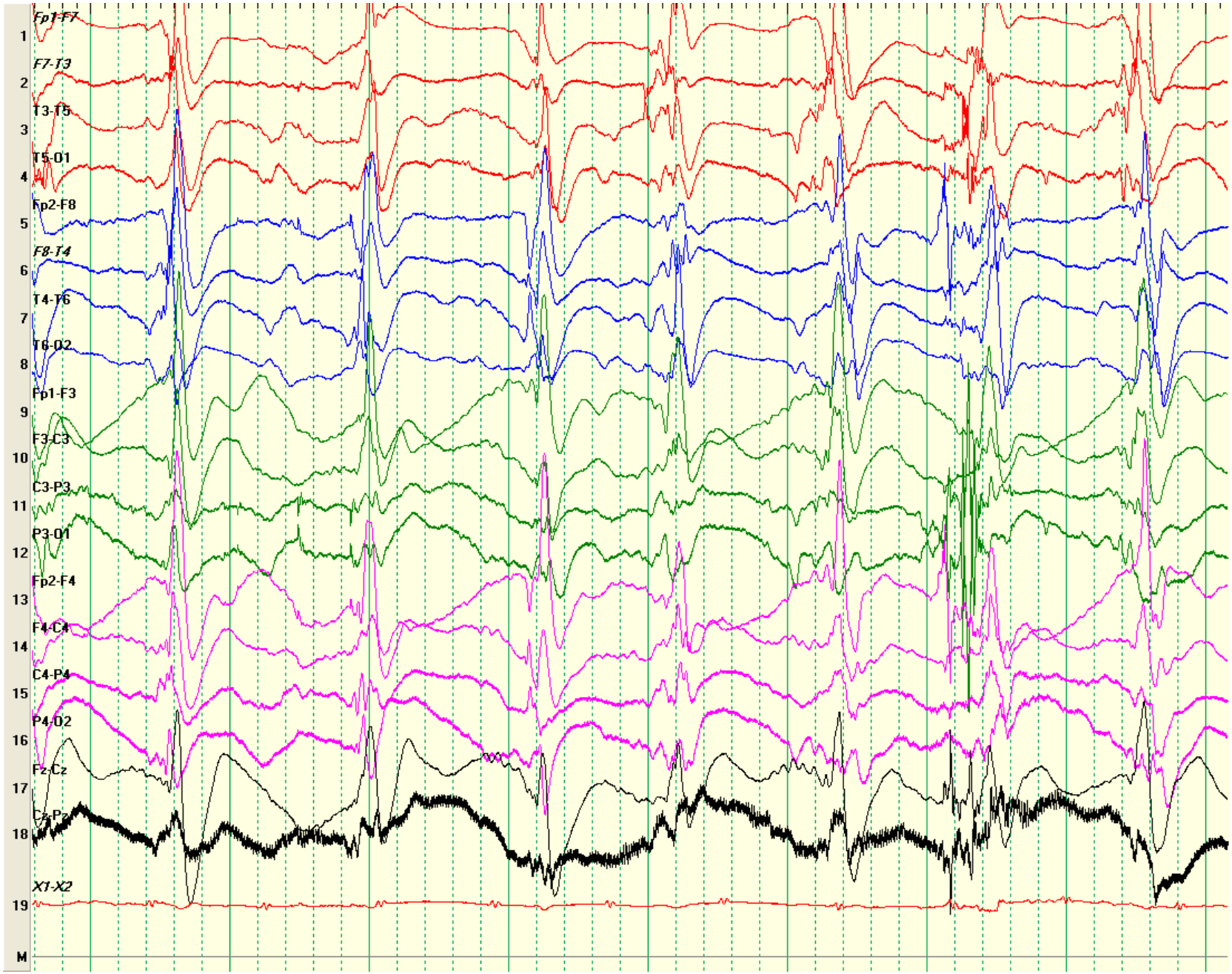
- Refractory status epilepticus (RSE) refers to status epilepticus that continues despite administration of therapeutic doses of two or more anti-seizure drugs.

- Treatment of refractory NCSE must be individualized. Examples of situations that may warrant aggressive therapy include subtle status epilepticus developing from generalized convulsive seizures, NCSE with acute brain injury, an cryptogenic new-onset refractory status epilepticus (NORSE).

- NORSE is a clinical presentation, not a specific diagnosis, in a patient without active epilepsy or other preexisting relevant neurological disorder, with new onset of refractory status epilepticus without a clear acute or active structural, toxic or metabolic cause.

Epilepsia. 2018;59:745–752.

