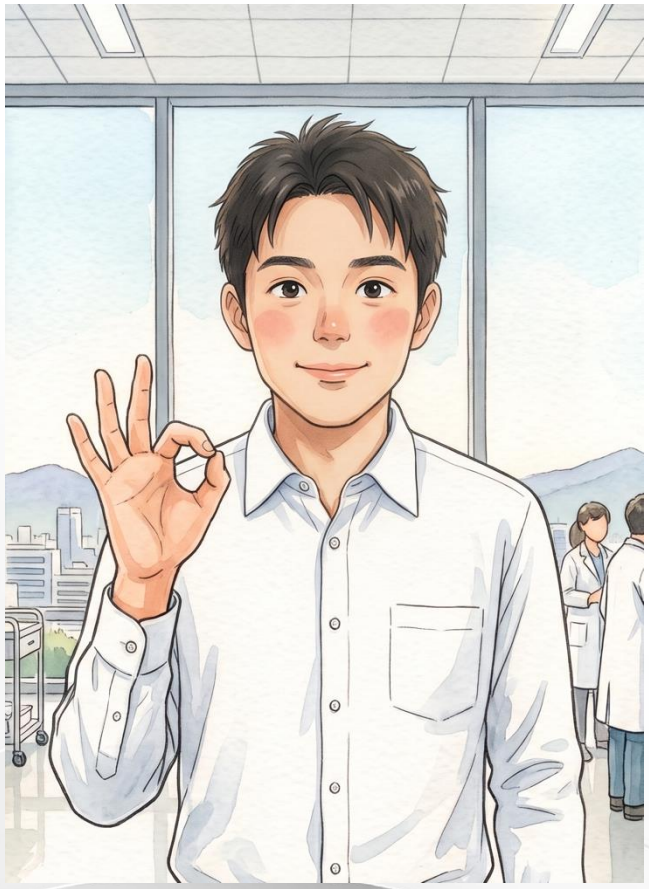
EST 30th ANNIVERSARY ANNUAL MEETING



First Episode Seizure

Treat or Not Treat

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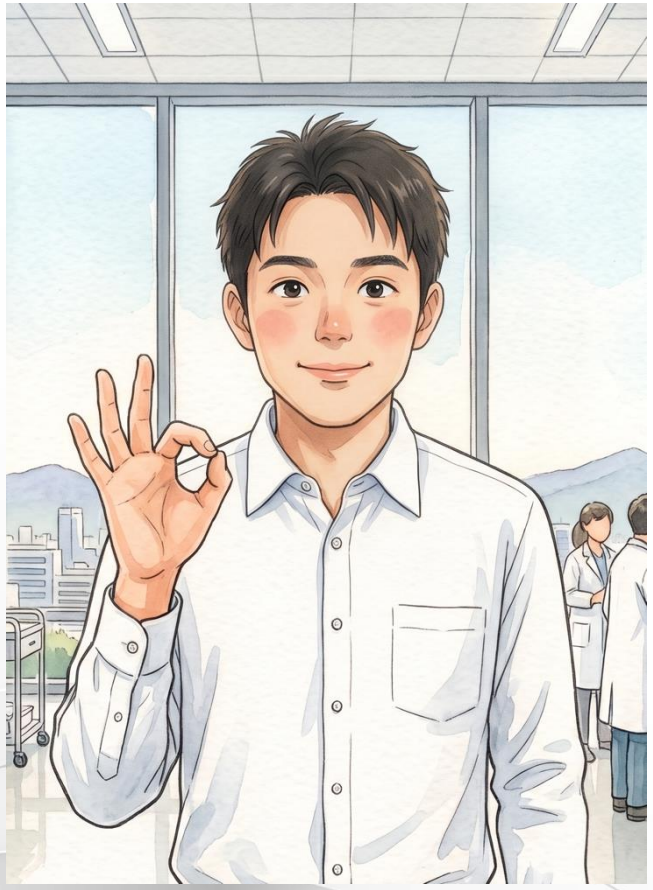

The "First Seizure" Dilemma – To Treat or Not to Treat

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Key Considerations

1. Predicting Recurrence

2. Evidence for Treatment Benefit

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Seizure vs. Epilepsy

SEIZURE

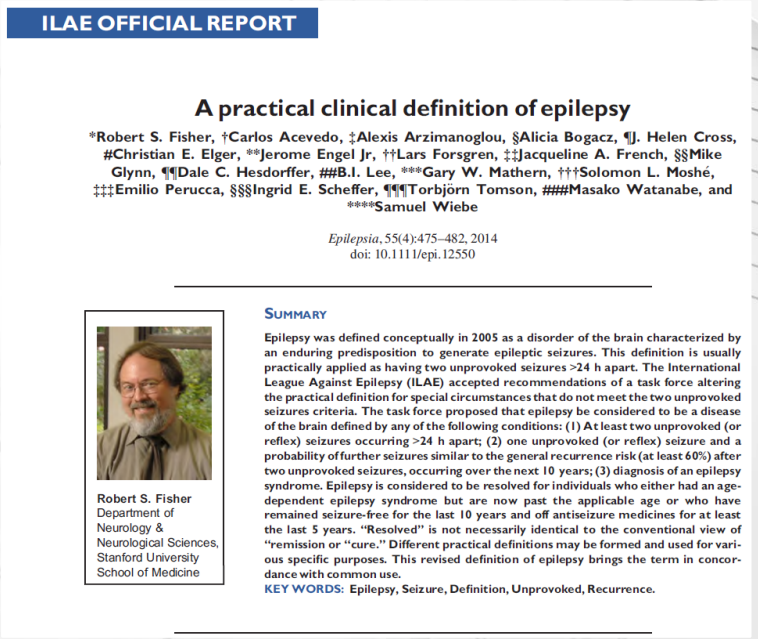
A single event

A transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain

EPILEPSY

An enduring disease

A disorder of the brain characterized by an enduring predisposition to generate epileptic seizures



ILAE OFFICIAL REPORT

A practical clinical definition of epilepsy

*Robert S. Fisher, †Carlos Acevedo, ‡Alexis Arzimanoglou, §Alicia Bogacz, ¶J. Helen Cross, #Christian E. Elger, **Jerome Engel Jr, ††Lars Forsgren, ‡‡Jacqueline A. French, §§Mike Glynn, ¶¶Dale C. Hesdorffer, ##B.I. Lee, ***Gary W. Mathern, †††Solomon L. Moshé, ‡‡‡Emilio Perucca, §§§Ingrid E. Scheffer, ¶¶¶Torbjörn Tomson, ###Masako Watanabe, and ****Samuel Wiebe

Epilepsia, 55(4):475–482, 2014
doi: 10.1111/epi.12550

Robert S. Fisher
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SUMMARY

Epilepsy was defined conceptually in 2005 as a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures. This definition is usually practically applied as having two unprovoked seizures >24 h apart. The International League Against Epilepsy (ILAE) accepted recommendations of a task force altering the practical definition for special circumstances that do not meet the two unprovoked seizures criteria. The task force proposed that epilepsy be considered to be a disease of the brain defined by any of the following conditions: (1) At least two unprovoked (or reflex) seizures occurring >24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome. Epilepsy is considered to be resolved for individuals who either had an age-dependent epilepsy syndrome but are now past the applicable age or who have remained seizure-free for the last 10 years and off antiseizure medicines for at least the last 5 years. "Resolved" is not necessarily identical to the conventional view of "remission or "cure." Different practical definitions may be formed and used for various specific purposes. This revised definition of epilepsy brings the term in concordance with common use.

KEY WORDS: Epilepsy, Seizure, Definition, Unprovoked, Recurrence.

~10% will have a seizure in their lifetime — only **2–3%** develop epilepsy

Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014; 55: 475–482.
Feyissa AM, Cascino GD. The Argument for a More Patient Attitude Toward a Single Unprovoked Seizure: Wait for It? Mayo Clin Proc. 2023 Jan;98(1):23-30.

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Provoked or Unprovoked?

PROVOKED

Acute cause, within ~1 week.

Stroke · head injury · CNS infection · metabolic · withdrawal

UNPROVOKED

No acute cause

Remote symptomatic · genetic · unknown

Table 1. Proposed cutoff values for acute symptomatic seizures in common metabolic disorders

Biochemical parameter	Value
Serum glucose	<36 mg/dl (2.0 mM) or >450 mg/dl (25 mM) associated with ketoacidosis (whether or not there is long-standing diabetes)
Serum sodium	<115 mg/dl (<5 mM)
Serum calcium	<5.0 mg/dl (<1.2 mM)
Serum magnesium	<0.8 mg/dl (<0.3 mM)
Urea nitrogen	<100 mg/dl (>35.7 mM)
Creatinine	>10.0 mg/dl (>884 μM)

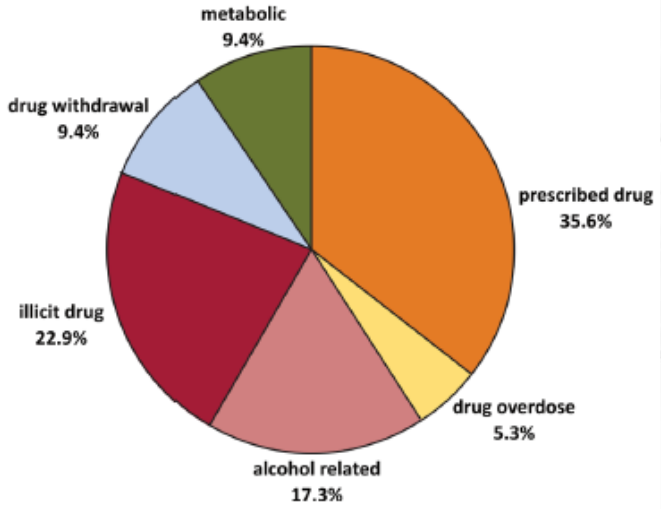
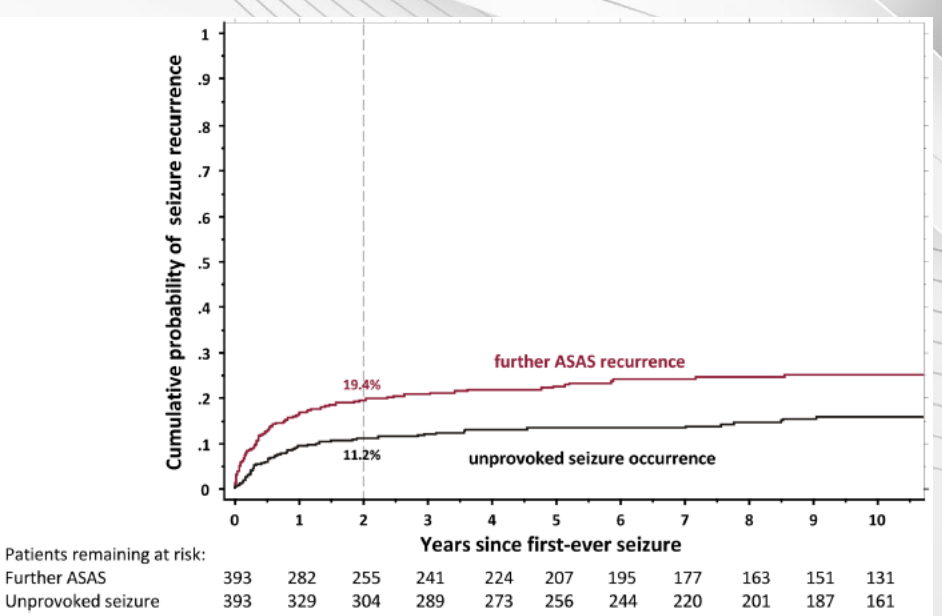
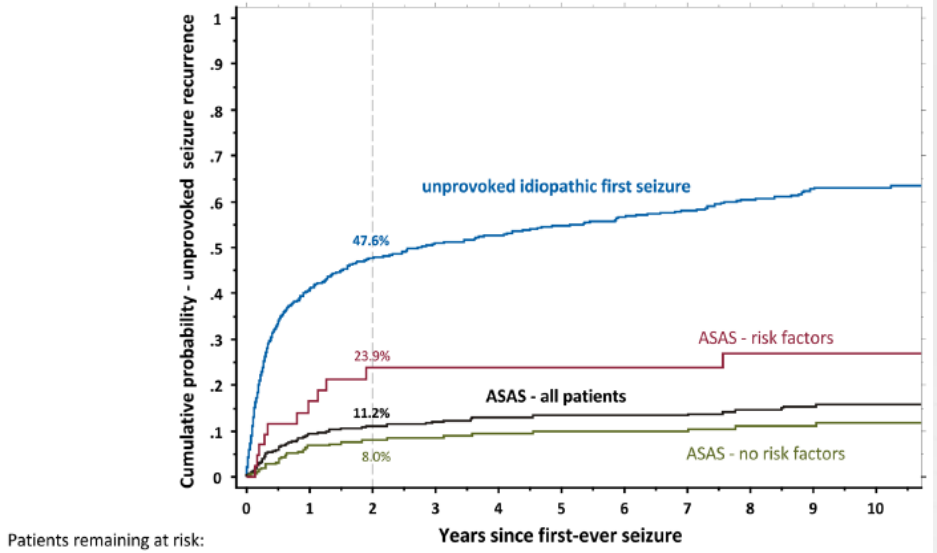


FIGURE 1 Etiologies of acute symptomatic seizure due to acute systemic causes.



