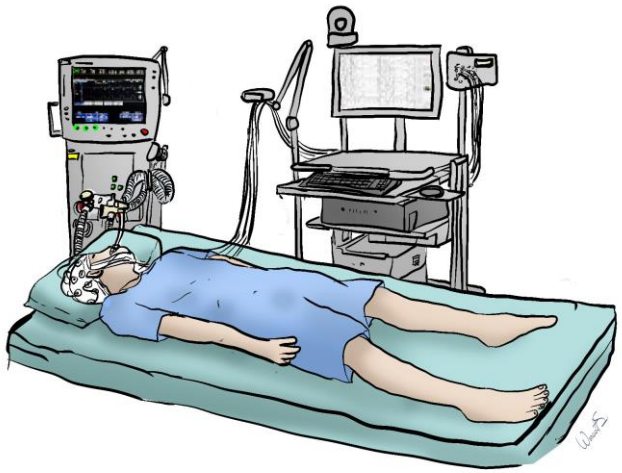
Cutting-edge treatment in status epilepticus

Assistant Professor. Apisit Boongird

Division of Neurology

Ramathibodi Hospital



Topics

- Definitions and criteria in status epilepticus
- Treatment in convulsive status epilepticus (CSE)
- Postanoxic status epilepticus

Veterans Affairs Status Epilepticus Cooperative Study (VA study)

- A comparison of four treatments for generalized convulsive status epilepticus.
- Veterans Affairs Status Epilepticus Cooperative Study Group established the primacy of lorazepam over phenytoin alone as first-line treatment of early CSE in hospital.

N Engl J Med. 1998 Sep 17;339(12):792-8.

	Year	References
Definition of Refractory Status Epilepticus (RSE)	2011	Lancet Neurol . 2011 Oct;10(10):922-30.
A definition and classification of status epilepticus--Report of the ILAE Task Force on Classification of Status Epilepticus	2015	Epilepsia, 56(10):1515–1523, 2015
Definition of Super-Refractory Status Epilepticus (SRSE)	2015 2016	Epilepsy Behav . 2015 Aug;49:131-4. J Clin Med. 2016 May 19;5(5):54.
Salzburg EEG consensus criteria for non-convulsive status epilepticus	2015	Epilepsy Behav: E&B 2015;49(August)158–63
Proposed consensus definitions for new-onset refractory status epilepticus (NORSE), febrile infection-related epilepsy syndrome (FIRES), and related conditions	2018	Epilepsia. 2018 Apr;59(4):739-744.

ESETT trial in 2019

Trial of Three Anticonvulsant Medications for Status Epilepticus			
MULTICENTER, RANDOMIZED, DOUBLE-BLIND TRIAL			
384 children and adults with benzodiazepine-refractory status epilepticus	Levetiracetam 60 mg/kg	Fosphenytoin 20mg/kg	Valproate 40 mg/kg
Disappearance of clinically evident seizures and improved responsiveness at 60 minutes	47%	45%	46%
In the context of benzodiazepine-refractory convulsive status epilepticus, the anticonvulsant drugs levetiracetam, fosphenytoin, and valproate each led to seizure cessation and improved alertness by 60 minutes in approximately half the patients, and the three drugs were associated with similar incidences of adverse events.			

N Engl J Med 2019;381:2103-13.

A definition of status epilepticus

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

Associations Between Time to Administration of Antiseizure Medications and Short-term Clinical Outcomes in Adult with Convulsive Status Epilepticus

Pongsakorn Kongsakorn, MD[1]; Apisit Boongird, MD[1]

[1]Division of Neurology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Correspondence: Pongsakorn Kongsakorn, MD

Keywords: Status epilepticus, mortality, antiseizure medications, mRS

Abstract

Background:

Status epilepticus (SE) is a time-sensitive emergency that requires immediate treatment.

Objective:

To analyze the associations between time to administration of antiseizure medications(ASM) and short-term clinical outcomes.

Material and Methods:

From January1, 2014 to December31, 2020, we performed a retrospective cohort study in adult patients who presented with convulsive SE. Primary outcome was to analyze association between timing of ASM administration and mortality. Secondary outcomes were to determine the relationship between timing of ASM administration and length of hospital stay, and mRS at discharge, respectively.

Results:

A total of 83 patients were enrolled. Mean age was 57. Mean length of hospital stay was 32 days. BDZ was prescribed as first ASM in 79 patients (95.2%). Levetiracetam was the second ASM most frequently administered (N=39, 47%), followed by phenytoin (N=28, 33.7%), and valproate (N= 13, 15.7%). Of 83, 71 patients (85.5%) had prolonged t_2 period. Therapy delay in SE, and underdosing of ASM was noted in both alive and dead group. The mortality rate was 20.5%, and was highest in super-refractory SE (N=15, 88.2%). For secondary outcomes including length of hospital stay and mRS, a statistically significant finding was only noted in the category of timing of seizure onset to first ASM, with p=0.002, and p=0.004, respectively.

Conclusion:

Although, this study showed no significant association between timing of ASM administration and in-hospital mortality. Prolonged duration of SE and therapy delay was associated with increased mortality. SE guidelines were not followed in a substantial proportion of SE patients.

Emergency department at Ramathibodi hospital

SE with prominent motor symptoms

Axis 1: Classification of status epilepticus (SE)

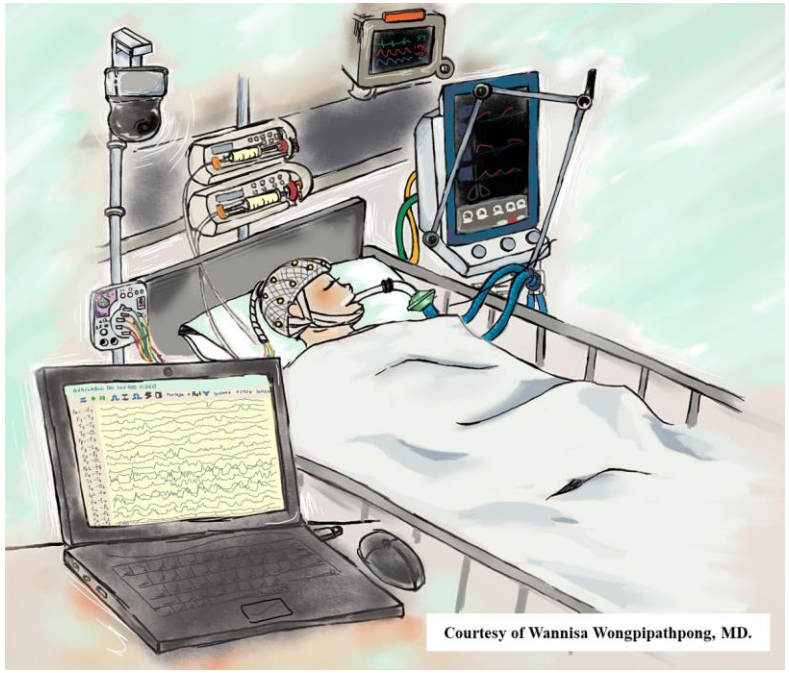
(A) With prominent motor symptoms

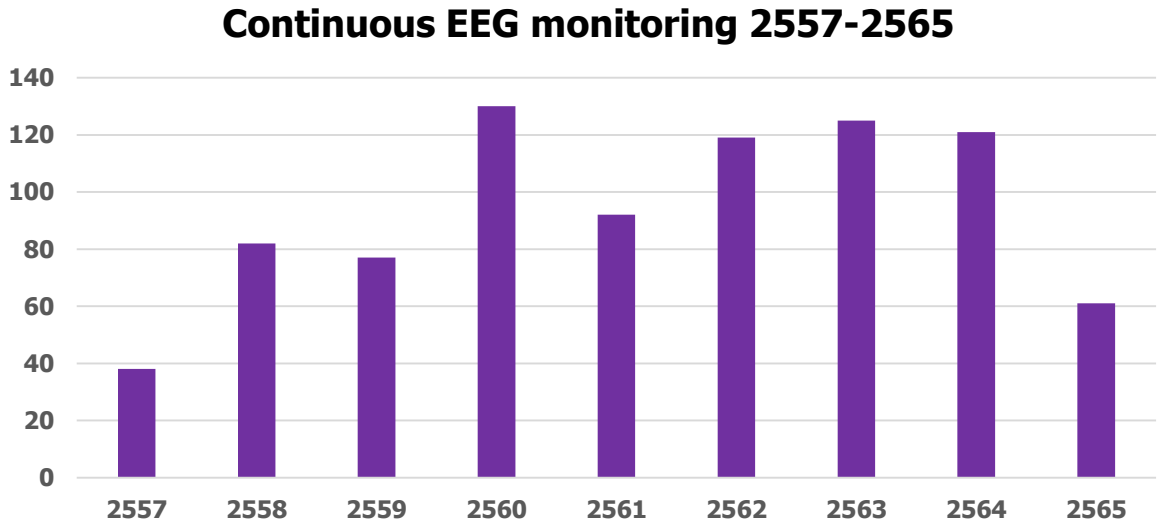
A.1 Convulsive SE (CSE)

- 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 jerks)

- A.2.a. With coma
- A.2.b. Without coma





Most SE patients have no history of epilepsy.