NCSE with coma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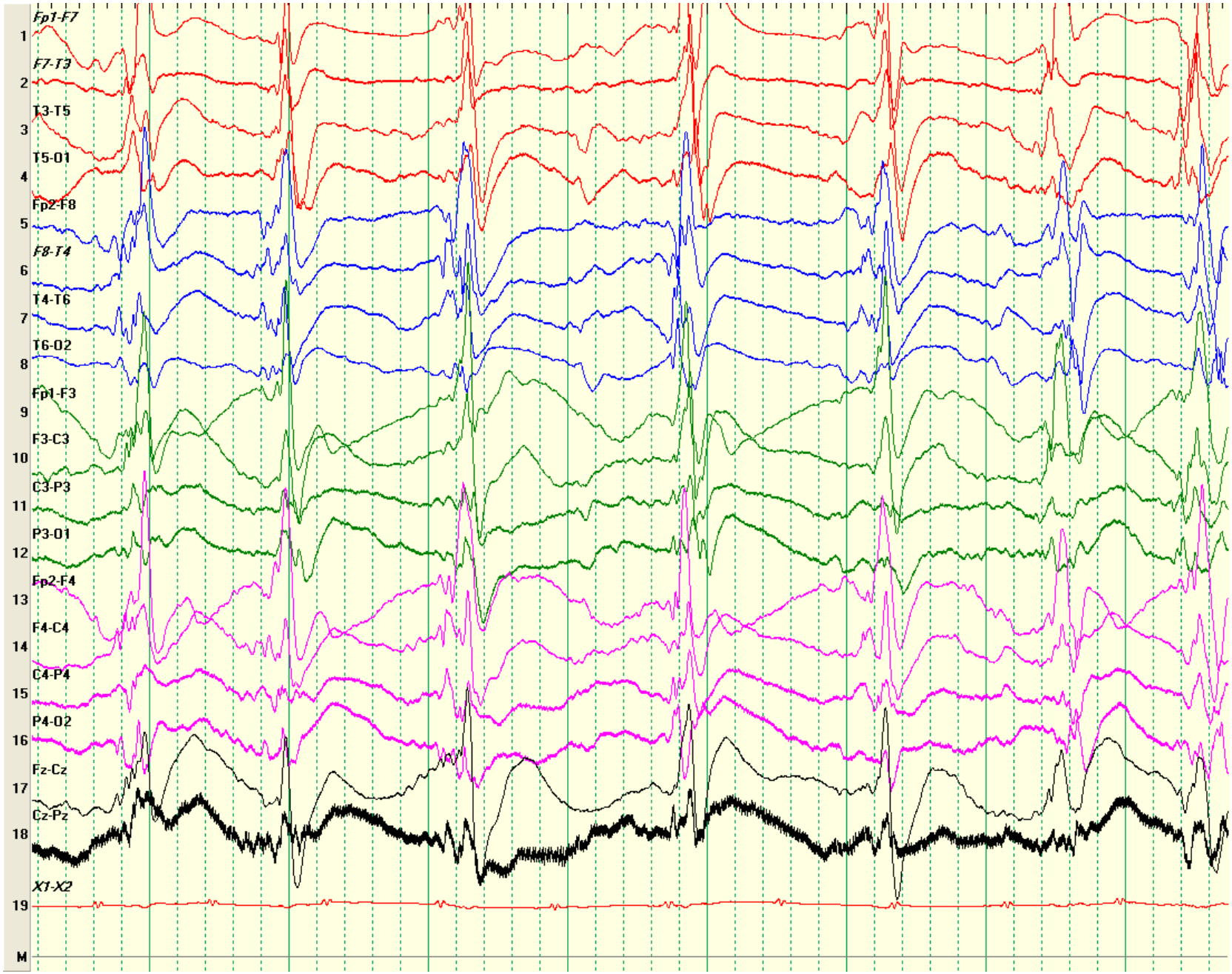
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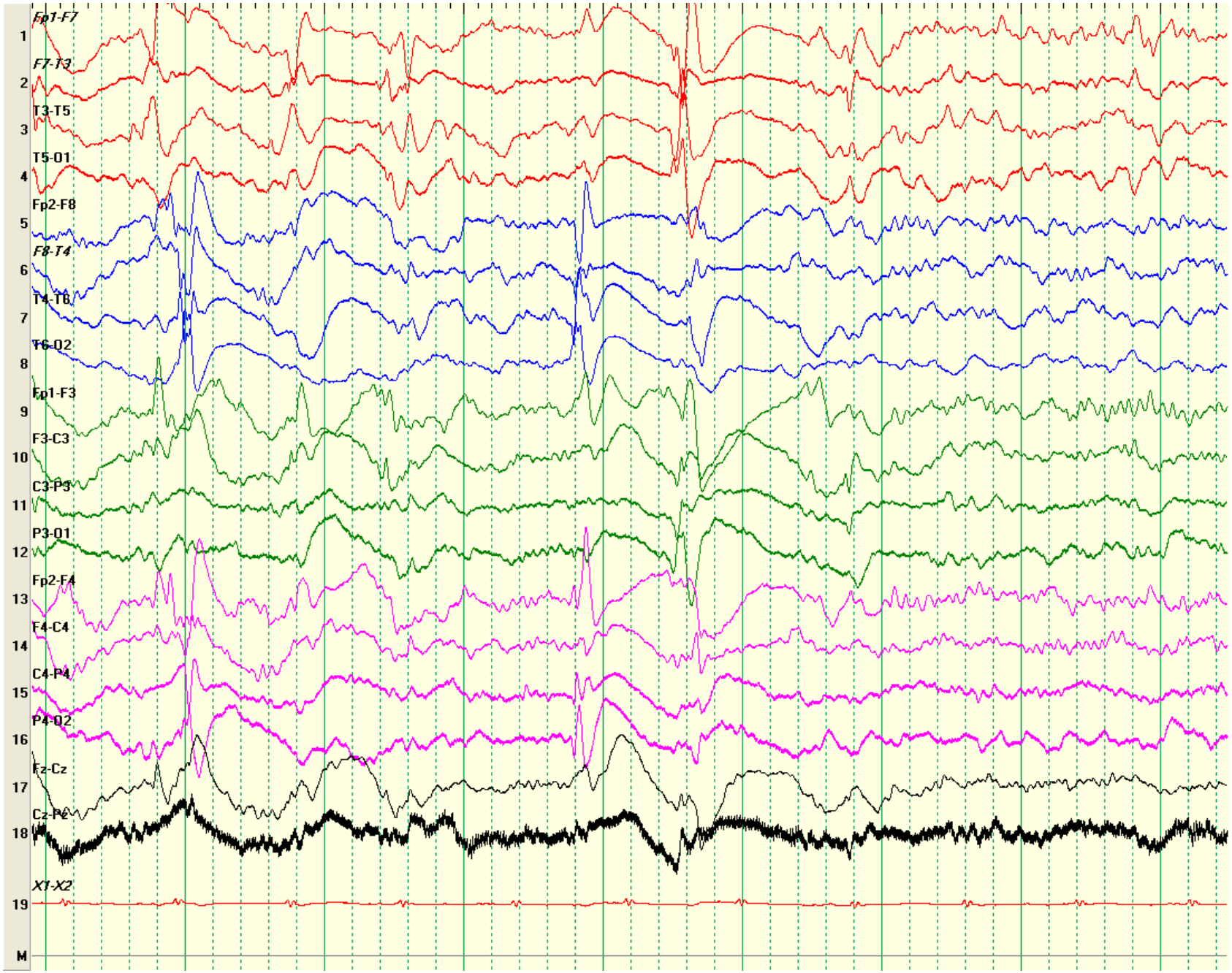