Patients remaining at risk:

Further ASAS	393	282	255	241	224	207	195	177	163	151	131
Unprovoked seizure	393	329	304	289	273	256	244	220	201	187	161



Patients remaining at risk:

Unprovoked idiopathic	874	489	388	339	295	256	211	174	140	110	89
ASAS - all patients	393	329	304	289	273	256	244	220	201	187	161

Beghi E, Carpio A, Forsgren L, Hesdorffer DC, Malmgren K, Sander JW, Tomson T, Hauser WA. Recommendation for a definition of acute symptomatic seizure. Epilepsia. 2010 Apr;51(4):671-5.

Lawn N, Wallefeld W, Lee J, Dunne J. Clinical features and prognosis of first-ever acute symptomatic seizures due to acute systemic causes. Epilepsia. 2025 Nov;66(11):4272-4282.

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Who's at Higher Risk?

Evidence-based guideline: Management of an unprovoked first seizure in adults

Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society

Presence of interictal epileptiform EEG discharges implies increased risk of recurrence after the first unprovoked seizure: Report of the International League Against Epilepsy and International Federation of Clinical Neurophysiology

Betül Baykan[1,2] | John Dunne[3,4] | Samuel Wiebe[5] | Louis Maillard[6] | Sandor Beniczky[7,8] | Michalis Koutroumanidis[9] | Margitta Seeck[10]

The overall proportion with seizure recurrence was higher in patients with IEDs (**60%**) compared to those without (**40%**), $p < .001$

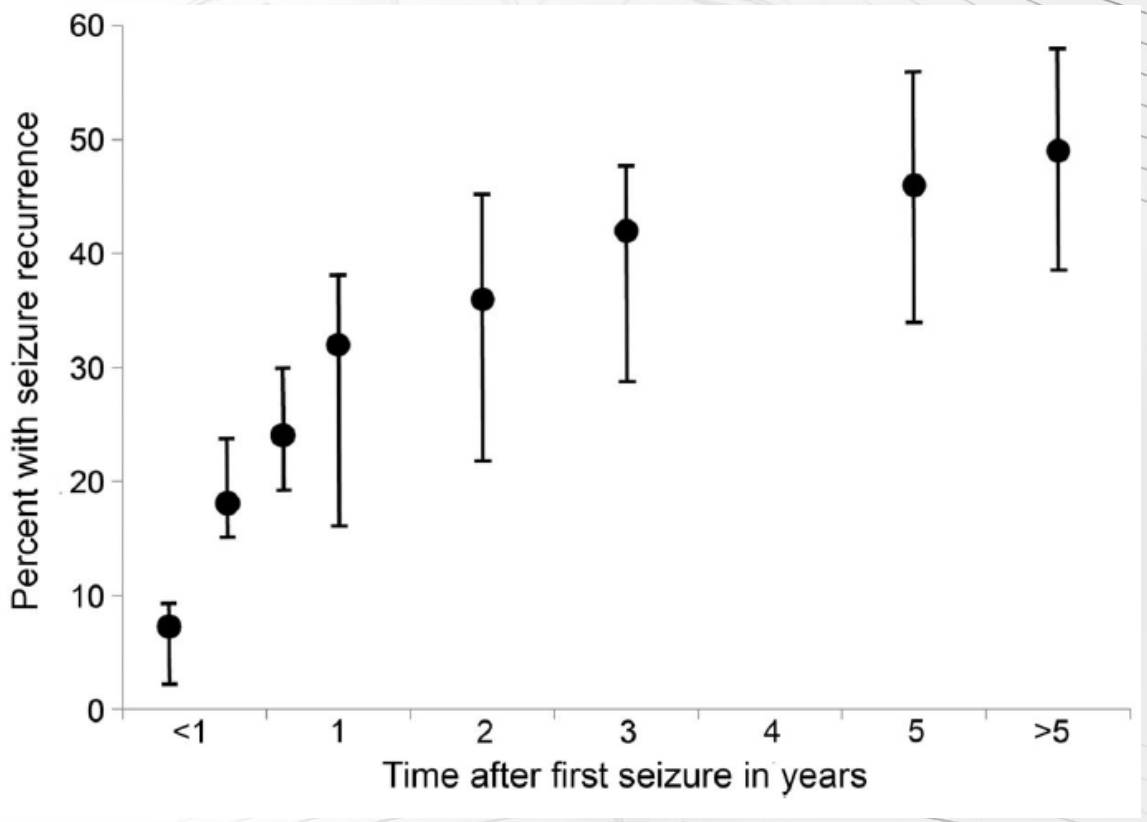
Not predictive: age, sex, family history, seizure type, first-presentation status epilepticus.

Krumholz A, Wiebe S, Gronseth GS, Gloss DS, Sanchez AM, Kabir AA, Liferidge AT, Martello JP, Kanner AM, Shinnar S, Hopp JL, French JA. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2015 Apr 21;84(16):1705-13.
Baykan B, Dunne J, Wiebe S, Maillard L, Beniczky S, Koutroumanidis M, Seeck M. Presence of interictal epileptiform EEG discharges implies increased risk of recurrence after the first unprovoked seizure: Report of the International League Against Epilepsy and International Federation of Clinical Neurophysiology. Epilepsia. 2025 Oct;66(10):3920-3936.

Risk of seizure recurrence is front-loaded — highest in year 1–2

Evidence-based guideline: Management of an unprovoked first seizure in adults

Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society



Krumholz A, Wiebe S, Gronseth GS, Gloss DS, Sanchez AM, Kabir AA, Liferidge AT, Martello JP, Kanner AM, Shinnar S, Hopp JL, French JA. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2015 Apr 21;84(16):1705-13.

When Does It Become Epilepsy?

≥60% Seizure risk in 10 years = Epilepsy

Prediction of risk of seizure recurrence after a single seizure and early epilepsy: further results from the MESS trial

Lois G Kim, Tony L Johnson, Anthony G Marson, David W Chadwick on behalf of the MRC MESS Study group

	Prognostic index
Starting value	
One seizure prior to presentation	0
Two or three seizures prior to presentation	1
Four or more seizures prior to presentation	2
Add if present	
Neurological disorder or deficit, learning disability, or developmental delay	1
Abnormal EEG	1
Risk classification group for seizure recurrence*	**Final score**
Low risk	0
Medium risk	1
High risk	2–4

	Treatment allocation	Probability of seizure by 1 year	Probability of seizure by 3 years	Probability of seizure by 5 years
Low risk	Start	0·26	0·35	0·39
	Delay	0·19	0·28	0·30
Medium risk	Start	0·24	0·35	0·39
	Delay	0·35	0·50	0·56
High risk	Start	0·36	0·46	0·50
	Delay	0·59	0·67	0·73

Kim LG, Johnson TL, Marson AG, Chadwick DW; MRC MESS Study group. Prediction of risk of seizure recurrence after a single seizure and early epilepsy: further results from the MESS trial. Lancet Neurol. 2006 Apr;5(4):317-22.

Part 1 Summary:

Who is at high risk of seizure recurrence or may benefit from treatment?

- High recurrence risk (> 60% in 10 years)
- Unprovoked seizure with prior brain insult
  - Post-stroke
  - Post CNS infection
  - Learning disability/Developmental delay
  - Neurological deficit
- Abnormal EEG
- Abnormal Imaging
  - Clinically relevant structural lesions
  - Judged the cause of the seizure
- Nocturnal (2.1x risk)

EVIDENCES FOR TREATMENT BENEFIT

FIRST Trial

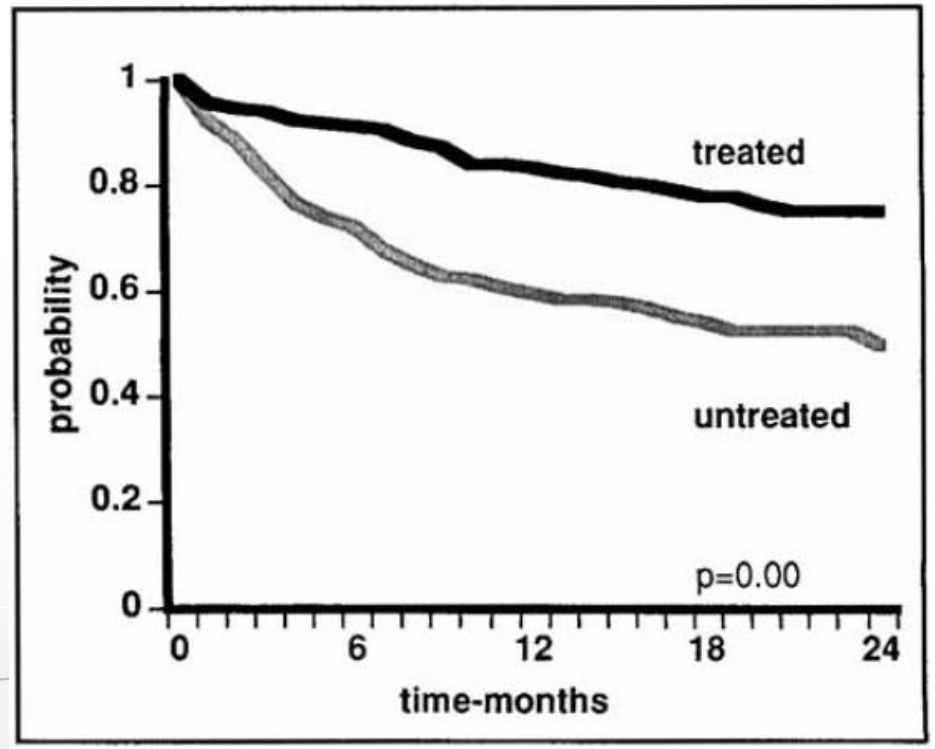


Figure. Cumulative probability of remaining seizure-free by treatment, all subjects.

Randomized clinical trial on the efficacy of antiepileptic drugs in reducing the risk of relapse after a first unprovoked tonic-clonic seizure

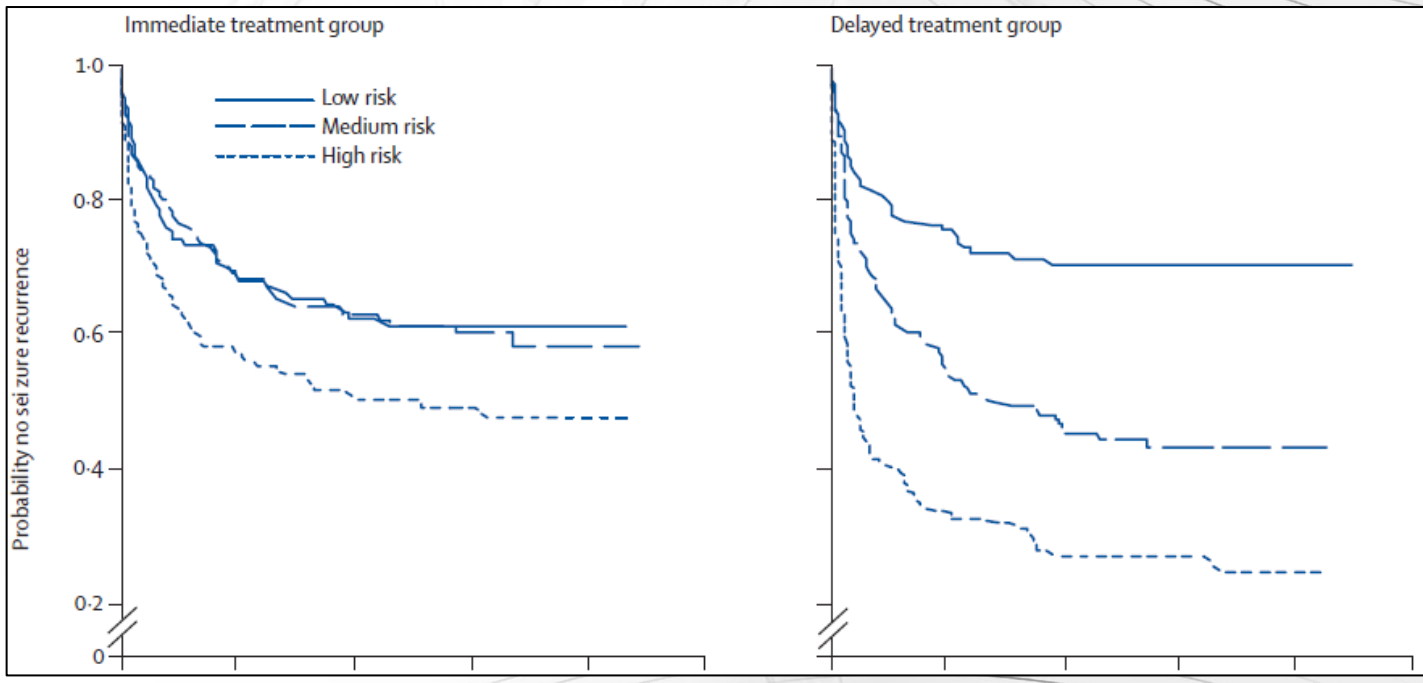
First Seizure Trial Group (FIR.S.T. GROUP)*

- The cumulative time-dependent risk of relapse among treated subjects was 25% by 24 months. The corresponding figure for untreated subjects was 51%.
- The risk of relapse was 2.8 times higher (95% CI, 1.9 to 4.2) for untreated subjects.