Table 1 Demographic and Clinical Variables

	All, N =83	Alive, N = 66	Dead, N = 17	p value
Age (years), Mean[range]	57 [18 - 95]	57 [18 - 95]	58 [19 - 88]	0.592
Male, N (%)	39 (47%)	33 (50%)	6 (35.3%)	0.279
History of epilepsy, N (%)	9 (10.8%)	8 (12.1%)	1 (5.9%)	0.461
Length of hospital stay (days), Mean[range]	32 [3 - 183]	32 [3 - 145]	32 [3 - 183]	0.531
Duration of status epilepticus, N (%)				
Within t_2	12 (14.5%)	11 (16.7%)	1 (5.9%)	0.26
More than t_2	71 (85.5%)	55 (83.3%)	16 (94.1%)	
Stage of status epilepticus (SE), N (%)				
Established status epilepticus (ESE)	20 (24.1%)	18 (27.3%)	2 (11.8%)	**0.018***
Refractory status epilepticus (RSE)	14 (16.9%)	14 (21.2%)	0 (0%)	
Super-refractory status epilepticus (SRSE)	49 (59%)	34 (51.5%)	15 (88.2%)	
Timing of seizure onset to first ASM (minutes), Mean[range]	43 [2 - 420]	48.58 [2 - 420]	21.35 [2 - 122]	0.134
< 10	40 (48.2%)	28 (42.4%)	12 (70.6%)	0.116
10-60	18 (21.7%)	16 (24.2%)	2 (11.8%)	
> 60	25 (30.1%)	22 (33.3%)	3 (17.6%)	
Timing of seizure onset to second ASM (minutes), Mean[range]	132.79 [17 - 1310]	140.17 [17 - 1310]	105.41 [29 - 303]	0.471
≤ 60	19 (22.9%)	15 (22.7%)	4 (23.5%)	0.981
> 60	61 (73.5%)	48 (72.7%)	13 (76.5%)	
Timing of first ASM to second ASM (minutes), Mean[range]	94.59 [9 - 1005]	97.57 [9 - 1005]	83.53 [10 - 300]	0.729
≤ 60	53 (63.9%)	42 (63.6%)	11 (64.7%)	0.879
> 60	27 (32.5%)	21 (31.8%)	6 (35.3%)	
mRS, N (%)				
1	0 (0%)			
2	5 (6%)			
3	13 (15.7%)			
4	27 (32.5%)			
5	21 (25.3%)			
6	17 (20.5%)			

ASM; antiseizure medication, SE; status epilepticus, mRS; modified Rankin Scale
*p value < 0.05 was statistically significance.

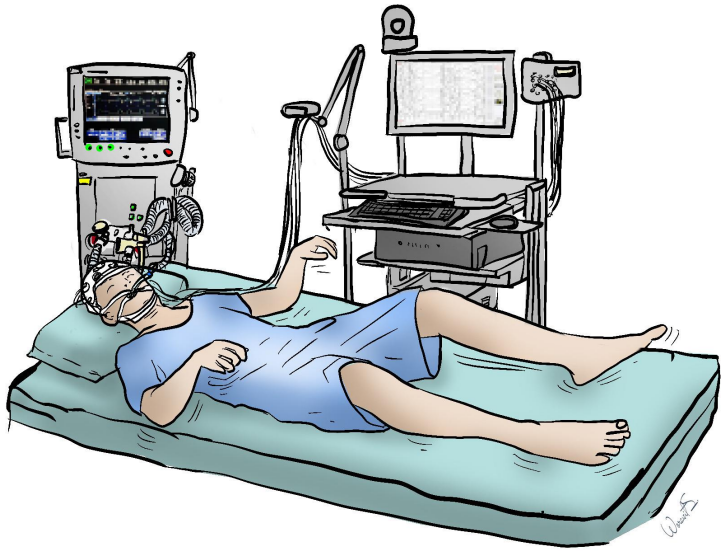
Classification of Status Epilepticus

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

	All, N =83	Alive, N = 66	Death, N = 17	p value
Axis 1 : Classification of status epilepticus with prominent motor symptoms, N (%)				
Generalized convulsive SE	36 (43.4%)	31 (47%)	5 (29.4%)	0.118
Focal onset evolving into bilateral convulsive SE	35 (42.2%)	28 (42.4%)	7 (41.2%)	
Myoclonic status epilepticus with coma	12 (14.5%)	7 (10.6%)	5 (29.4%)	

Generalized CSE 36 pts

Focal onset evolving to bilateral CSE 35 pts



Myoclonic SE with coma 12 pts

Worawit Sukpakkit

Classification of Status Epilepticus

AXIS 1
Semiology

AXIS 2
Etiology

AXIS 3
EEG

AXIS 4
Age

	All, N =83	Alive, N = 66	Death, N = 17	p value
Axis 2 : Etiology of status epilepticus, N (%)				
Acute symptomatic seizure				
Acute ischemic stroke	5 (6%)	4 (6.1%)	1 (5.9%)	0.735
Acute hemorrhagic stroke	8 (9.6%)	7 (10.6%)	1 (5.9%)	
Metabolic disturbance	7 (8.4%)	5 (7.6%)	2 (11.8%)	
Drug induced seizure	1 (1.2%)	1 (1.5%)	0 (0%)	
Hypoxic brain injury	12 (14.5%)	7 (10.6%)	5 (29.4%)	
CNS infection	8 (9.6%)	5 (7.6%)	3 (17.6%)	
Systemic infection	7 (8.4%)	6 (9.1%)	1 (5.9%)	
Traumatic brain injury	0 (0%)	0 (0%)	0 (0%)	
CNS autoimmune disease	6 (7.2%)	5 (7.6%)	1 (5.9%)	
Systemic autoimmune disease	4 (4.8%)	3 (4.5%)	1 (5.9%)	
Poor ASM compliance	3 (3.6%)	3 (4.5%)	0 (0%)	
Substance intoxication	1 (1.2%)	1 (1.5%)	0 (0%)	
Remote symptomatic seizure				
Post-ischemic stroke lesion	7 (8.4%)	7 (10.6%)	0 (0%)	
Post-hemorrhagic stroke lesion	3 (3.6%)	3 (4.5%)	0 (0%)	
Progressive symptomatic seizure				
Brain Tumor	11 (13.3%)	9 (13.6%)	2 (11.8%)	

Classification of Status Epilepticus

AXIS 1
Semiology

AXIS 2
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AXIS 3
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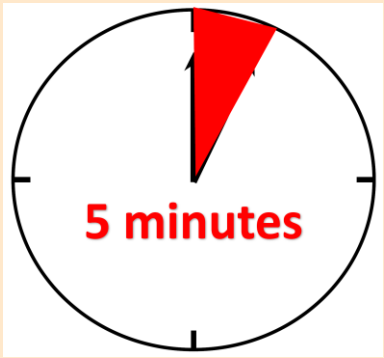
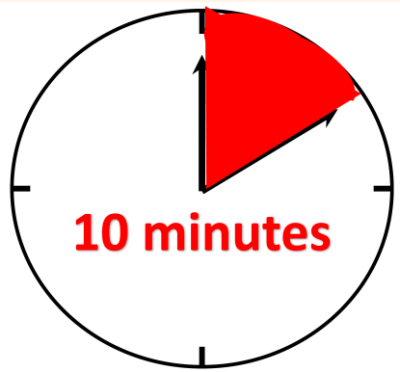
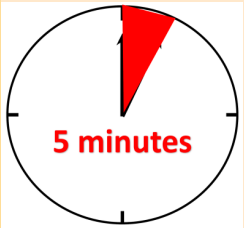
A definition of status epilepticus

Type of SE	Time (t1)	Time (t2)
Tonic- clonic SE		30 min
Focal SE with impaired consciousness		> 60 min

A definition of status epilepticus

Type of SE	Time (t1)	Time (t2)
Tonic- clonic SE		30 min
Focal SE with impaired consciousness		> 60 min

Most SE patients had prolonged t2 and subsequently developed SRSE later on.

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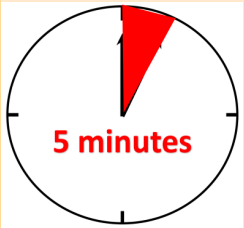
Tonic- clonic SE		30 min
Focal SE with impaired consciousness		> 60 min

Delayed SE treatment is observed.

Mortality rate is 20%.

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ASM; antiseizure medication, SE; status epilepticus, mRS; modified Rankin Scale
*p value < 0.05 was statistically significance.

Table 1 Demographic and Clinical Variables; Continued

	All, N =83	Alive, N = 66	Death, N = 17	p value
Type of first ASM, N (%)				
Benzodiazepine	79 (95.2%)	62 (93.9%)	17 (100%)	0.582
Levetiracetam	3 (3.6%)	3 (4.5%)	0 (0%)	
Valproate	1 (1.2%)	1 (1.5%)	0 (0%)	
Adequate dose of first ASM according to SE guideline	66 (79.5%)	52 (78.8%)	14 (82.4%)	0.745
Type of second ASM, N (%)				
Levetiracetam	39 (47%)	27 (40.9%)	12 (70.6%)	0.161
Valproate	13 (15.7%)	11 (16.7%)	2 (11.8%)	
Phenytoin	28 (33.7%)	25 (37.9%)	3 (17.6%)	
No usage of second ASM	3 (3.6%)	3 (4.5%)	0 (0%)	
Adequate dose of second ASM according to SE guideline	12 (14.5%)	10 (15.2%)	2 (11.8%)	0.674
Usage of ASM (not including benzodiazepine and anesthetic agent), N (%)				
One ASM	19 (22.9%)	18 (27.3%)	1 (5.9%)	0.151
Two ASMs	24 (28.9%)	19 (28.8%)	5 (29.4%)	
Three ASMs	20 (24.1%)	16 (24.2%)	4 (23.5%)	
≥ Four ASMs	20 (24.1%)	13 (19.7%)	7 (41.2%)	
Usage of anesthetic agent, N (%)	55 (66.3%)	40 (60.6%)	15 (88.2%)	**0.032***
Midazolam	52 (62.7%)	37 (56.1%)	15 (88.2%)	**0.014***
Propofol	7 (8.4%)	3 (4.5%)	4 (23.5%)	**0.012***
Thiopental	2 (2.4%)	1 (1.5%)	1 (5.9%)	0.295
Use 1 type of anesthetic agent	50 (60.2%)	39 (59.1%)	11 (64.7%)	**0.001***
Use ≥ 2 types of anesthetic agents	5 (6%)	1 (1.5%)	4 (23.5%)	
No usage of anesthetic agent	28 (33.7%)	26 (39.4%)	2 (11.8%)	
Complication, N (%)				
Systemic hypotension requiring vasopressors and inotropes	40 (48.2%)	24 (36.4%)	16 (94.1%)	**<0.001***
Nosocomial Infection	45 (54.2%)	34 (51.5%)	11 (64.7%)	0.330

ASM; antiseizure medication
*p value < 0.05 was statistically significance.

Underdosing of ASM is observed.

Midazolam is the most commonly used.

Most common complications are systemic hypotension and infection.