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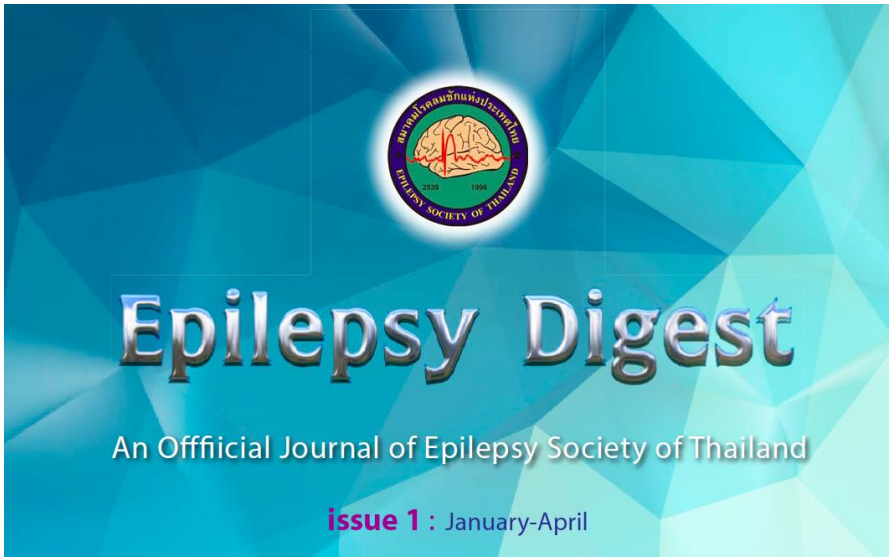
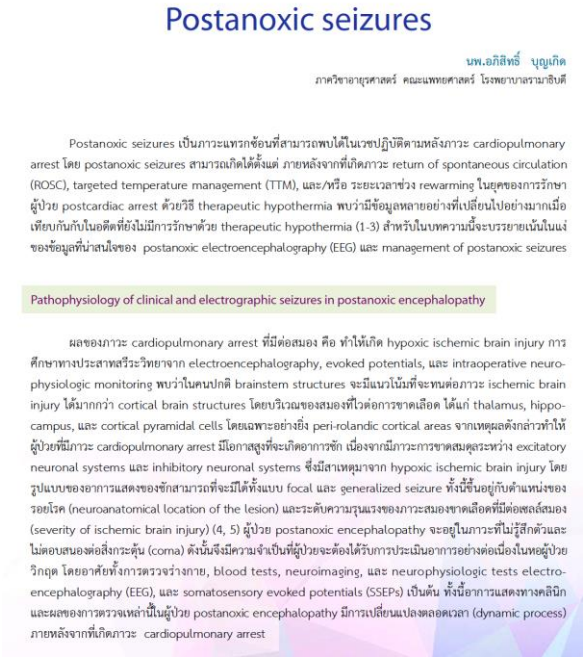
American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 version