Randomized clinical trial on the efficacy of antiepileptic drugs in reducing the risk of relapse after a first unprovoked tonic-clonic seizure. First Seizure Trial Group (FIR.S.T. Group). Neurology. 1993 Mar;43(3 Pt 1):478-83.

MESS Trial

- Reduces Recurrence Risk: Significantly delays and reduces the risk of further seizures (HR 1.4)
- Concentrated Benefit (Years 1–3): Clinical efficacy is most prominent during the first 2–3 years post-diagnosis
  - High-Risk Group Benefits (Delay vs. Start)
    - 1-Year Risk: Reduced from 59% to 36%
    - 3-Year Risk: Reduced from 67% to 46%
    - 5-Year Risk: Reduced from 73% to 50%
  - Medium-Risk Group Benefits (Delay vs. Start)
    - 1-Year Risk: Reduced from 35% to 24%
    - 3-Year Risk: Reduced from 50% to 35%
    - 5-Year Risk: Reduced from 56% to 39%



- Prevents Psychosocial Impact: Avoids social complications, such as threats to driving and employment
- Does NOT alter long-term terminal remission rates at 3–5 years

Kim LG, Johnson TL, Marson AG, Chadwick DW; MRC MESS Study group. Prediction of risk of seizure recurrence after a single seizure and early epilepsy: further results from the MESS trial. Lancet Neurol. 2006 Apr;5(4):317-22.

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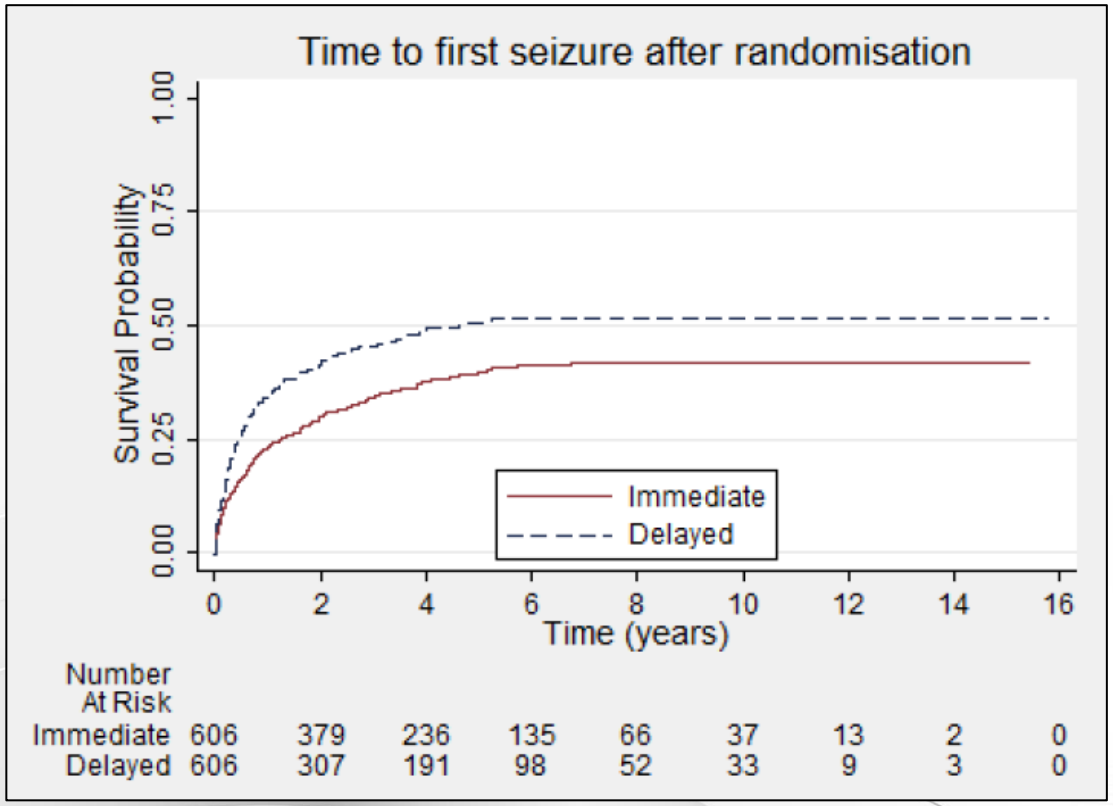
Cochrane 2021



Cochrane Library

Cochrane Database of Systematic Reviews

Immediate antiepileptic drug treatment, versus placebo, deferred, or no treatment for first unprovoked seizure (Review)

Leone MA, Giussani G, Nevitt SJ, Marson AG, Beghi E

Percentages of participants who experienced seizure recurrence from the immediate treatment group compared to the control group were

- 23.4% versus 34.3% at one year
- 30.2% versus 41.4% at two years
- 39.6% versus 50.6% at five years

A log rank test showed a highly significant difference between the treatment groups ($P < 0.001$)

Leone MA, Giussani G, Nevitt SJ, Marson AG, Beghi E. Immediate antiepileptic drug treatment, versus placebo, deferred, or no treatment for first unprovoked seizure. Cochrane Database Syst Rev. 2021 May 4;5(5):CD007144.

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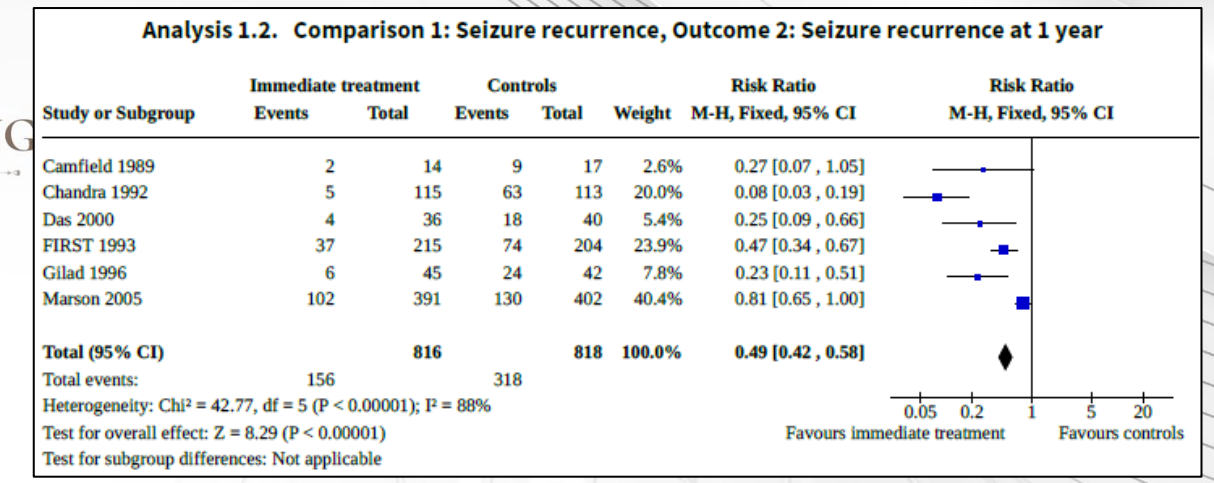
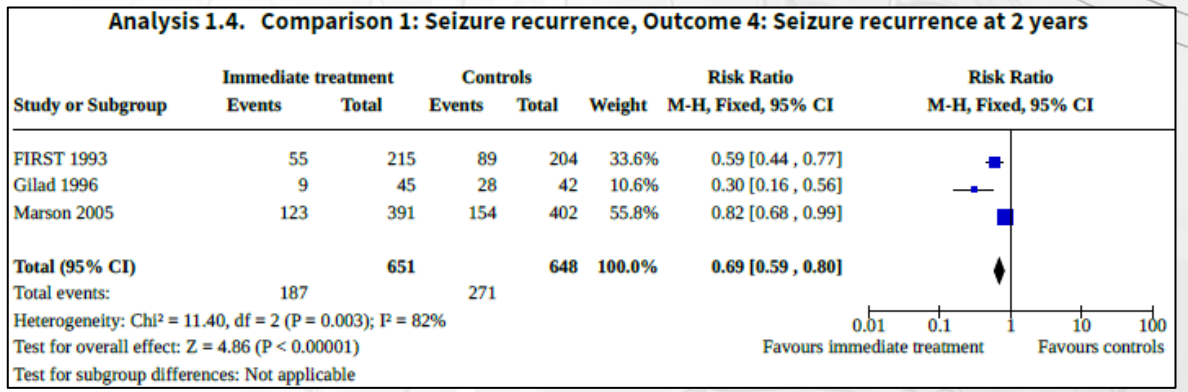
Cochrane 2021

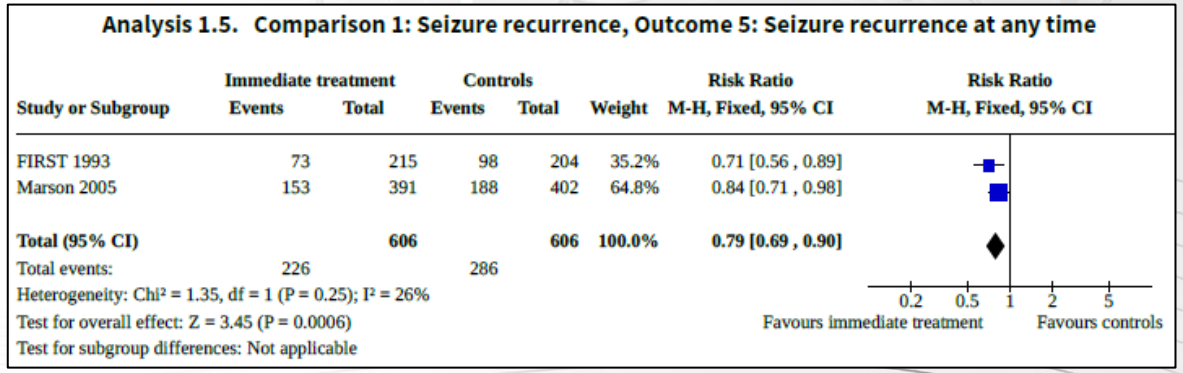
Immediate treatment lowers recurrence risk across all timeframes

- At 12 Months: Recurrence risk reduced by 51% (RR 0.49, 95% CI 0.42 to 0.58)
- At 24 Months: Recurrence risk reduced by 31% (RR 0.69, 95% CI 0.59 to 0.80)
- At any time: Recurrence risk reduced by 21% (RR 0.79, 95% CI 0.69 to 0.90)

Delayed Seizure Occurrence: Significantly increases the time to first seizure (HR 0.70, 95% CI 0.59 to 0.83)







Leone MA, Giussani G, Nevitt SJ, Marson AG, Beghi E. Immediate antiepileptic drug treatment, versus placebo, deferred, or no treatment for first unprovoked seizure. Cochrane Database Syst Rev. 2021 May 4;5(5):CD007144.