StEp Audit

- Most people with SE have no history of epilepsy.
- Outcome depends on etiology.
- First-line treatment was delayed and not in line with current guidelines.
- Treatment was delayed compared with current SE guidelines.

SENSE registry

- Factors predicting cessation of SE in clinical practice
  - Time
  - Adequate doses of benzodiazepines and anti-seizure medications

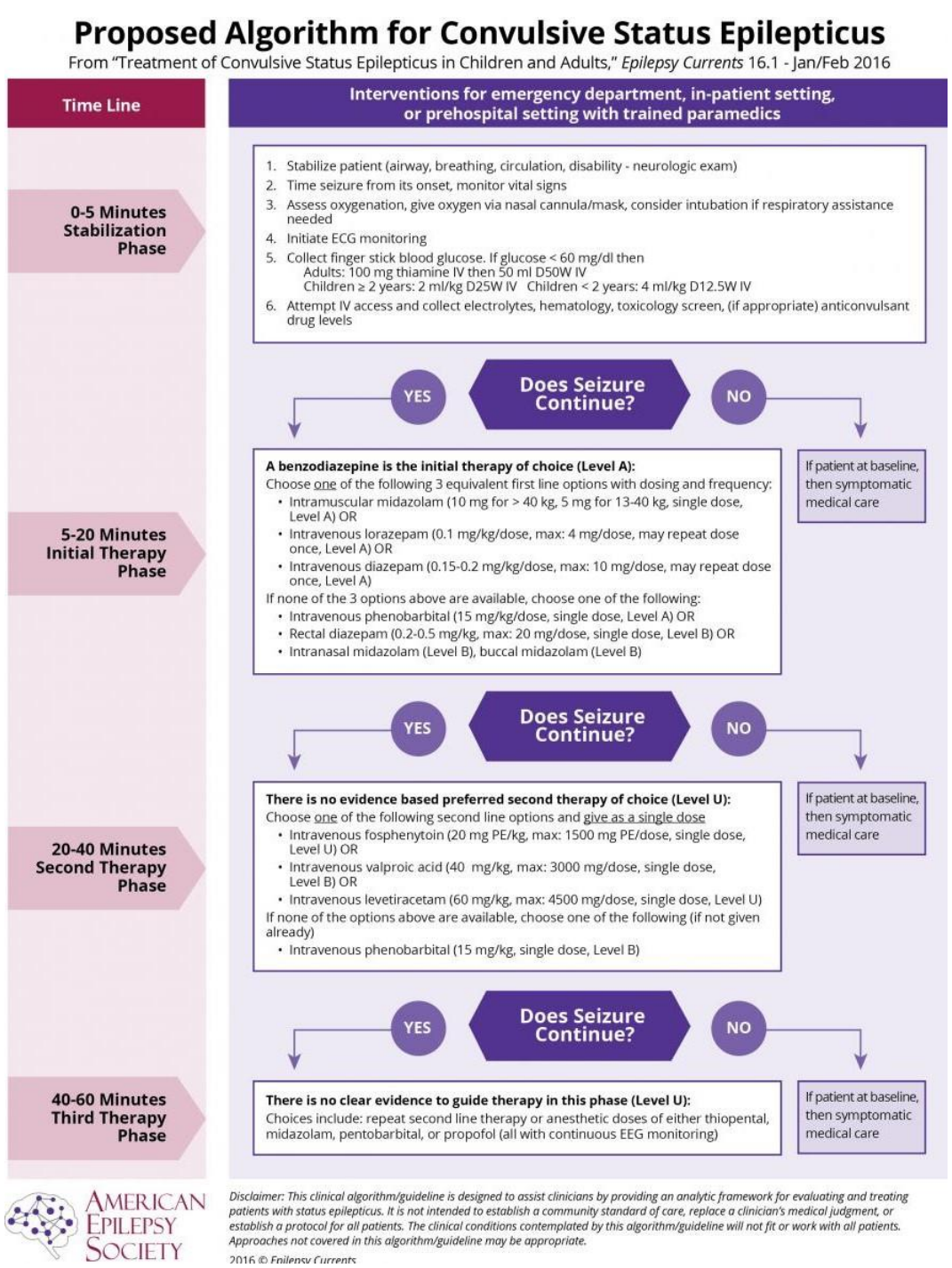
The bolus dose is lower than recommended in most cases and, in a relevant number of patients, benzodiazepines were not used as first-line agents.

TABLE 3 First treatment steps

First step		Successful (%)	Bolus dose
Lorazepam	318	52 (16)	0.03 mg/kg
Diazepam	44	11 (25)	0.13 mg/kg
Midazolam	85	20 (23)	0.1 mg/kg
Clonazepam	211	29 (14)	0.013 mg/kg
Several benzodiazepines	188	35 (19)	
Levetiracetam	158	36 (22)	15 mg/kg
Other	45	6 (13)	
Total	1049	154 (15)	
Second step		**Successful (%)**	**Bolus dose**
Latency first step to second step	Median	40 min IQR 10-120 min	
Lorazepam	38	8 (21)	0.025 mg/kg
Diazepam	4	1 (25)	0.13 mg/kg
Midazolam	8	2 (25)	0.07 mg/kg
Clonazepam	30	10 (33)	0.014 mg/kg
Levetiracetam	534	233 (44)	21 mg/kg
Valproate	111	47 (42)	20 mg/kg
Lacosamide	38	10 (27)	2.5 mg/kg
Phenytoin	13	3 (23)	10 mg/kg
Propofol	48	23 (48)	2.3 mg/kg
Other	28	10 (36)	
Total	852	347 (41)	

IQR, 25/75 interquartile range.

Epilepsia.2018 Oct;59 Suppl 2:150-154



- Current SE guidelines recommend a rapid stepwise treatment using benzodiazepines in monotherapy as the first line treatment, targeting $GABA_A$ synaptic receptors.

https://www.aesnet.org

Are we following the guideline?

- Time to SE treatment ?
- Type and dosage of ASM ?

Cutting-edge treatment in status epilepticus

- **Patient and Public**
  - time is the brain
  - seizure first aid
  - increasing awareness and education about status epilepticus
- **Healthcare professions**
  - time is the brain
  - importance of definition and classification of SE
  - follow the SE guideline
  - novel drugs and treatment strategies in status epilepticus?

Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults

- A benzodiazepine (specifically IM midazolam, IV lorazepam, or IV diazepam) is recommended as the initial therapy of choice, given their demonstrated efficacy, safety, and tolerability (level A, four class I RCTs).

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

Treatment of Refractory Convulsive Status Epilepticus: A Comprehensive Review by the American Epilepsy Society Treatments Committee

- No class I or II randomized controlled trials have been performed on the treatment of CRSE.

- Mostly insufficient evidence exists on the efficacy of stopping clinical CRSE using brivaracetam(BRV), lacosamide(LCS), levetiracetam (LEV), valproate(VPA), ketamine, midazolam (MDZ), pentobarbital (PTB; and thiopental), and propofol (PRO) either as the last ASM or compared to others of these drugs.

- Adrenocorticotropic hormone, IVIG, corticosteroids, magnesium sulfate, and pyridoxine have been used in special situations but have not been studied for CRSE.

Epilepsy Currents 2020, Vol. 20(5) 245-264

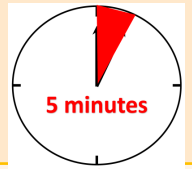
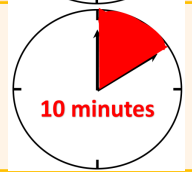
Adults with super-refractory status epilepticus (SRSE)

	Level of evidence	Comment
Therapeutic hypothermia	insufficient evidence	
Vagus nerve stimulation	insufficient evidence	
Inhalational anesthetics	insufficient evidence	
Brain surgery	insufficient evidence	Focal resection of a well-localized ictal zone in noneloquent cortex is recommended.
Perampanel	insufficient evidence	Possible role in the treatment of postanoxic seizure
Pregabalin	insufficient evidence	
Topiramate	insufficient evidence	

2020 American Epilepsy Society (AES) comprehensive review
Epilepsy Curr. 2021 Mar 10:1535759721999670.

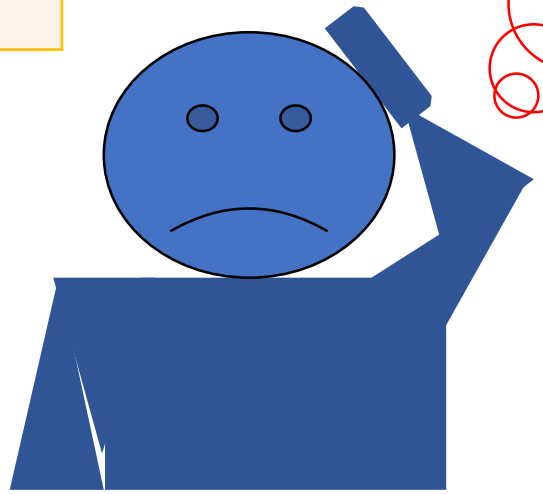
Novel drugs and treatment strategies in status epilepticus

A definition of status epilepticus (SE)

Type of SE	Time (t1)	Time (t2)
Tonic- clonic SE		30 min
Focal SE with impaired consciousness		> 60 min

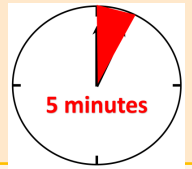
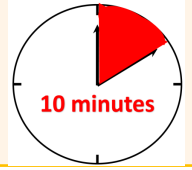
One of the biggest challenges is that SE patients may already have been in status epilepticus for quite a long period of time before coming to the hospital.

The first 1 to 2 hours are the critical time in achieving SE control. Very often, we have already lost most of that time.