J Clin Neurophysiol 2013;30: 1–27)

Postanoxic status epilepticus (PSE)

- Thai epilepsy society (http://thaiepilepsysociety.com/epilepsy-digest-2017-issue-1-jan-april/)





Postanoxic seizures

นพ.อภิสิทธิ์ บุญเกิด
ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี

Postanoxic seizures เป็นภาวะแทรกซ้อนที่สามารถพบได้ในเวชปฏิบัติตามหลังภาวะ cardiopulmonary arrest โดย postanoxic seizures สามารถเกิดได้ตั้งแต่ ภายหลังจากที่เกิดภาวะ return of spontaneous circulation (ROSC), targeted temperature management (TTM), และ/หรือ ระยะเวลาช่วง rewarming ในยุคของการรักษาผู้ป่วย postcardiac arrest ด้วยวิธี therapeutic hypothermia พบว่ามีข้อมูลหลายอย่างที่เปลี่ยนไปอย่างมากเมื่อเทียบกับในอดีตที่ยังไม่มีการรักษาด้วย therapeutic hypothermia (1-3) สำหรับในบทความนี้จะบรรยายเน้นในแง่ของข้อมูลที่น่าสนใจของ postanoxic electroencephalography (EEG) และ management of postanoxic seizures

Pathophysiology of clinical and electrographic seizures in postanoxic encephalopathy

ผลของภาวะ cardiopulmonary arrest ที่มีต่อสมอง คือ ทำให้เกิด hypoxic ischemic brain injury การศึกษาทางประสาทสรีระวิทยาจาก electroencephalography, evoked potentials, และ intraoperative neurophysiologic monitoring พบว่าในคนปกติ brainstem structures จะมีแนวโน้มที่จะทนต่อภาวะ ischemic brain injury ได้มากกว่า cortical brain structures โดยบริเวณของสมองที่ไวต่อการขาดเลือด ได้แก่ thalamus, hippocampus, และ cortical pyramidal cells โดยเฉพาะอย่างยิ่ง peri-rolandic cortical areas จากเหตุผลดังกล่าวทำให้ผู้ป่วยที่มีภาวะ cardiopulmonary arrest มีโอกาสสูงที่จะเกิดอาการชัก เนื่องจากมีภาวะการขาดสมดุลระหว่าง excitatory neuronal systems และ inhibitory neuronal systems ซึ่งมีสาเหตุมาจาก hypoxic ischemic brain injury โดยรูปแบบของอาการแสดงของชักสามารถที่จะมีได้ทั้งแบบ focal และ generalized seizure ทั้งนี้ขึ้นอยู่กับตำแหน่งของรอยโรค (neuroanatomical location of the lesion) และระดับความรุนแรงของภาวะสมองขาดเลือดที่มีต่อเซลล์สมอง (severity of ischemic brain injury) (4, 5) ผู้ป่วย postanoxic encephalopathy จะอยู่ในภาวะที่ไม่รู้สึกตัวและไม่ตอบสนองต่อสิ่งกระตุ้น (coma) ดังนั้นจึงมีความจำเป็นที่ผู้ป่วยจะต้องได้รับการประเมินอาการอย่างต่อเนื่องในหอผู้ป่วยวิกฤต โดยอาศัยทั้งการตรวจร่างกาย, blood tests, neuroimaging, และ neurophysiologic tests electroencephalography (EEG), และ somatosensory evoked potentials (SSEPs) เป็นต้น ทั้งนี้อาการแสดงทางคลินิกและผลของการตรวจเหล่านี้ในผู้ป่วย postanoxic encephalopathy มีการเปลี่ยนแปลงตลอดเวลา (dynamic process) ภายหลังจากที่เกิดภาวะ cardiopulmonary arrest

The end