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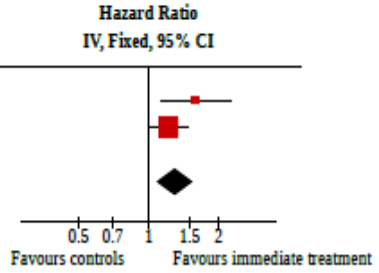
Analysis 2.5. Comparison 2: Remission, Outcome 5: Time to immediate 2-year remission

Study or Subgroup	log[Hazard Ratio]	SE	Immediate treatment Total	Controls Total	Weight	Hazard Ratio IV, Fixed, 95% CI
FIRST 1993	0.46021	0.17632	215	204	22.4%	1.58 [1.12 , 2.24]
Marson 2005	0.19568	0.09481	391	402	77.6%	1.22 [1.01 , 1.46]
Total (95% CI)			**606**	**606**	**100.0%**	**1.29 [1.10 , 1.52]**

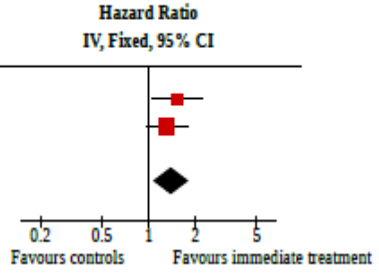
Heterogeneity: Chi² = 1.75, df = 1 (P = 0.19); I² = 43%
Test for overall effect: Z = 3.05 (P = 0.002)
Test for subgroup differences: Not applicable



Analysis 2.6. Comparison 2: Remission, Outcome 6: Time to immediate 5-year remission

Study or Subgroup	log[Hazard Ratio]	SE	Immediate treatment Total	Controls Total	Weight	Hazard Ratio IV, Fixed, 95% CI
FIRST 1993	0.42308	0.19532	215	204	39.1%	1.53 [1.04 , 2.24]
Marson 2005	0.26611	0.15665	391	402	60.9%	1.30 [0.96 , 1.77]
Total (95% CI)			**606**	**606**	**100.0%**	**1.39 [1.09 , 1.76]**

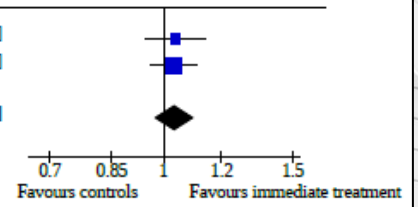
Heterogeneity: Chi² = 0.39, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 2.68 (P = 0.007)
Test for subgroup differences: Not applicable



Analysis 2.3. Comparison 2: Remission, Outcome 3: 2-year remission at any time

Study or Subgroup	Immediate treatment Events	Total	Controls Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FIRST 1993	176	215	161	204	35.0%	1.04 [0.94 , 1.14]
Marson 2005	312	391	311	402	65.0%	1.03 [0.96 , 1.11]
Total (95% CI)		**606**		**606**	**100.0%**	**1.03 [0.98 , 1.09]**
Total events:	488		472			

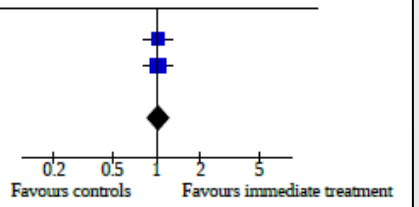
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.12 (P = 0.26)
Test for subgroup differences: Not applicable



Analysis 2.4. Comparison 2: Remission, Outcome 4: 5-year remission at any time

Study or Subgroup	Immediate treatment Events	Total	Controls Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
FIRST 1993	88	215	82	204	44.1%	1.02 [0.81 , 1.28]
Marson 2005	108	391	108	402	55.9%	1.03 [0.82 , 1.29]
Total (95% CI)		**606**		**606**	**100.0%**	**1.02 [0.87 , 1.21]**
Total events:	196		190			

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.28 (P = 0.78)
Test for subgroup differences: Not applicable



Immediate AED Treatment

- Speeds Up Initial Remission: Accelerates the time it takes for patients to achieve their first 2-year (HR 1.29) and 5-year (HR 1.39) seizure-free periods
- No Ultimate Remission Benefit: Does not increase the final likelihood of achieving long-term seizure freedom (2-year RR 1.03; 5-year RR 1.02)

Leone MA, Giussani G, Nevitt SJ, Marson AG, Beghi E. Immediate antiepileptic drug treatment, versus placebo, deferred, or no treatment for first unprovoked seizure. Cochrane Database Syst Rev. 2021 May 4;5(5):CD007144.

Part 2 summary:

- High risk recurrence in: prior brain insult, abnormal EEG/imaging, neurological deficit
- Recurrence risk is front-loaded
- Immediate treatment will reduce the risk of recurrence by 20-50% depending on the time frame
- Immediate treatment accelerates initial remission but does not improve long-term remission rates
- Psychosocial and lifestyle considerations: driving and employment

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The "First Seizure" Dilemma – To Treat or Not to Treat

Sattawut Wongwiangjunt, M.D.

Division of Neurology, Siriraj Hospital, Mahidol University

When to start ASM?

Diagnosis of epilepsy

1. ≥ 2 unprovoked (or reflex) SZs occurring >24 hours apart

Fisher et al. Epilepsia 2014

What if?

A 50-year-old man presented with unprovoked GTC SZ
He had history of seizure when he was 7 years old.
Would you diagnose this patient EPILEPSY?

No clear time interval

When to start ASM?

Diagnosis of epilepsy

1. ≥ 2 unprovoked (or reflex) SZs occurring >24 hours apart
2. 1 unprovoked (or reflex) SZ with probability of further SZs (>60%) over the next 10 yr
3. Diagnosis of epileptic syndrome

Similar to general recurrent risk after 2 unprovoked SZs

Fisher et al. Epilepsia 2014

SPECIAL ARTICLE

Evidence-based guideline: Management of an unprovoked first seizure in adults

Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society

21-45% (36%)

				Seizure recurrences at various times, n (%)								
Ref.	Class	Age, y	No.	Treated	1 mo	3 mo	6 mo	1 y	2 y	3 y	5 y	>5 y
10, 11	I	70% >19	238	164 (69)	—	—	—	38 (16)	50 (21)	60 (29)	70 (34)	81 (39)
12, 13	I	72% >16	397	204 (51)	24 (6)	58 (15)	75 (19)	98 (25)	111 (28)	—	—	—
17	II	≥16	147	62 (42)	—	—	39 (27)	50 (34)	60 (41)	61 (41)	—	—
18	II	Mean >20	76	36 (47)	2 (3)	18 (24)	20 (26)	22 (29)	—	—	—	—
16	II	≥16	306	41 (13)		55 (18)	79 (26)	111 (36)	136 (44)	144 (47)	—	—
19	II	75% >15	424	?	38 (9)	89 (21)	127 (30)	153 (36)	191 (45)	204 (48)	237 (56)	244 (58)
20	II	14-91	497	127 (26)	—		—	191 (38)	—	—	—	—
15	II	60% >20	812	404 (50)	—		179 (22)	—	288 (35)	—	378 (46)	398 (49)
21	II	≥16	228	113 (50)	—	—	—	68 (30)	—	—	—	—
22	II	18-50	87	45 (52)	—		—	30 (34)	37 (43)	39 (45)	—	—
Total			3,212	1,196 (43)	64 (7)	220 (18)	519 (24)	761 (32)	873 (36)	508 (42)	685 (46)	723 (49)

Krumholz et al. Neurology 2015

SPECIAL ARTICLE

AMERICAN ACADEMY OF NEUROLOGY

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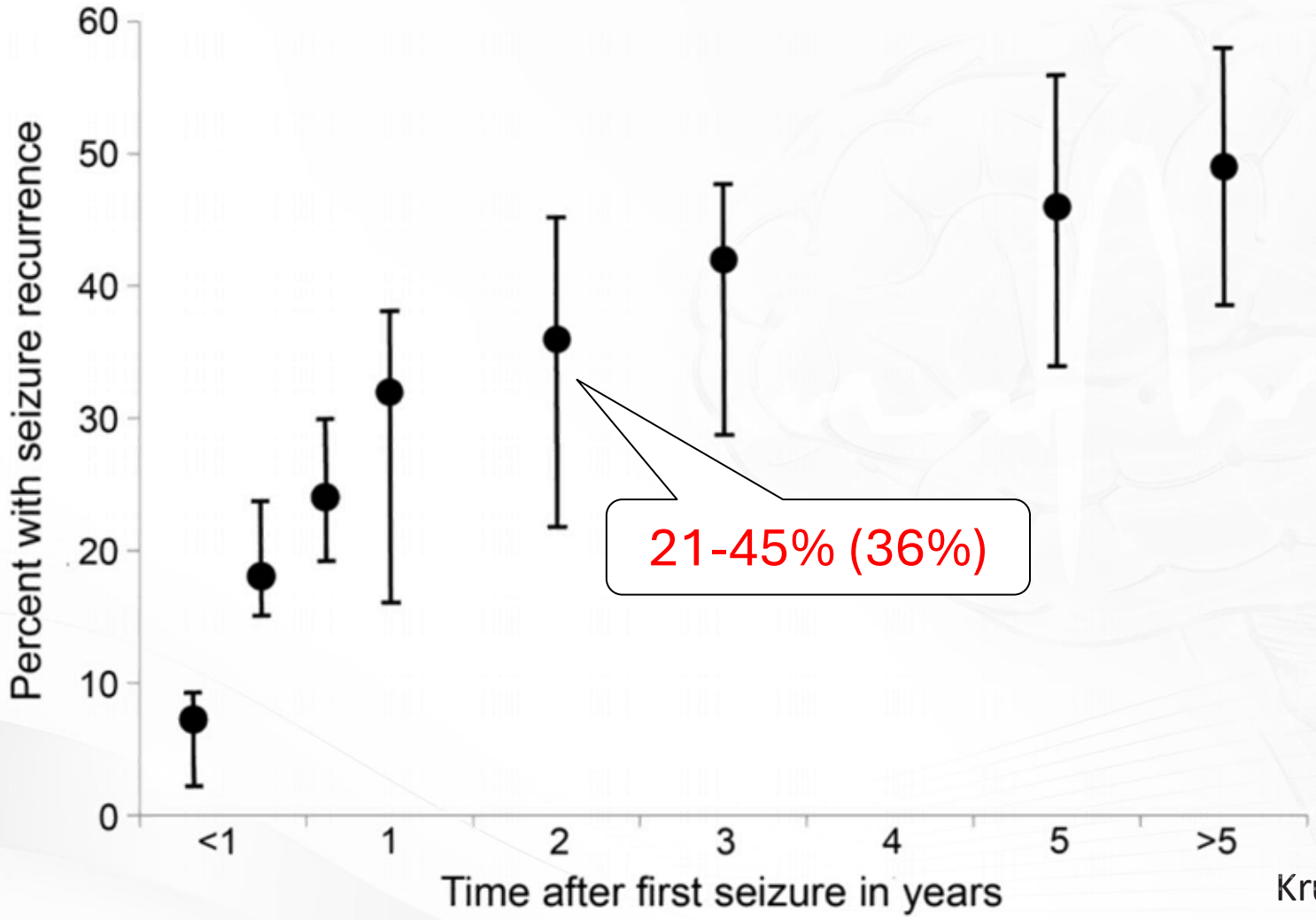

Krumholz et al. Neurology 2015

SPECIAL ARTICLE

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Management → What to consider?

1. Short-term risk for a seizure recurrence
2. Longer-term potential for seizure remission

3. Adverse effects

Krumholz et al. Neurology 2015

SPECIAL ARTICLE

Evidence-based guideline: Management of an unprovoked first seizure in adults

Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society

Management → What to consider?

1. **<u>Short-term risk for a seizure recurrence</u>**
2. Longer-term potential for seizure remission

3. Adverse effects

Krumholz et al. Neurology 2015

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SPECIAL ARTICLE

AMERICAN ACADEMY OF NEUROLOGY

Evidence-based guideline: Management of an unprovoked first seizure in adults

Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society

Short-term

Table 2 Rates for short-term (1 and 2 years) seizure recurrence after an unprovoked first seizure in adults as related to immediate antiepileptic drug treatment (Class I and II studies)

Ref.	Class	No.	Treated, n (%)	Recur. rate treated, n (%)	Recur. rate untreated, n (%)	Length of follow-up, y
12-14	I	397	204 (51)	36 (18)[a]	75 (39)	2
18	II	76	36 (47)	4 (11)[a]	18 (45)	1
15	II	812	404 (50)	129 (32)	159 (39)	2
21	II	228	113 (50)	5 (4)[a]	63 (55)	1
22	II	87	45 (52)	9 (20)[a]	28 (66)	2
Total		1,600	804 (50)	183 (23)	343 (43)	1 or 2

Krumholz et al. Neurology 2015

Treat 14 pts with a single seizure

in order to prevent a single seizure recurrence within the first 2 years.

Epilepsia, 49(Suppl. 1):26–28, 2008

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Received: 6 September 2025 | Accepted: 17 March 2026

DOI: 10.1002/epd2.70234

Epileptic Disorders

ORIGINAL ARTICLE

The second unprovoked seizure in a cohort of treated patients with a first unprovoked seizure

Revital Gandelman-Marton[1,2] | Jacques Theitler[1,2]

TABLE 2 Types of ASMs at first and last observations.

	First observation	Last observation[a]
LEV	35 (58.3)	31 (51.7)
PHT	10 (16.7)	2 (3.3)
CBZ	5 (8.3)	3 (5)
VPA	2 (3.3)	3 (5)
GBP	3 (5)	3 (5)
LTG	1 (1.7)	5 (8.3)
PRM	–	1 (1.7)
LEV + LCS	1 (1.7)	3 (5)
LEV + VPA	–	1 (1.8)
LEV + LTG	–	2 (3.3)
VPA + LTG		1 (1.7)
PHT + LTG	3 (5)	–
CBZ + LTG	–	2 (3.3)

- 2nd unprovoked seizure occurred in 43% (24/60)
- 75% of the recurrences occurred at 3 years.
- Risks higher in younger (32.9 vs. 46.9 years) (p = 0.010) and more likely to be women (64% vs. 28.6%) (p = 0.009)
- Women and younger patients may deserve closer monitoring following a 1st unprovoked seizure

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Long-term

Rates of 2-year seizure remission over the longer term (>3 years), comparing immediate with deferred antiepileptic drug treatment of an unprovoked first seizure in adults (Class I and II studies)

Ref.	Class	No.	Immediate treatment, n (%)	Remission, immediate treatment, n (%)	Remission, deferred treatment, n (%)	Length of follow-up
12-14	I	419	215 (51)	174 (81), NS	159 (78)	More than 3 y[a]
15	II	812	404 (50)	372 (92), NS	375 (92)	5 y[b]
Total		1,231	619 (50)	546 (88)	534 (87)	

Krumholz et al. Neurology 2015

“ASMs are symptomatic treatments,

not disease-modifying or antiepileptogenic therapies.”