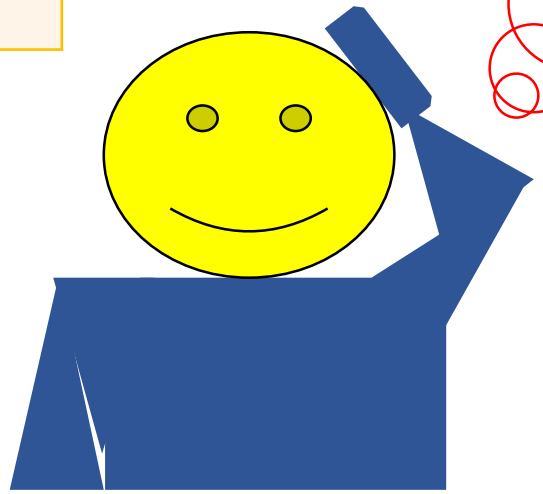
Worawit Sukpakkit

A definition of status epilepticus (SE)

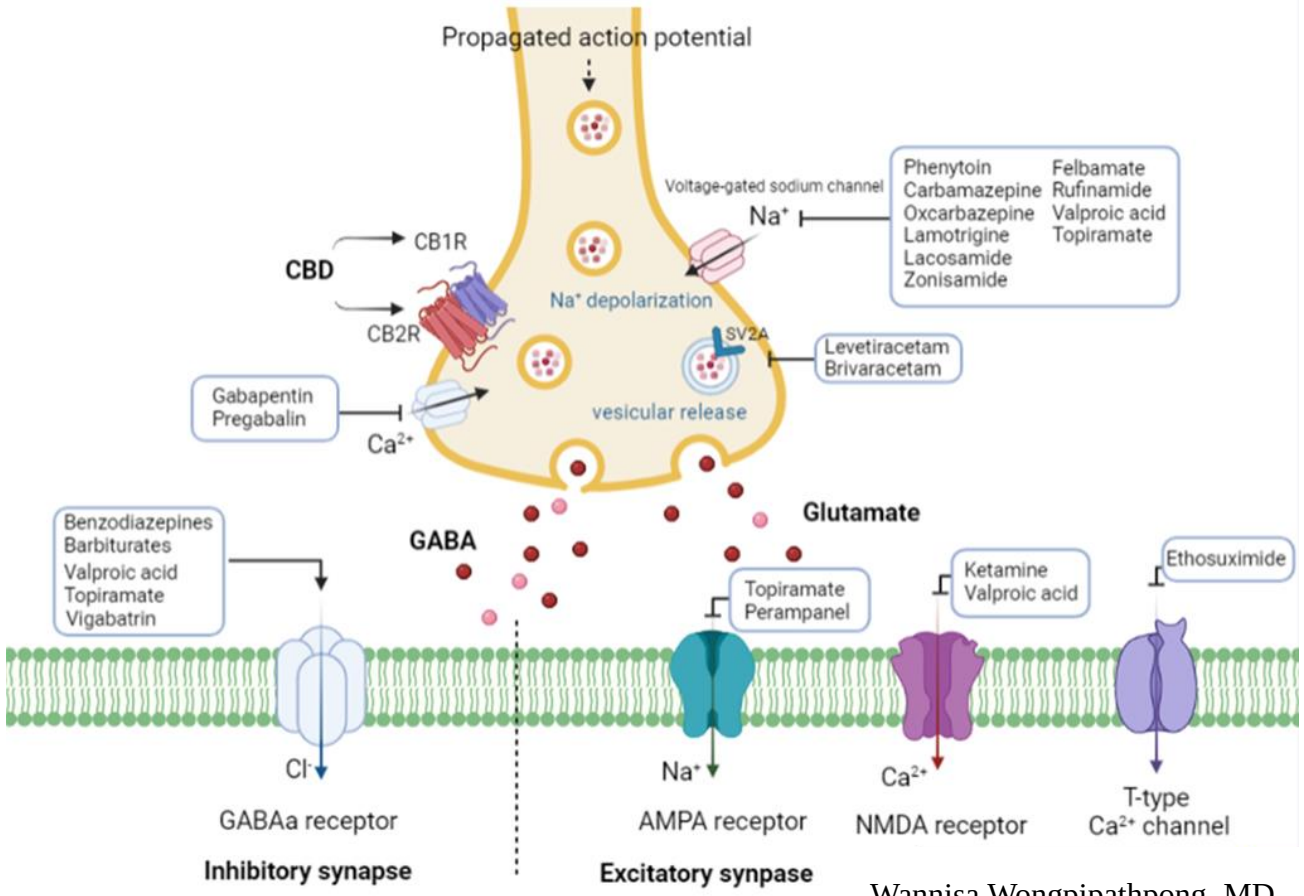
Type of SE	Time (t1)	Time (t2)
Tonic- clonic SE		30 min
Focal SE with impaired consciousness		> 60 min

Novel drugs target the underlying pathophysiology of SE?

Early polypharmacotherapy ?



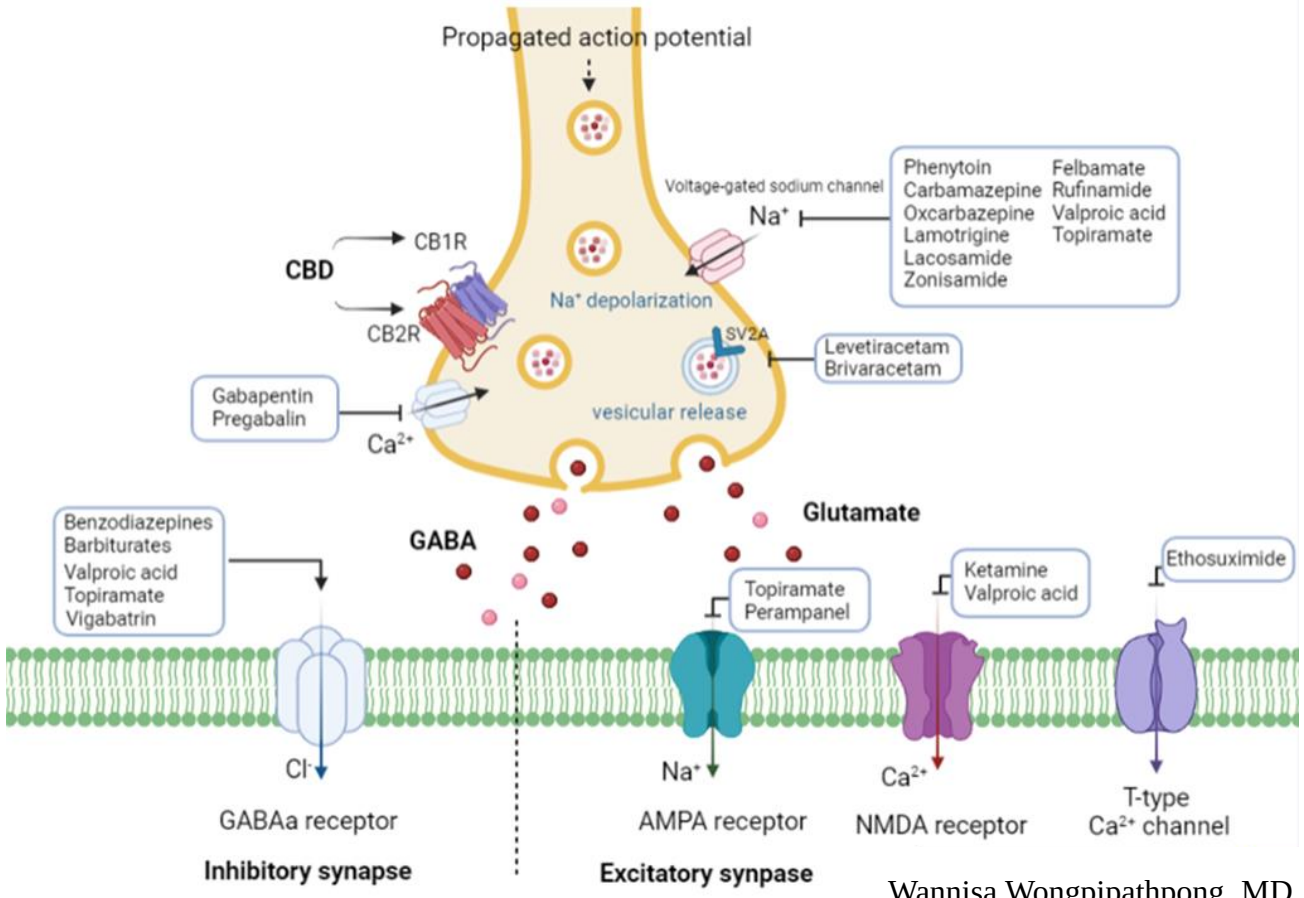
Novel drugs target the underlying pathophysiology of SE



- Brivaracetam
- Cannabinoids
- Ketamine
- Neurosteroid
- Topiramate
- Perampanel

Wannisa Wongpipathpong, MD

Brivaracetam (BRV)



Wannisa Wongpipathpong, MD

Mechanism of action: SV2A modulation

BRV is more selective than LEV with a higher affinity to the target.

BRV is more lipophilic than LEV, and has been shown an animal models to penetrate BBB more quickly than LEV.