Immediate treatment buys time and safety over the first 1–2 years, but withholding medication until a 2nd seizure does not compromise the patient's ultimate chance of long-term seizure freedom."

Guidelines and epilepsy practice: Antiseizure medication initiation following an unprovoked first seizure in adults

Shir Levi-Abayo [a], Shimon Ben-Shabat [a], Revital Gandelman-Marton [b,c,*]

- **Objective:** Evaluated the translation and impact of the 2015 AAN/AES Practice Guideline into real-world clinical decision-making
- ASMs were initiated in **100% of admitted patients post-guideline publication** (compared to 86% pre-guideline).
- In pre-guideline real-world practice, decisions to start treatment were significantly influenced by **epileptiform discharges on EEG**.
- Ensuring that clinicians consistently integrate:
  - structural neuroimaging
  - remote symptomatic histories
  - EEG findings when calculating recurrence risk.

S. Levi-Abayo, et al. Epilepsy Research 200 (2024) 107304

SPECIAL ARTICLE

Evidence-based guideline: Management of an unprovoked first seizure in adults

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2. Longer-term potential for seizure remission

3. **<u>Adverse effects</u>**

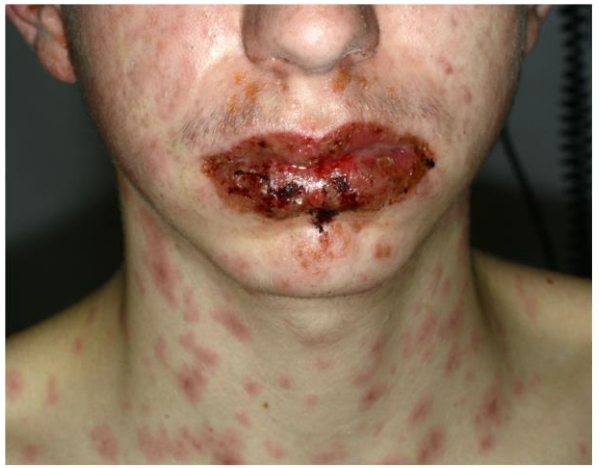
Krumholz et al. Neurology 2015

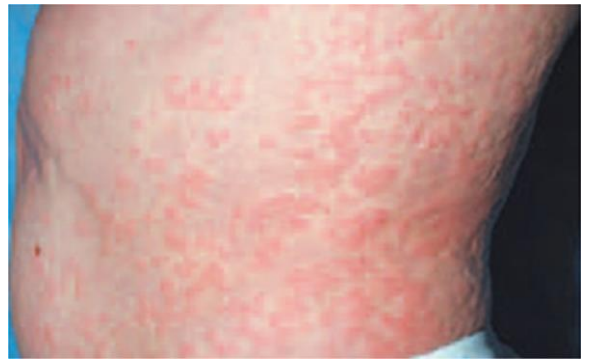
Immediate versus deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial

A Marson, A Jacoby, A Johnson, L Kim, C Gamble, D Chadwick, on behalf of the Medical Research Council MESS Study Group*

	Immediate treatment (n=722)	Deferred treatment (n=721)	Total
No follow-up	37	26	63
None reported	415 (61%)	481 (69%)	896 (65%)
At least one reported	270 (39%)	214 (31%)	484 (35%)
Depression, anxiety	40	31	71
Dizziness, unsteadiness	37	32	69
Gastrointestinal symptoms	41	24	65
Tiredness, drowsiness	41	23	64
Headache	37	13	50
Injury, scalds	28	22	50
Rash, acne	31	14	45
Surgery	21	21	42
Chest pain, myocardial infarction	21	21	42
Impaired memory, concentration	19	15	34
Weight gain, increased appetite	14	19	33
Behaviour problem	20	12	32
Tremor	17	6	23

Table 3: **Patients reporting adverse events at any follow-up**





Lancet 2005; 365: 2007-13

Treat the Risk, Not Just the Seizure

Ask, *"Does this patient meet the >60% recurrence threshold?"*
rather than *"Is one seizure enough to treat?"*

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- 23 studies evaluated
- 5,918 total participants (children and adults)
- Follow-up period of at least 6 months

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Prognostic factors predicting an unprovoked seizure recurrence in children and adults following a first unprovoked seizure

Guleed Adan, Aidan Neligan, Sarah J Nevitt, Laura J Bonnett, Josemir W Sander, Anthony G Marson
Authors' declarations of interest

Version published: 10 October 2025 Version history
https://doi.org/10.1002/14651858.CD013848.pub2

Category	Key Findings / Details	Evidence Certainty
Strong Predictors (Higher Risk)	• **Abnormal EEG:** Associated with roughly **double the risk** of recurrence	**Moderate to Low**
Possible Predictors (Increased Risk)	• **Abnormal brain imaging** (CT or MRI) • **Nocturnal seizures** (occurring during sleep) • **Todd's paresis** (temporary post-seizure muscle weakness) • **Family history of epilepsy**	**Low**
Uncertain / Inconclusive Factors	• History of febrile seizures • Focal seizure onset or neurological deficits • Initial presentation as status epilepticus • Age (under 16) and male sex	**Very Low**
Main Conclusion	• An **abnormal EEG** is currently the most reliable single predictor. • Broader findings are limited by study inconsistencies and reporting gaps, highlighting the need for better standardized prospective studies.	—

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Pitfalls in Diagnosis

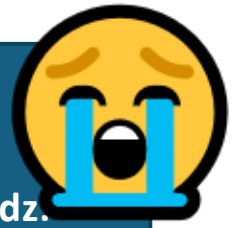
First Episode Seizure?

Seizure ?

Yes

Is it the real first SZ?

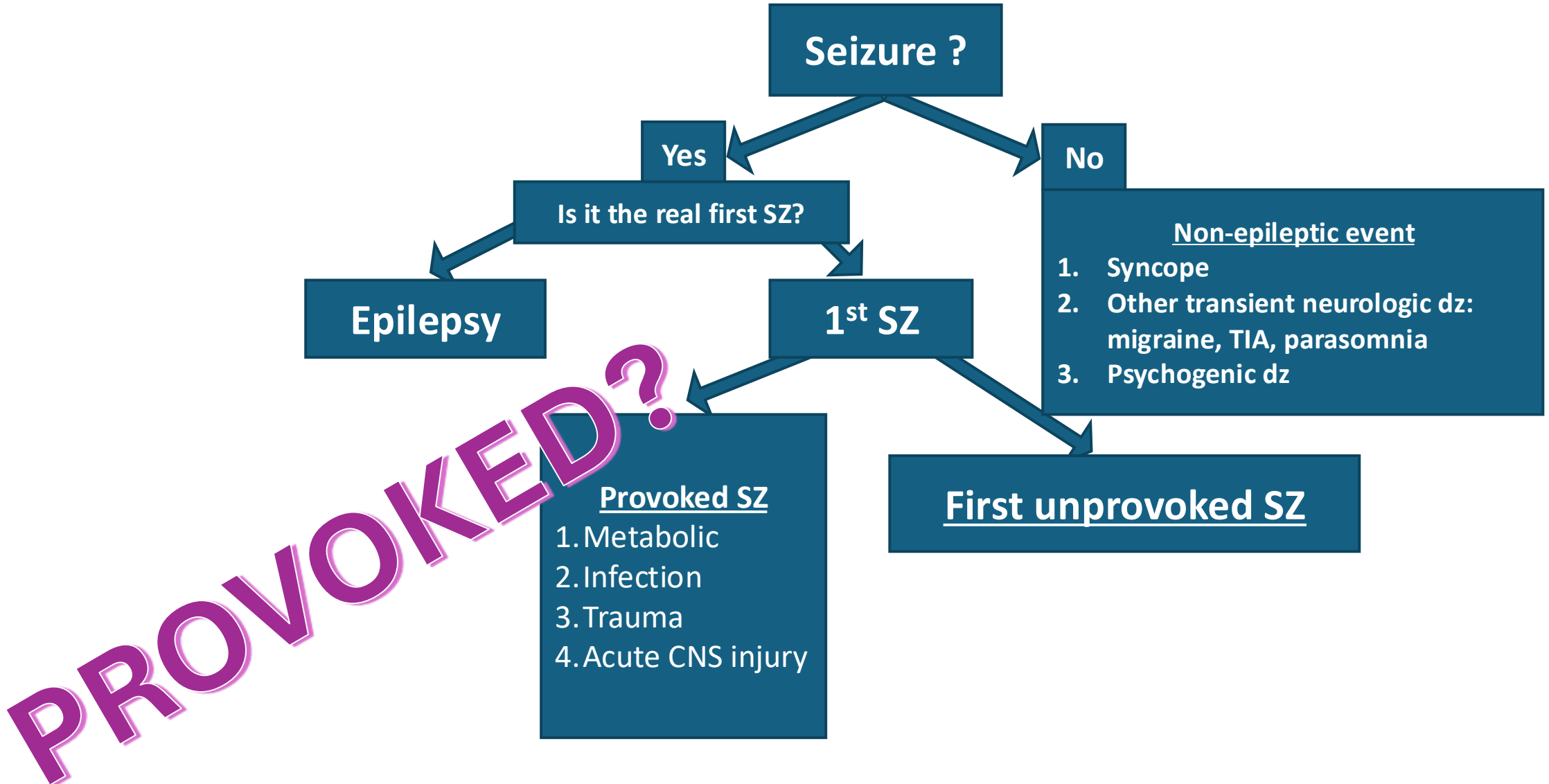
No



Non-epileptic event

1. Syncope
2. Other transient neurologic dz: migraine, TIA, parasomnia
3. Psychogenic dz

First Episode Seizure?



Recommendation for a definition of acute symptomatic seizure

*[1]Ettore Beghi, †Arturo Carpio, ‡Lars Forsgren, §Dale C. Hesdorffer, ¶Kristina Malmgren, #Josemir W. Sander, **Torbjorn Tomson, and §W. Allen Hauser

Biochemical parameter	Value
Serum glucose	<36 mg/dl (2.0 mM) or >450 mg/dl (25 mM) associated with ketoacidosis (whether or not there is long-standing diabetes)
Serum sodium	<115 mg/dl (<5 mM)
Serum calcium	<5.0 mg/dl (<1.2 mM)
Serum magnesium	<0.8 mg/dl (<0.3 mM)
Urea nitrogen	<100 mg/dl (>35.7 mM)
Creatinine	>10.0 mg/dl (>884 μM)

SZs associated with febrile illness

- Minimum rectal temp 38.5°C (101.0°F)

Epilepsia, 51(4):671–675, 2010

TABLE 1-2

Categories of Toxins Causing Provoked Seizures

Category	Mechanism	Other clinical findings	Examples
Increased excitation			
Stimulants	Increased release of dopamine, serotonin, norepinephrine, and/or epinephrine or blocking their reuptake	Anxiety, delusions, delirium, diaphoresis, hypertension, tachycardia, hyperthermia, hyperreflexia, mydriasis, piloerection ECG monitoring should be considered for QRS and QTc prolongation and arrhythmias	Cocaine Amphetamines Phenethylamines Bath salts Serotonergic agents Bupropion Venlafaxine Synthetic cannabinoids Phencyclidine
Cholinergic agents	Binding of nicotinic or muscarinic receptors or inhibiting acetylcholinesterase	DUMBBELS (defecation, urination, miosis, bradycardia, bronchospasm, emesis, lacrimation, and salivation)	Organophosphates Nicotine Nerve gases (sarin and VX)
Glutamate agonists	Binding of *N*-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA), or kainate receptors	Somnolence, hallucinations, delirium, nausea and vomiting, diarrhea, salivation	Domoic acid (shellfish poisoning) *Amanita muscaria* mushroom ingestion

CONTINUUM (MINNEAP MINN) 2022;28(2, EPILEPSY):230–260.

Category	Mechanism	Other clinical findings	Examples
Increased excitation or withdrawal of central nervous system (CNS) depressants			
γ-Aminobutyric acid (GABA) antagonists	Blockage of GABA-ergic neurons or abrupt withdrawal of CNS depressants	Tremor, tachycardia, hypertension, diaphoresis, nausea, anxiety, irritability, insomnia, hallucinations	Tramadol Antibiotics: isoniazid (depletes pyridoxine, which inhibits GABA synthesis from glutamate), penicillin, cephalosporins, carbapenems, fluoroquinolones Abrupt withdrawal of GABA-ergic agents such as alcohol, benzodiazepines, baclofen, barbiturates Antidepressants and antipsychotics including tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), phenothiazines
Decreased CNS inhibition			
Histamine antagonists	Antagonism at histamine receptors	Confusion, ataxia, hallucinations, delirium, dry mucous membranes, mydriasis	Histamine antagonists including diphenhydramine, doxylamine, hydroxyzine, chlorpheniramine
Adenosine antagonists	Antagonism of adenosine	Cardiac dysrhythmias	Theophylline, caffeine

May not truly PROVOKED

ECG = electrocardiogram.