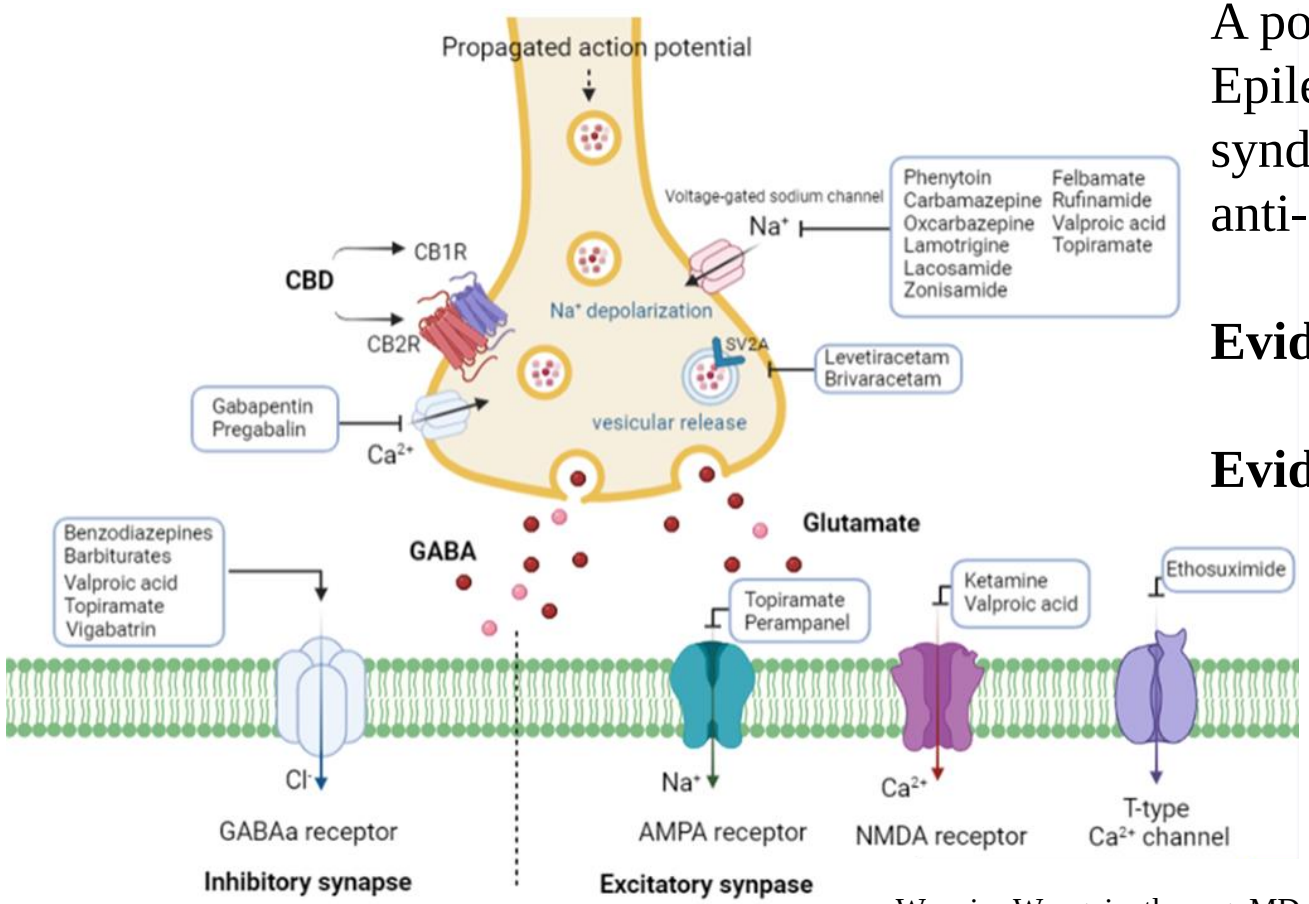
BRV is very attractive for use in emergency situations and critically ill SE patients (SE, RSE, SRSE).

Evidence in SE, RSE, SRSE: insufficient evidence

Epilepsy Behav. 2017 May;70(Pt A):177-181.

Epilepsia. 2019 Aug;60(8):1593-1601.

Cannabinoids



Wannisa Wongpipathpong, MD

Mechanism of action: CB1R, CB2R

A potential treatment in New-Onset Refractory Status Epilepticus (NORSE)/ febrile infection–related epilepsy syndrome (FIRES) → anti-inflammatory and anti-seizure effects*

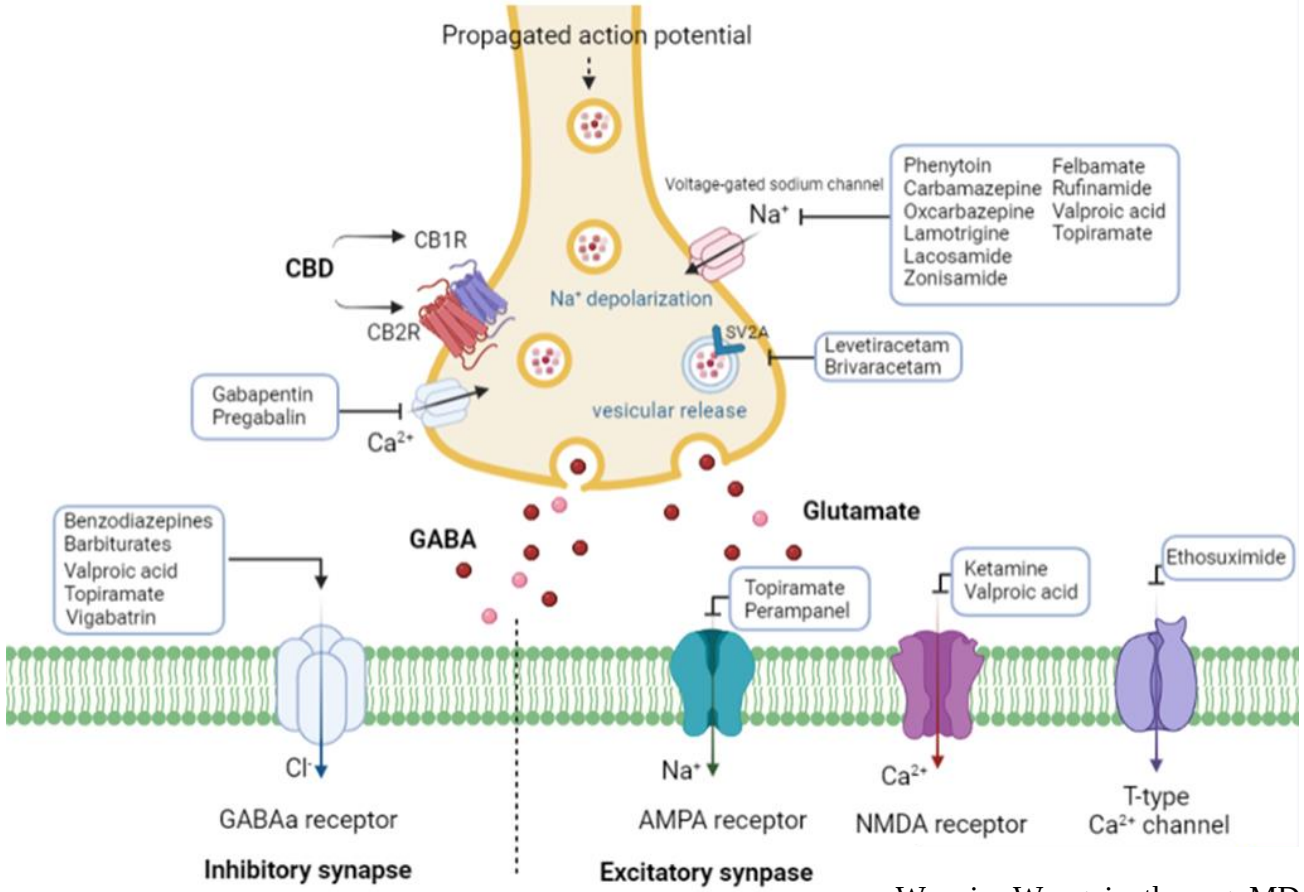
Evidence in SE, RSE: insufficient evidence

Evidence in SRSE: case report**

*Seizure. 2022 Jan;94:126-128.

**Seizure. 2016 Feb;35:56-8.

Ketamine



Wannisa Wongpipathpong, MD

Mechanism of action: N-methyl D-aspartate (NMDA) receptor antagonists

Ketamine is often selected after 5–6 ASMs have failed.

Earlier vs late implementation of ketamine ?

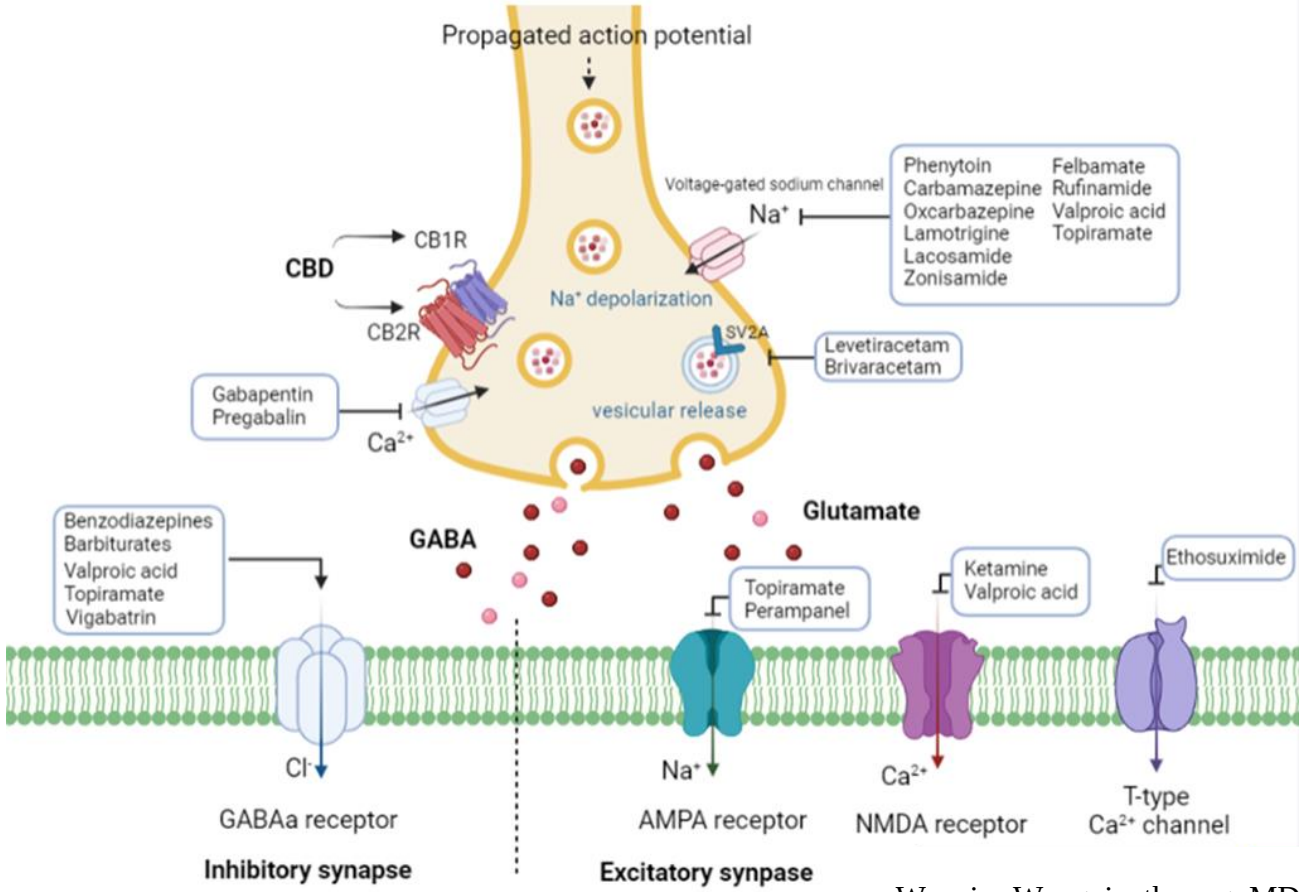
Evidence in SE, RSE: Ketamine appears to be effective on refractory SE (low level of evidence).

Evidence in SRSE: Class IV evidence. Ketamine treatment was associated with a decrease in seizure burden , decreased vasopressor requirements without increased intracranial pressure, n= 68 SRSE pts.*

Adverse effects: elevation of blood pressure, increased intracranial pressure

*Neurology. 2020 Oct 20;95(16):e2286-e2294.

Neurosteroid



Wannisa Wongpipathpong, MD

Neurosteroid → Allopregnanolone (AP), Brexanolone (GNX)

Mechanism of action: target $GABA_A$ synaptic and $GABA_A$ extrasynaptic receptors

Neurosteroids could be a therapeutic option for SE since they target extrasynaptic $GABA_A$ receptors > $GABA_A$ synaptic receptors.

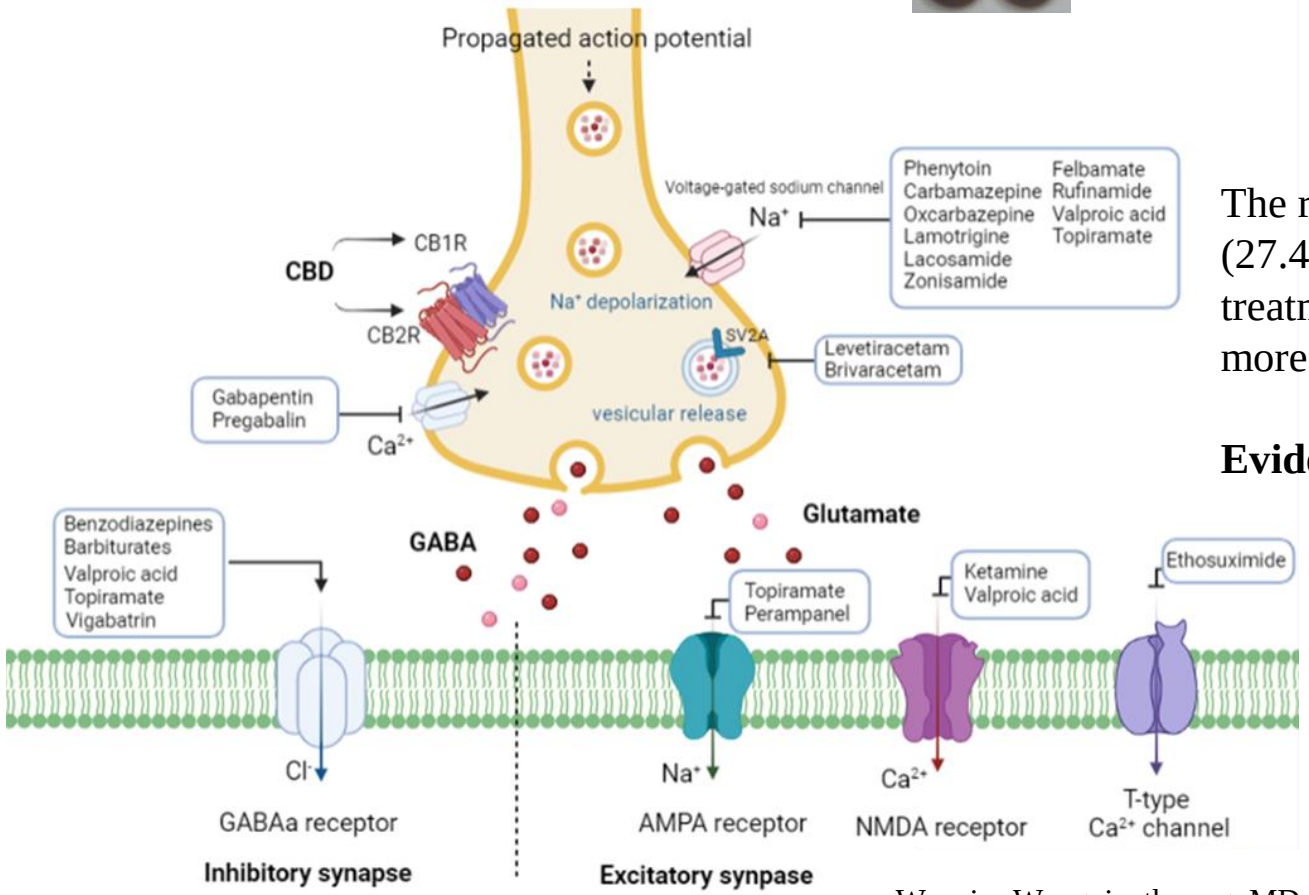
Neurosteroids are reduced in status epilepticus.

Decreased allopregnanolone levels in cerebrospinal fluid obtained during status epilepticus*

Evidence in SE, RSE, SRSE: insufficient evidence**

*Epilepsia. 2017 Feb;58(2):e16-e20.
**Epilepsia.2018;59(S2):216–219.

Topiramate (TPM)



Wannisa Wongpipathpong, MD

Mechanism of action:

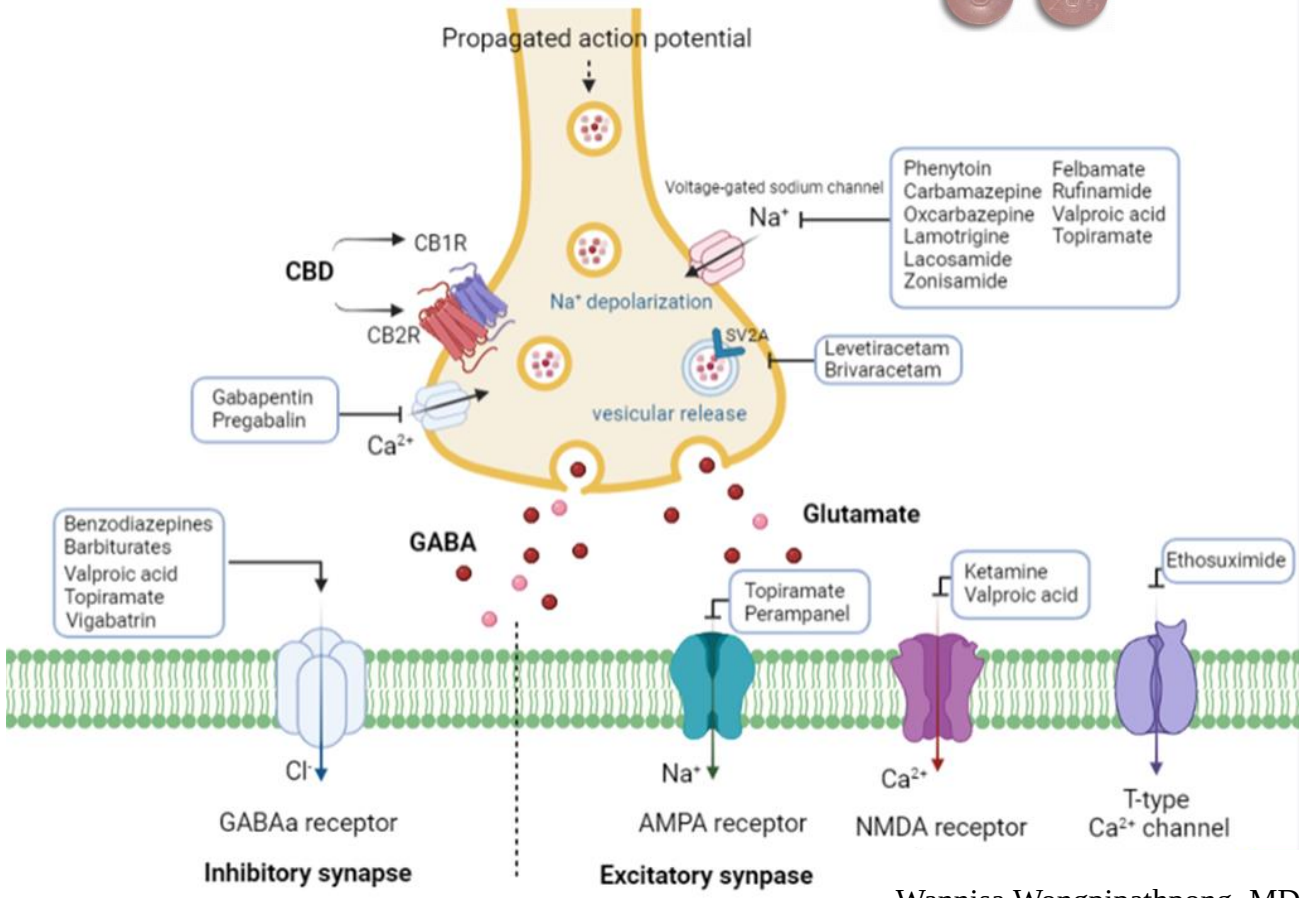
Blockade of the ionotropic glutamatergic AMPA/kainate receptors
Blocks neuronal voltage-dependent sodium channels
Enhancement of GABAergic activity
Inhibition of L-type calcium channels
Inhibition of carbonic anhydrase

The rate of SE cessation attributed to TPM treatment (27.4%) represents a relevant response given the late treatment position of TPM and the treatment latency of more than 8 days.*

Evidence in SE, RSE, SRSE: insufficient evidence

*Epilepsia. 2019 Dec;60(12):2448-2458.

Perampanel (PER)



Wannisa Wongpipathpong, MD

Perampanel (PER)

Mechanism of action: selective, non-competitive alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor agonist

Dosages of up to 32 mg/day have been assessed with overall good tolerability

Efficacy and tolerability of high dosages at intervals shorter than 24 h should be studied.