Investigations: Pitfalls

- **Electroencephalography**
- **Neuroimaging**

Electroencephalography

- 18 – 56% of children and 12-50% of adults presenting with new-onset seizures have epileptiform abnormality found on routine EEG
- More diagnostic yield in early EEG and sleep deprivation EEG

- Pitfalls: 3% of people without epilepsy may show epileptiform discharges → False positive

CONTINUUM (MINNEAP MINN) 2022;28(2, EPILEPSY):230–260.

Electroencephalogram epileptiform abnormalities in candidates for aircrew training

R.P. Gregory, T. Oates and R.T.G. Merry

Princess Alexandra Hospital, Royal Air Force Wroughton, Swindon (UK)

(Accepted for publication: 11 September 1992)

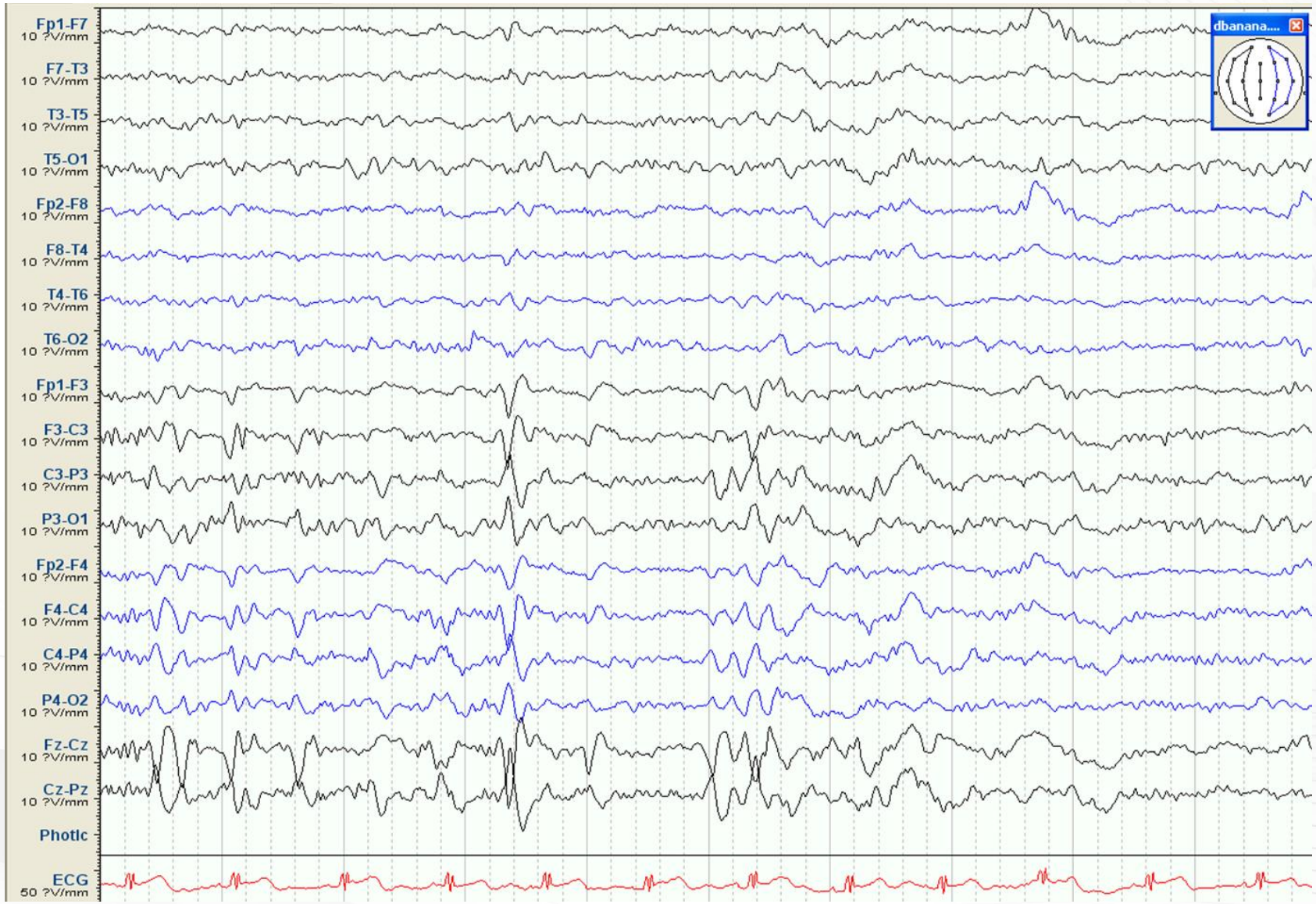
- 30 years the Royal Air Force has used the EEG as part of the medical screening of candidates for aircrew training.
- A total of 13,658 males aged 17-25 years.
- 0.5% of these showed unequivocal epileptiform discharges, 58% occurring only on photic stimulation.
- Exclude → 6 and 14 Hz positive spikes, 6 Hz spike and wave
- Chance of healthy individuals with EEG abnormalities epileptiform discharges is **2-3%.**

Electroencephalography and clinical Neurophysiology, 86 (1993) 75- 77

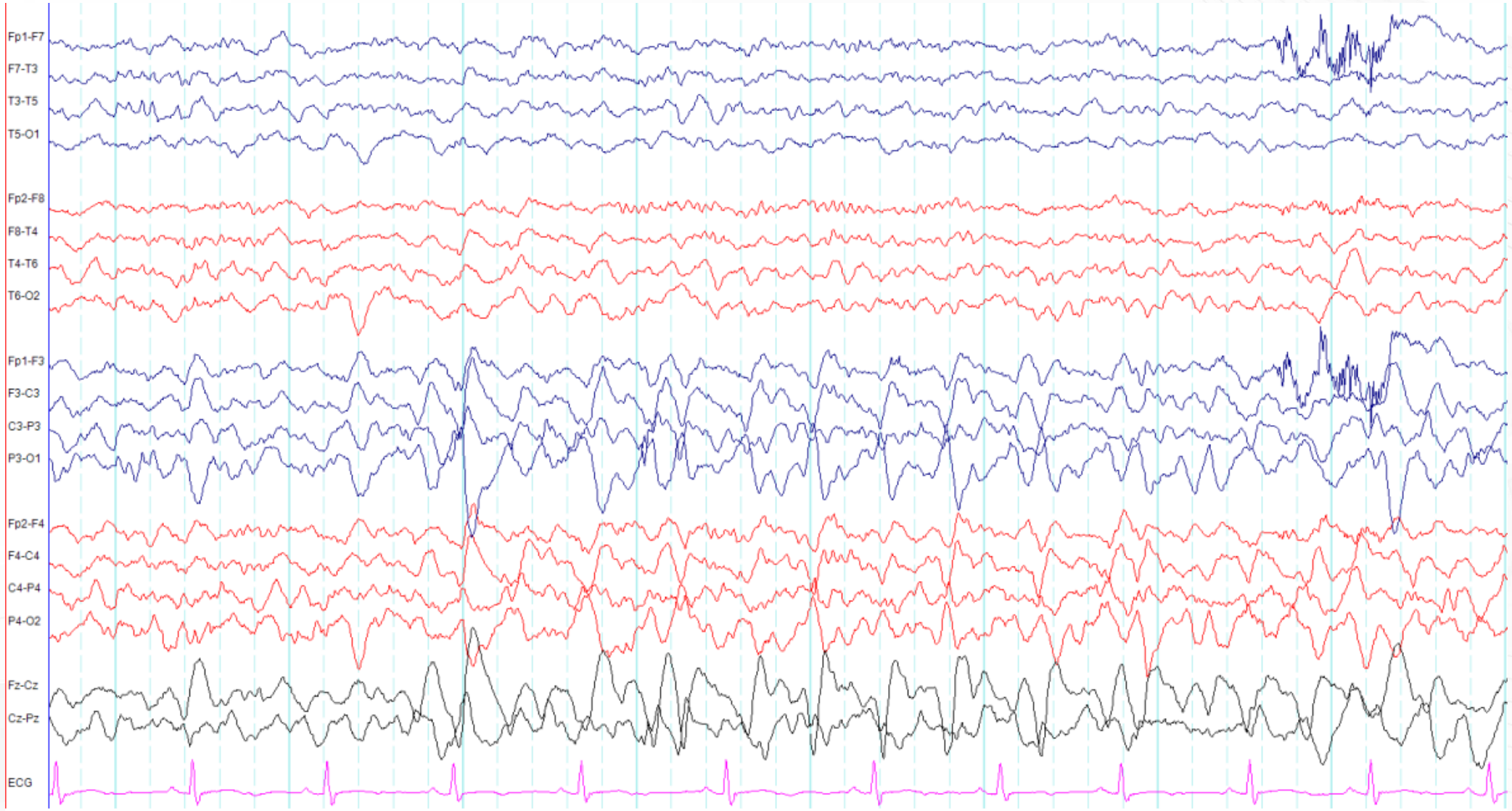
Caveats; normal/normal variants

- Children: vertex sharp waves, hypnagogic hypersynchrony
- Adolescents and adults: wicket waves and rhythmic temporal theta of drowsiness