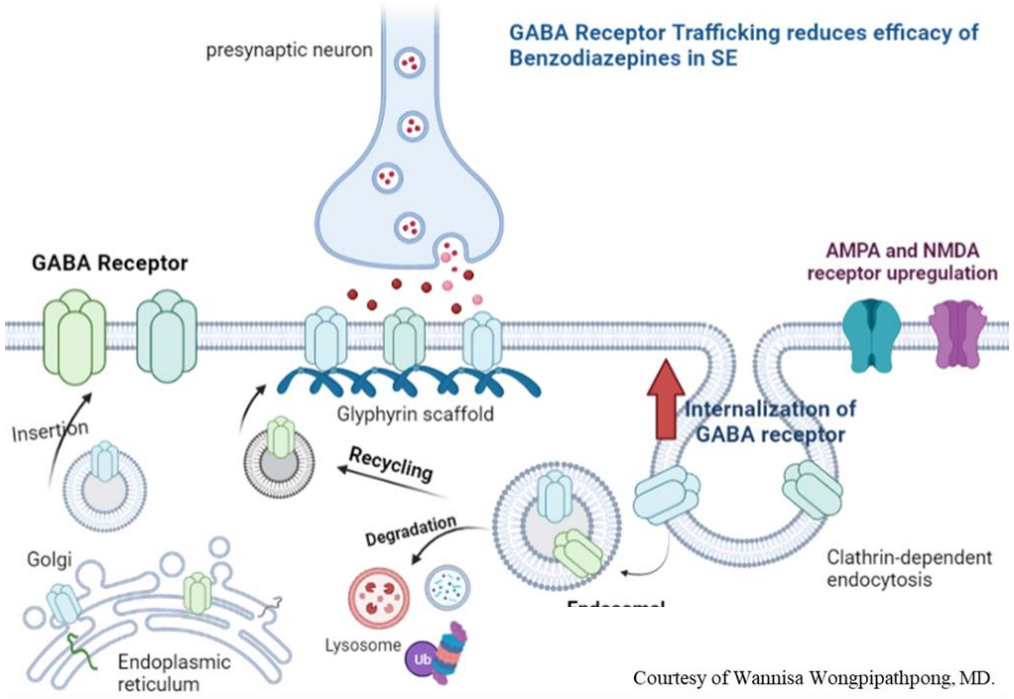
Evidence in SE, RSE, SRSE: insufficient evidence*

*Epilepsy Behav. 2022 Mar;128:108583.

Treatment strategies in status epilepticus

Convulsive status epilepticus

Prolonged time (t1)

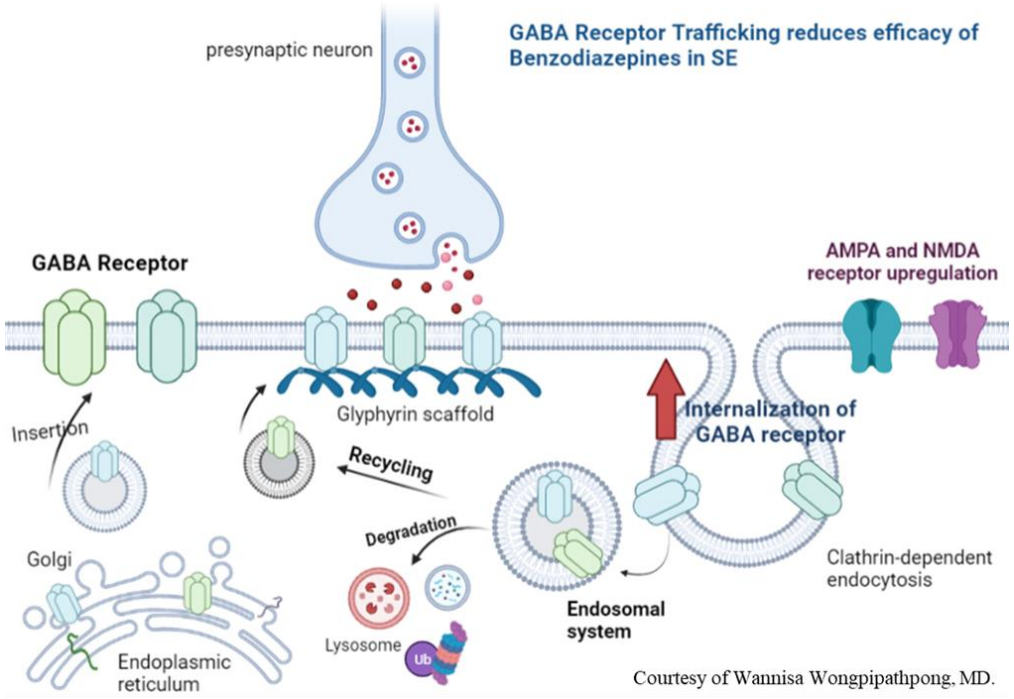


Receptor trafficking hypothesis

Changes at the synapse level during SE include a progressive decrease in synaptic $GABA_A$ receptors and increase in synaptic NMDA receptors. These changes tend to promote self-sustaining seizures, and pharmacoresistance.

Convulsive status epilepticus

Prolonged time (t1)



Receptor trafficking hypothesis

Treatment strategies in status epilepticus

Cardiovascular and metabolic support

Reduced time to SE treatment

Adequate AEDs dosage and administration

Early switch from benzodiazepines to other AEDs

A timely transition to non-benzodiazepine AED

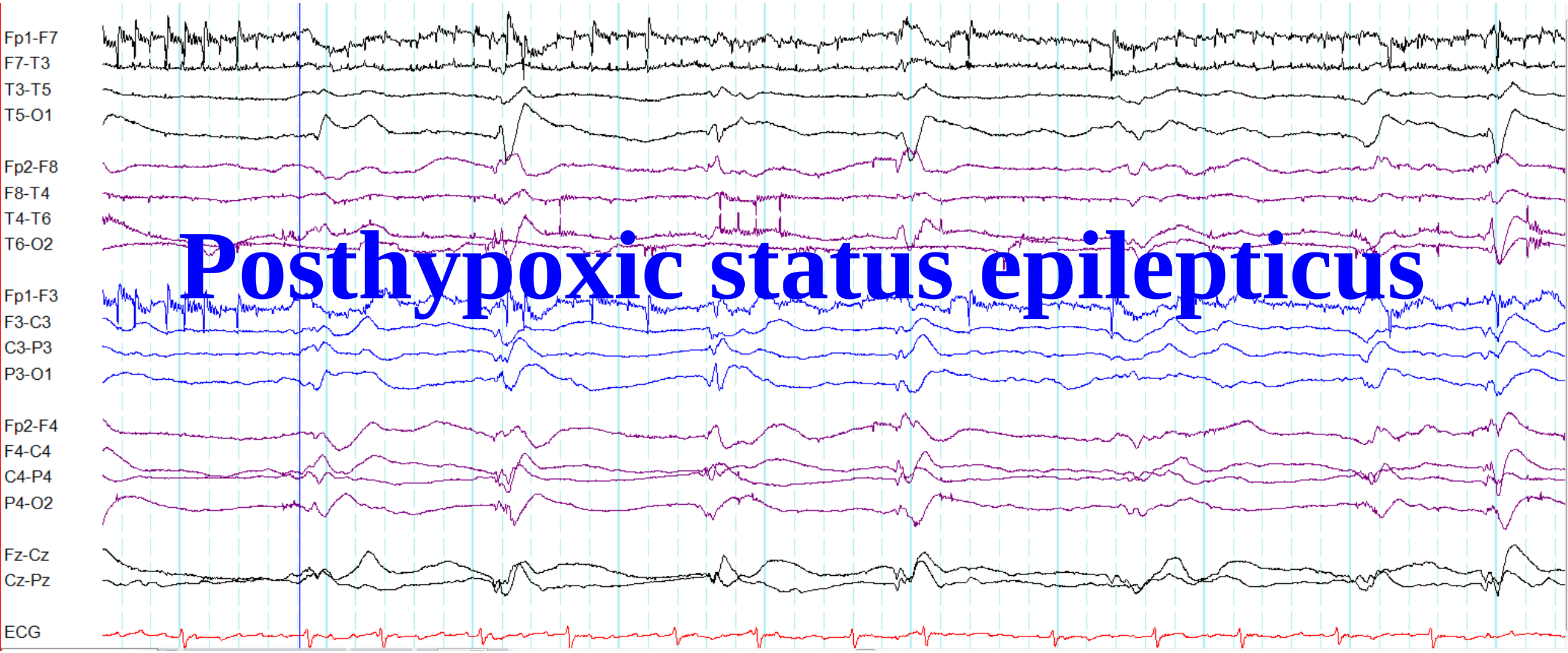
Targeting extrasynaptic $GABA_A$ receptor: allopregnanolone

Early polytherapy(limited number of clinical studies)