Vertex sharp transients

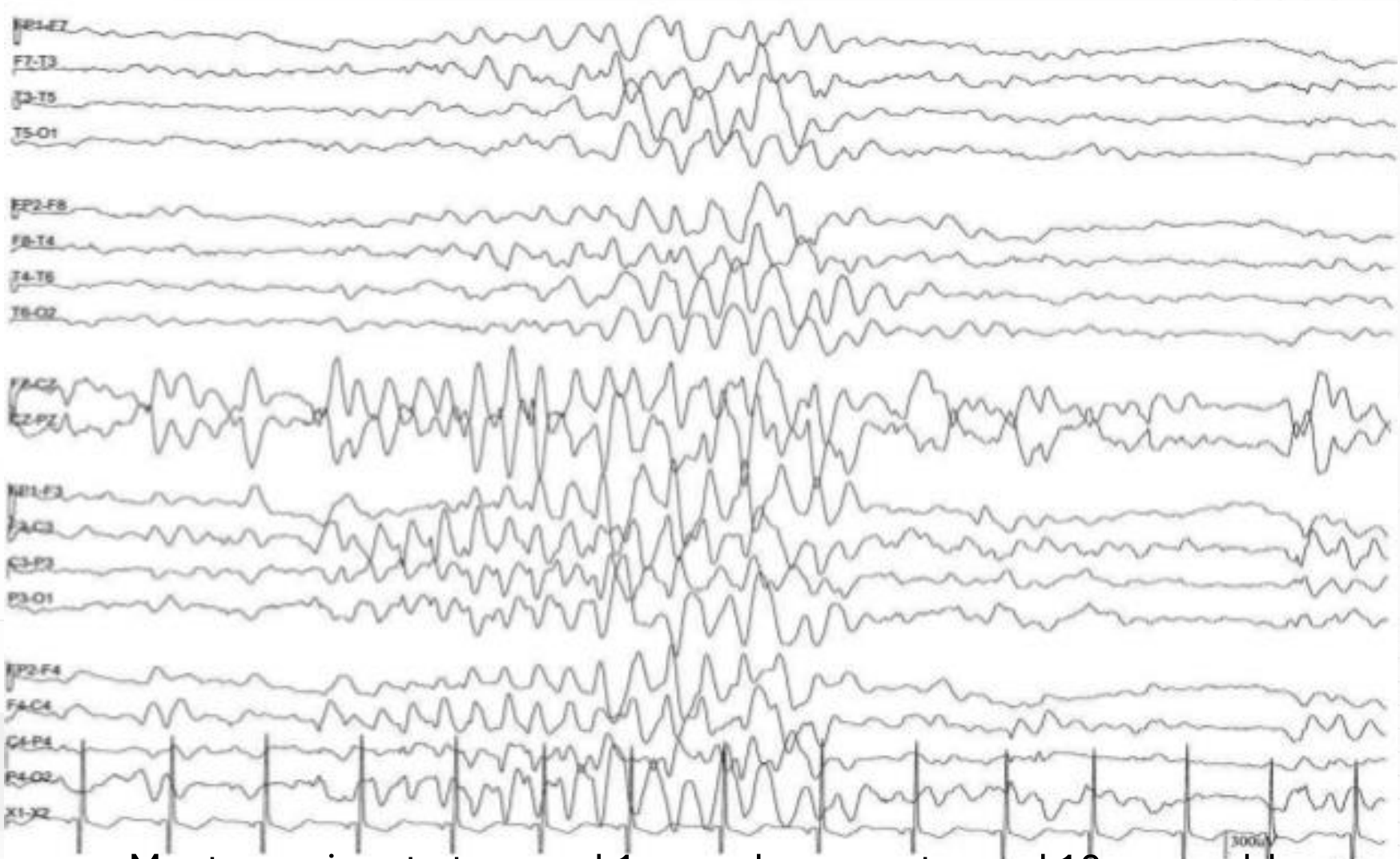


Vertex waves in runs



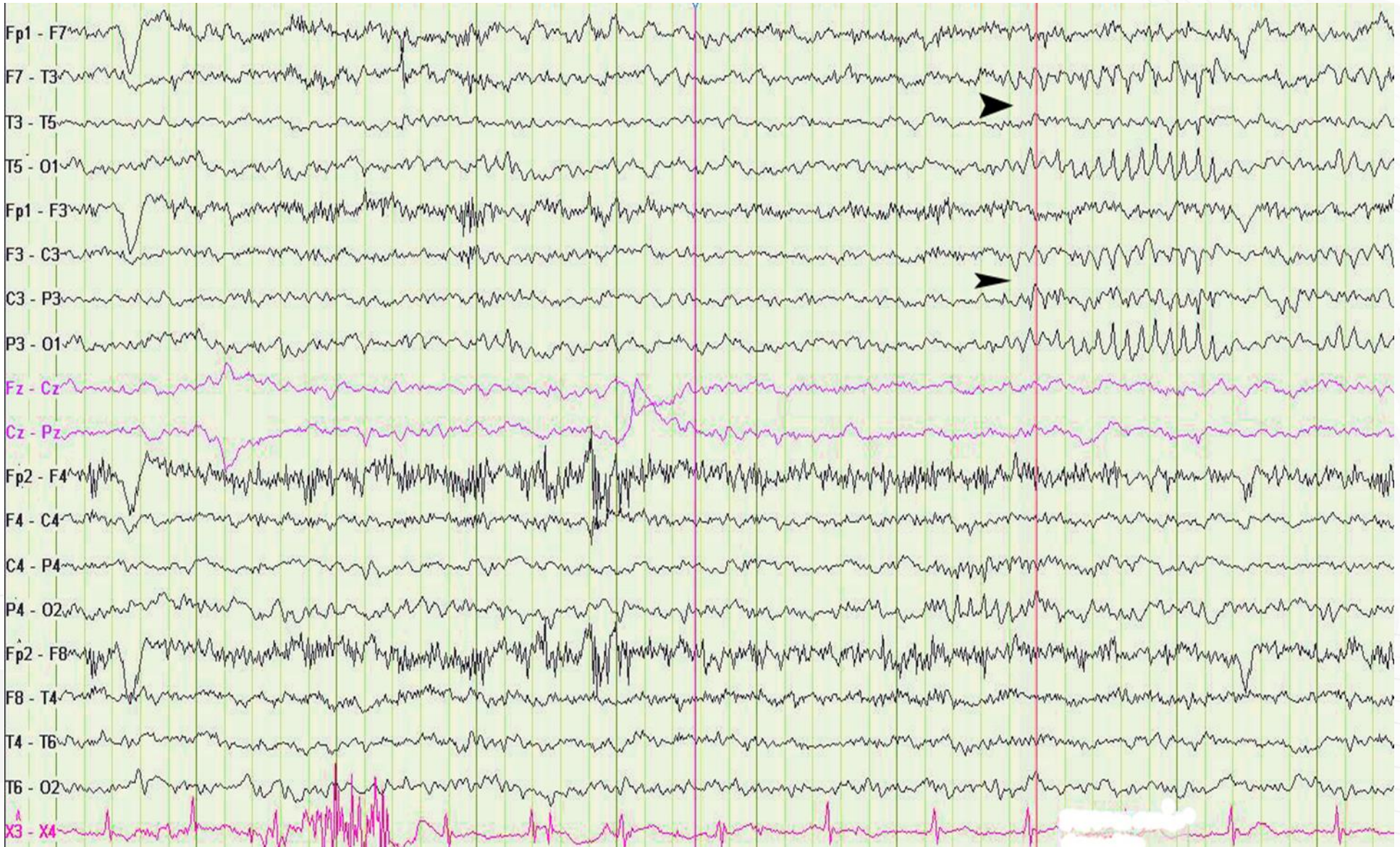
Hypnagogic hypersynchrony

Rhythmic bilateral synchronous high amplitude theta with widely distribution

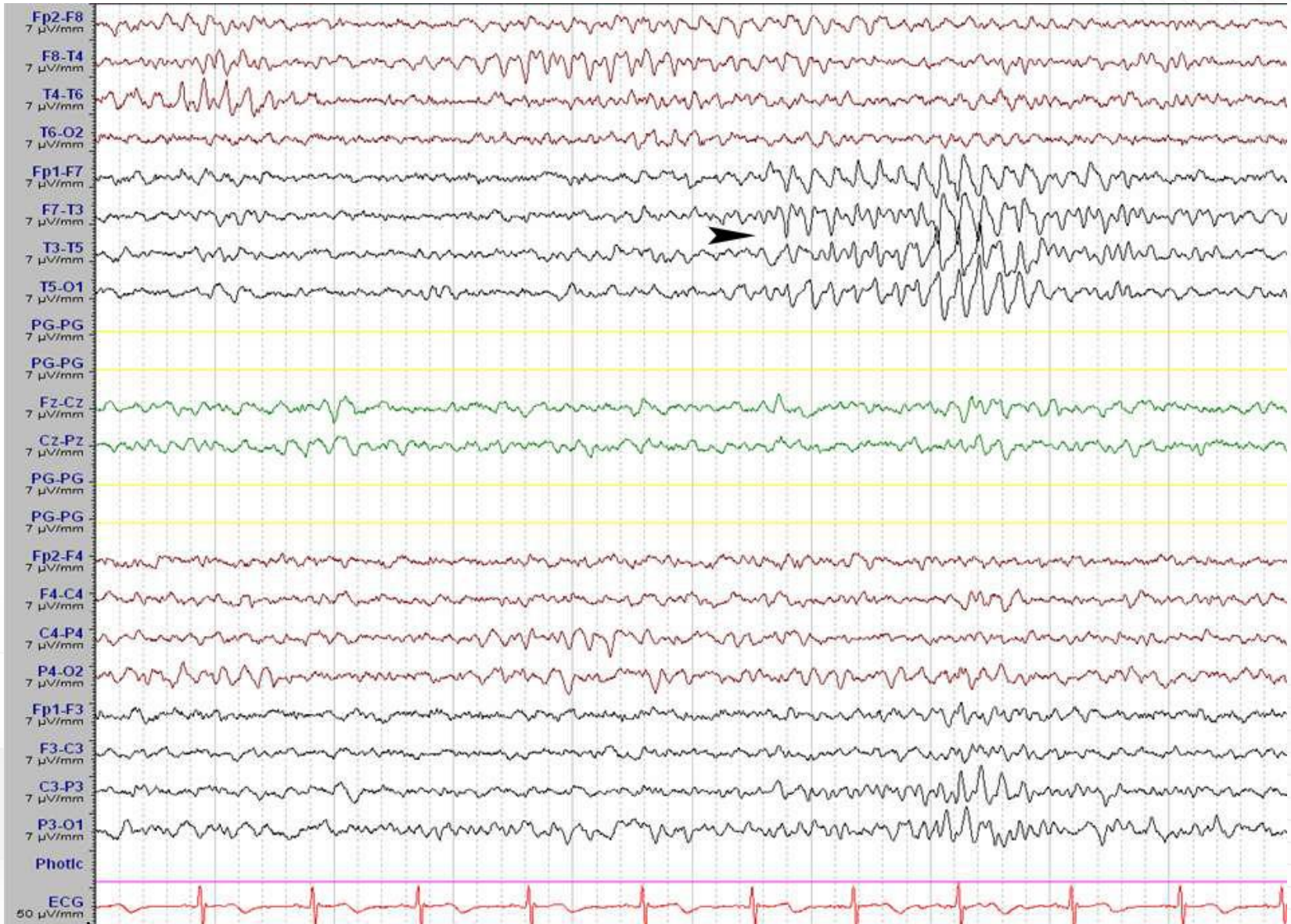


Most prominent at around 1 year, decrease toward 10 years old

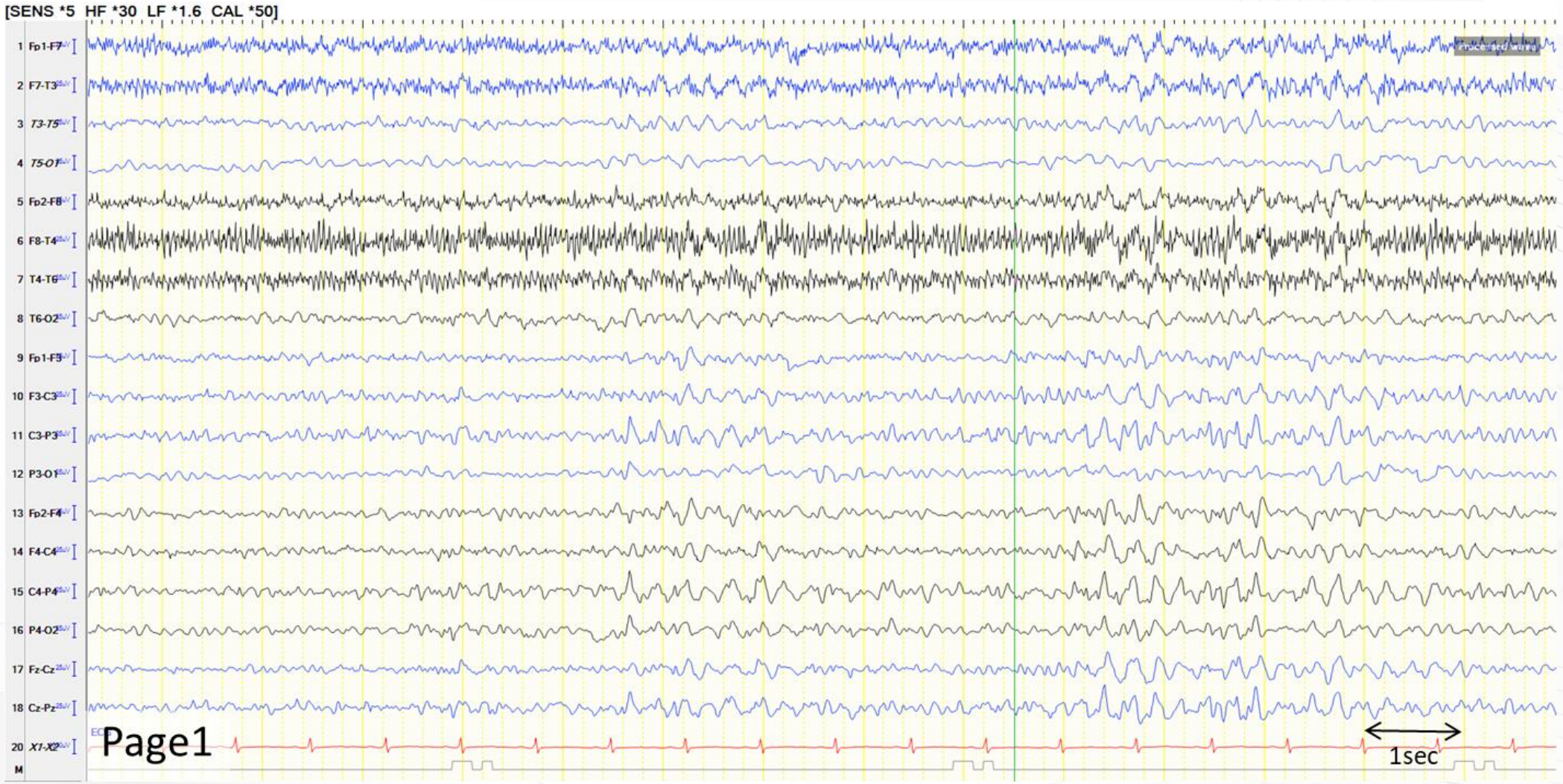
Wicket spikes



RMTD


Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F7
F7-T3
T3-T5
T5-O1
PG-PG
PG-PG
Fz-Cz
Cz-Pz
PG-PG
PG-PG
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Photic
ECG
7 µV/mm
50 µV/mm