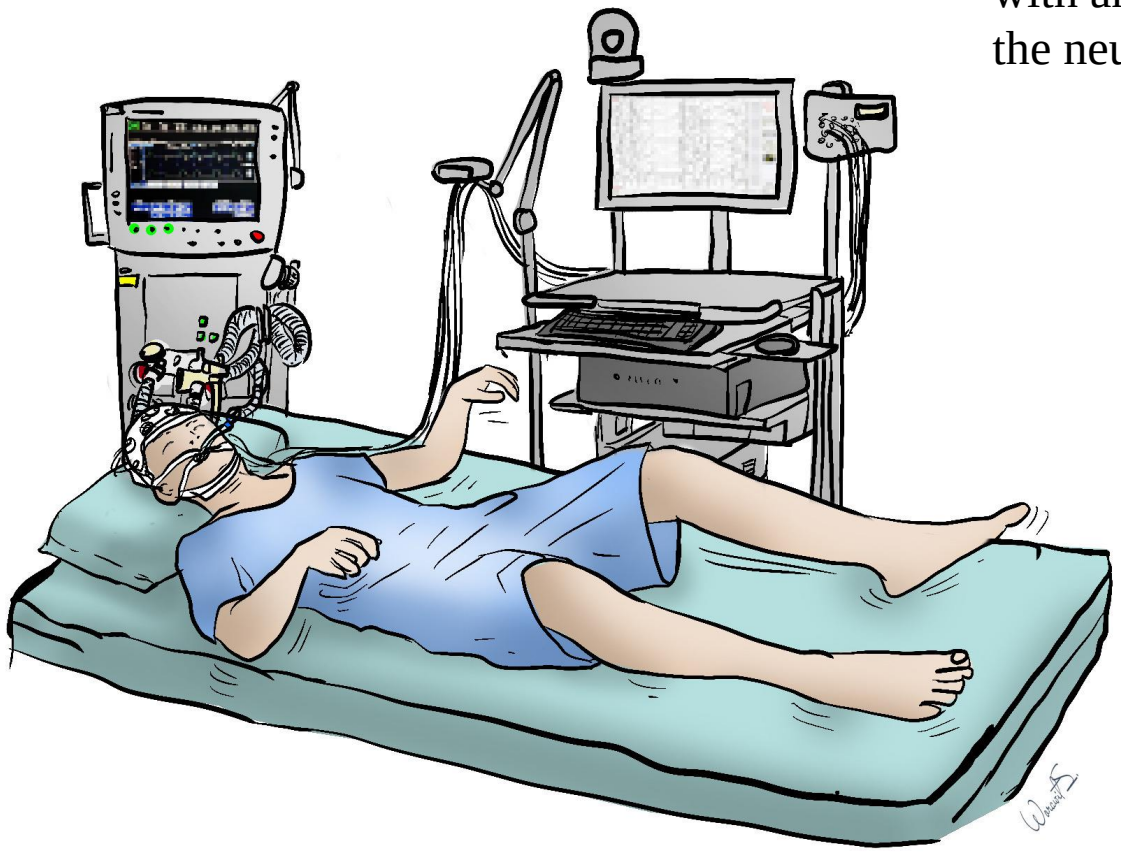
Early polytherapy for benzodiazepine-refractory status epilepticus

- Limited number of clinical studies

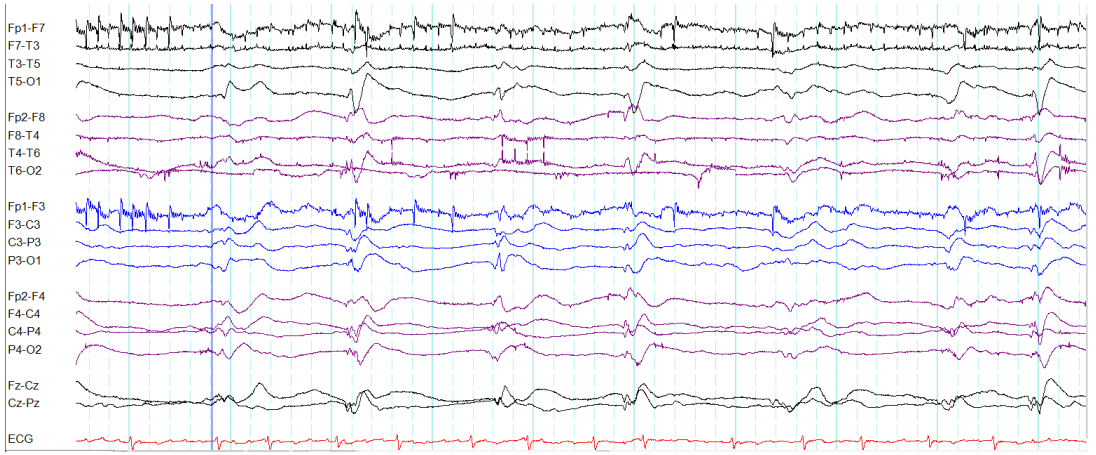
- Currently, evidence is lacking to recommend specific combinations of AEDs.



Posthypoxic status epilepticus



Whether rhythmic and periodic EEG patterns should be treated with antiseizure medications, with the goal of improving the neurologic outcome, is unclear.



Myoclonic SE with coma

Worawit Sukpakkit

(TELSTAR trial)

RESEARCH SUMMARY

Treating Rhythmic and Periodic EEG Patterns in Comatose Survivors of Cardiac Arrest

Ruijter BJ et al. DOI: 10.1056/NEJMoa2115998

CLINICAL PROBLEM

Periodic and rhythmic electroencephalographic (EEG) patterns have been reported in 10 to 35% of comatose survivors of cardiac arrest, potentially indicating electrographic seizures. Whether aggressively suppressing this EEG activity would improve neurologic outcomes is unknown.

CLINICAL TRIAL

Design: A pragmatic, open-label, multicenter, randomized trial assessed neurologic outcomes among comatose survivors of cardiac arrest whose rhythmic and periodic EEG activity was treated with an aggressive antiseizure strategy or with standard care.

Intervention: 172 patients were assigned to receive either stepped antiseizure treatment aimed at suppressing rhythmic and periodic EEG activity for at least 48 consecutive hours or standard care, which could include sedative medication. Both groups received targeted temperature management. The primary outcome was neurologic outcome according to the score on the Cerebral Performance Category (CPC) scale.

RESULTS

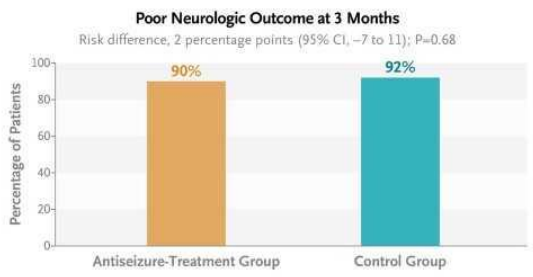
Efficacy: Complete or partial suppression of periodic or rhythmic activity for 48 consecutive hours occurred in 56% of patients in the aggressive treatment group and 2% of those in the control group. At 3 months, the incidence of a poor neurologic outcome (CPC score indicating severe disability, coma, or death) was similar in the two groups.

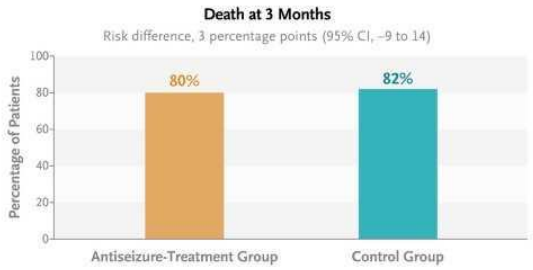
Safety: The incidence of serious adverse events was high in both groups.

LIMITATIONS AND REMAINING QUESTIONS

- Decisions regarding withdrawal of life-sustaining treatments may have been imbalanced in the two groups, because mortality at 48 hours was higher in the control group.
- Patients in the antiseizure-treatment group were more likely to receive sedatives, and withdrawal of life-sustaining treatment may have been delayed in this group.
- Treating clinicians were aware of trial-group assignments, which could have affected medication treatment choices and decisions about withdrawal of care.

Links: Full Article | NEJM Quick Take





CONCLUSIONS

An intensive strategy of suppressing rhythmic and periodic EEG patterns with antiseizure treatment did not improve neurologic outcomes over standard care in comatose survivors of cardiac arrest, but outcomes were very poor in both groups.

Table 1. Characteristics of the 172 Patients at Baseline.*

Characteristic	Antiseizure Treatment (N=88)	Control (N=84)†
Demographic characteristics		
Median age (IQR) — yr	64 (56–73)	66 (59–74)
Male sex — no./total no. (%)	60/88 (68)	58/83 (70)
Characteristics of cardiac arrest		
Location of cardiac arrest — no./total no. (%)		
Out of hospital	84/88 (95)	78/83 (94)
In hospital	4/88 (5)	5/83 (6)
Presumed cause of cardiac arrest — no./total no. (%)		
Cardiac	70/88 (80)	64/83 (77)
Other	9/88 (10)	14/83 (17)
Unknown	9/88 (10)	5/83 (6)
Bystander-witnessed cardiac arrest — no./total no. (%)	62/88 (70)	53/83 (64)
First monitored rhythm — no./total no. (%)		
Shockable	51/85 (60)	58/81 (72)
Nonshockable	34/85 (40)	23/81 (28)
Median time from cardiac arrest (IQR) — min		
To start of basic life support	5 (1–8)	5 (3–10)
To return of spontaneous circulation	16 (10–30)	19 (12–25)
Clinical characteristics at randomization		
Median APACHE IV score (IQR)‡	103 (76–119)	106 (87–119)
Nystagmus — no./total no. (%)	2/65 (3)	4/61 (7)
Myoclonus — no./total no. (%)	50/82 (61)	48/75 (64)
Standard care — no./total no. (%)		
Targeted temperature management, 33°C	21/88 (24)	20/83 (24)
Targeted temperature management, 33–36°C	67/88 (76)	63/83 (76)
EEG monitoring		
Median time from return of spontaneous circulation to start of continuous EEG monitoring (IQR) — hr	15 (9.4–19.2)	12 (6.9–17.7)
Median time from resuscitation to onset of RPP (IQR) — hr	36 (27.4–43.3)	33 (25.4–43.9)
EEG pattern at randomization — no./total no. (%)		
Generalized periodic discharges, 0.5–2.5 Hz	68/88 (77)	67/83 (81)
Electrographic seizures, ≥2.5 Hz	9/88 (10)	8/83 (10)
Evolving patterns, 0.5–2.5 Hz§	2/88 (2)	3/83 (4)
Other rhythmic or periodic patterns, 0.5–2.5 Hz	9/88 (10)	5/83 (6)
Background continuity of EEG at start of RPP — no./total no. (%)		
Continuous	56/88 (64)	40/83 (48)
Discontinuous	19/88 (22)	29/83 (35)
Suppressed	13/88 (15)	14/83 (17)
Somatosensory evoked potential — no./total no. (%)		
Evoked potential measured	61/88 (69)	60/83 (72)
N20 bilaterally absent¶	20/61 (33)	17/60 (28)

N Engl J Med 2022;386:724-34.

Conclusion

- Status epilepticus is a time-sensitive, life-threatening medical emergency. The sooner treatment is initiated, the better the chances of success, and the lower the risk for adverse consequences.

- Achieving seizure control within the first 1-2 hours after seizure onset is a significant determinant of outcome.

Thank you

- Pongsakorn Kongsakorn, MD
- Wannisa Wongpipathpong, MD
- Worawit Sukpakkit, MD

สมาคมโรคลมชักแห่งประเทศไทย
Epilepsy Society of Thailand

Thank you