SREDA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6 F8-T4
7 T4-T6
8 T6-O2
9 Fp1-F3
10 F3-C3
11 C3-P3
12 P3-O1
13 Fp2-F4
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20 X1-X2
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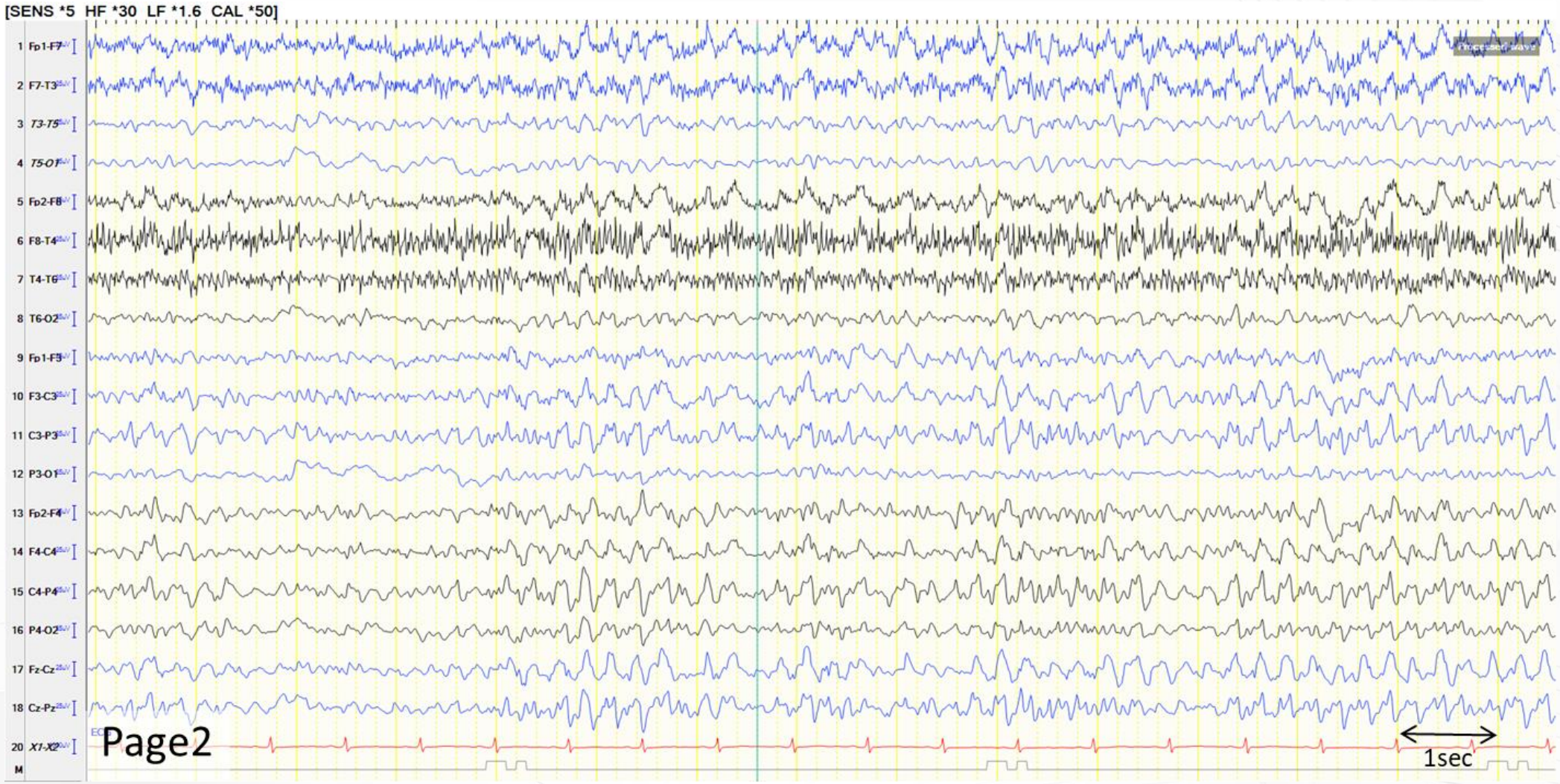
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10 F3-C3
11 C3-P3
12 P3-O1
13 Fp2-F4
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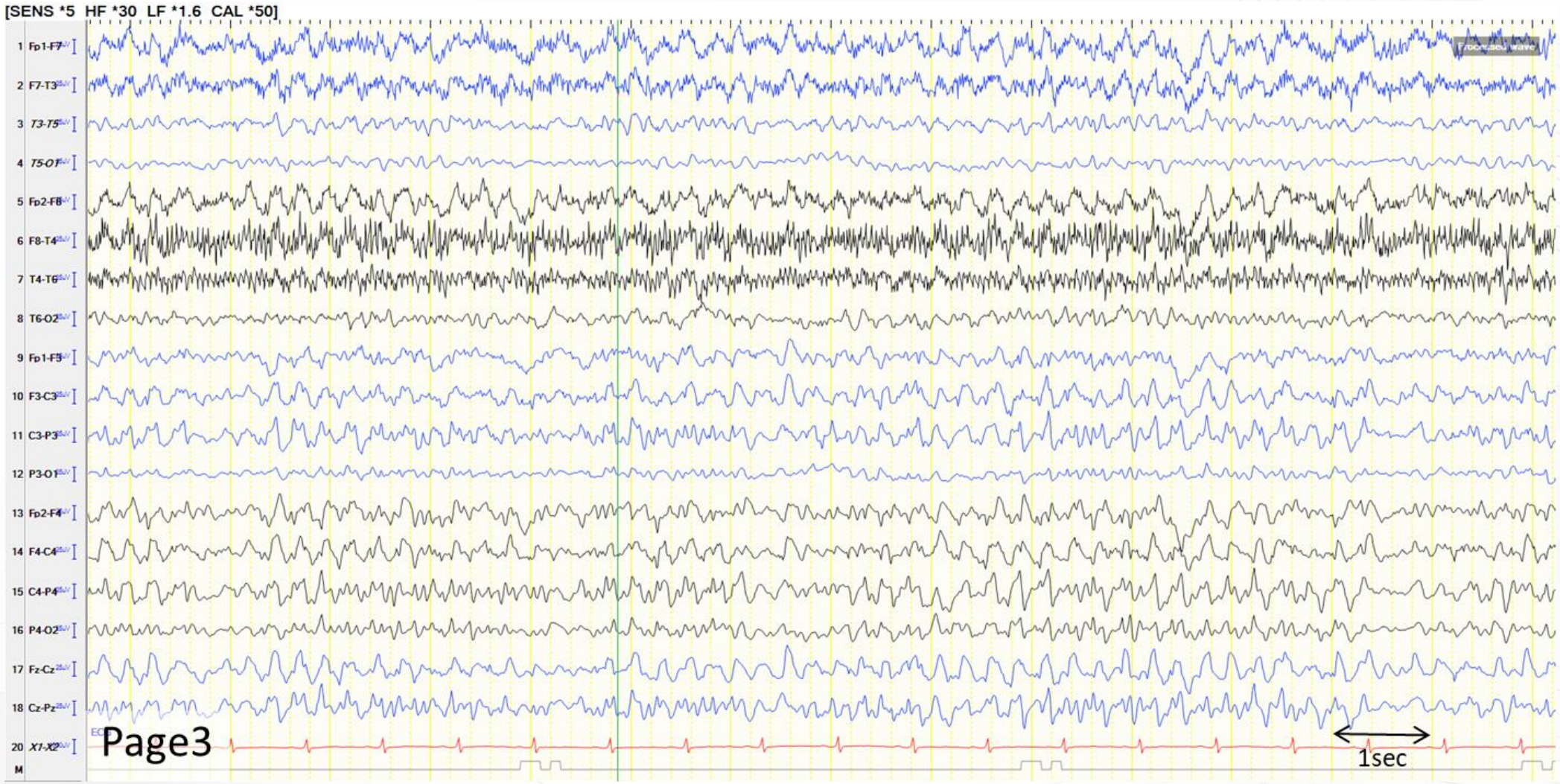
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10 F3-C3
11 C3-P3
12 P3-O1
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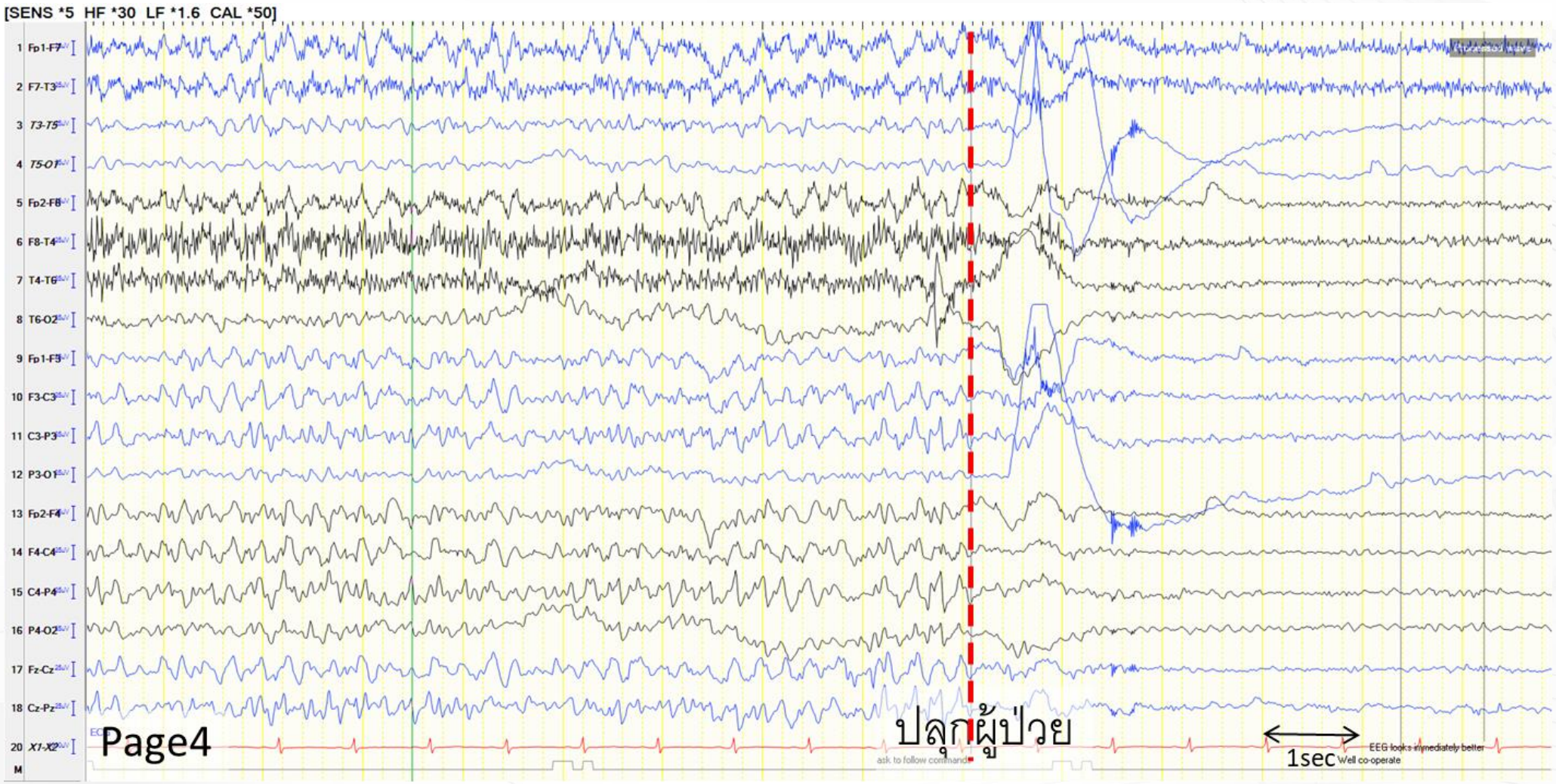
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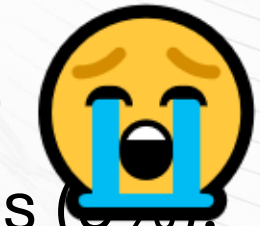
7 T4-T6
8 T6-O2
9 Fp1-F3
10 F3-C3
11 C3-P3
12 P3-O1
13 Fp2-F4
14 F4-C4
15 C4-P4
16 P4-O2
17 Fz-Cz
18 Cz-Pz
20 X1-X2
M
Page4
ปลุกผู้ป่วย
1sec
EEG looks immediately better
Well co-operate
ask to follow command

MRI-identified pathology in adults with new-onset seizures

- potentially epileptogenic lesions were detected in 23%.
- **epileptic seizure (28%) vs nonepileptic event (8%) (p,0.001)**
- gliosis or encephalomalacia (49%), tumors (15%), cavernomas (6%), and mesial temporal sclerosis (9%)
- EEG normal in 55% of pts with epileptogenic lesions



Hakami T, et al. Neurology 2013;81:920–927

The "First Seizure" Dilemma – To Treat or Not to Treat

- Immediate ASM treatment delays 2nd SZ
- 14 pts to prevent 1 SZ in 1-2 year
- Long-term remission: no different
- AE and stigma need to be considered
- Investigation may have false positive

Clinical Decision making

Clinical Scenario	Estimated Recurrence Risk	Recommended Action
Normal EEG, Normal MRI, No prior insult	Low (~20–30% at 2 years)	**Defer treatment.** Counsel on lifestyle, driving restrictions, and seizure precautions.
Epileptiform EEG OR Structural lesion on MRI	High (>60% at 10 years)	**Initiate ASM monotherapy.** (Meets ILAE epilepsy criteria).
High-risk occupation / Driving necessity / Patient anxiety	Variable	**Shared decision-making.** Weigh ASM side effects vs. psychosocial/occupational consequences of a second event.