EEG patterns in status epilepticus and coma

Dr. Chusak Limotai, MD., M.Sc., CSCN (C)

Chulalongkorn Comprehensive Epilepsy Center of Excellence (CCEC)

Talk overview

- Anatomic localization and EEG pattern
- EEG patterns of acute encephalopathy
- EEG patterns in post cardiac arrest
- Ictal-interictal continuum EEG patterns

  - Which patterns warrant treatment?
- Ictal EEG patterns and criteria for nonconvulsive status epilepticus in comatose patients

Introduction

- The EEG has been available but often neglected as a quick, noninvasive, inexpensive, first test for evidence of organic confusion in favor of its use more specifically for seizures and epilepsy

Kaplan PW and Sutter R; J Clin Neurophysiol 2013

- EEG enables rapid bedside electrophysiological monitoring providing dynamic real-time information on neocortical brain activity and dysfunction

Sutter R et al; *J Clin Neurophysiol 2015*

Usefulness of EEG in critically ill patients

- Identifying epileptic states or interictal patterns
- Identifying whether altered mental status is because of
  - lateralized focal dysfunction
  - cortical or subcortical dysfunction
  - excessive sleepiness
  - problem of arousal
  - possible medication intoxication

**** EEG may at times reveal the preponderant cause of encephalopathy e.g. TWs suggest that hepatic failure dominate the clinical picture****

Anatomic localization and EEG pattern

- Investigations with clinical-EEG-imaging correlations should expedite appropriate triage and management of patients in the ICU, ER, and general ward

Kaplan PW and Rossetti AO et al; J Clin Neurophysiol 2011

TABLE 3. Anatomic Localization and EEG Pattern

Anatomic Localization	EEG Frequency/Pattern
Cortical	Decreased α amplitude Slowing of posterior α background frequency
Subcortical/white matter	Increased polymorphic or arrhythmic δ-activity TWs Frontal intermittent δ-activity
Cortical and subcortical	Slow posterior basic rhythm (background activity) *with* slow-wave intrusion (arrhythmic δ-activity)
Brain stem	Arrhythmic δ-activity, rhythmic δ-activity Impaired arousal patterns Spindle activity

Kaplan PW and Rossetti AO et al; J Clin Neurophysiol 2011

Anatomic localization

- Slowing of EEG background activity without slow-wave activity in the delta range has been linked to **cortical impairments** that spare subcortical structures
- **Subcortical/white matter abnormalities or hydrocephalus** can lead to projected slow-wave activity or to TWs
- Clinical entities involving **both cortical and subcortical regions** (diffuse cerebral abnormalities) engender both background slowing and slow-wave activity

Kaplan PW and Rossetti AO et al; J Clin Neurophysiol 2011

Locations of the lesions	EEG findings
Diffuse cortical and subcortical gray matter disease, whether or not this pathology was associated with lesions in the white matter	**Generalized bilaterally synchronous paroxysmal discharges** *(abnormal interactions between cortical and subcortical neuronal systems)*
White matter diseases	**Continuous non-paroxysmal polymorphic delta activity** Absence of paroxysmal discharges
Diffuse encephalopathies involving gray and white matters	Generalized bilaterally synchronous paroxysmal discharges **+** Continuous non-paroxysmal polymorphic delta activity

Gloor P et.al; Electroenceph Clin Neurophysiol 1955

EEG patterns of acute encephalopathy

- Encephalopathy is a term often used by electroencephalographer, referred to as delirium in psychiatry and as altered mental status or acute confusional states in neurology

Multiple symptoms of encephalopathy

Kaplan PW and Sutter R; J Clin Neurophysiol 2013

EEG patterns in acute encephalopathy

- FIRDA
- TWs
- Theta pattern
- Theta/delta pattern
- Polymorphic high-voltage delta pattern

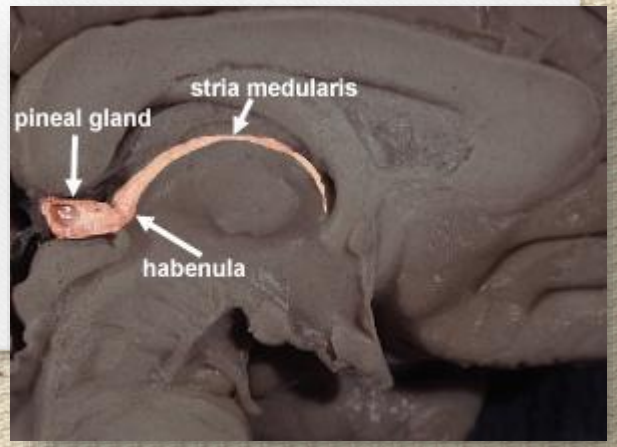
FIRDA

- a repetitive appearance of up to 2 seconds of frontal rhythmic slow (delta) waves activity at < 4 Hz, usually is reactive to external noxious stimulation
- Generally reflects an old fixed structural problem (e.g., stroke)

FIRDA

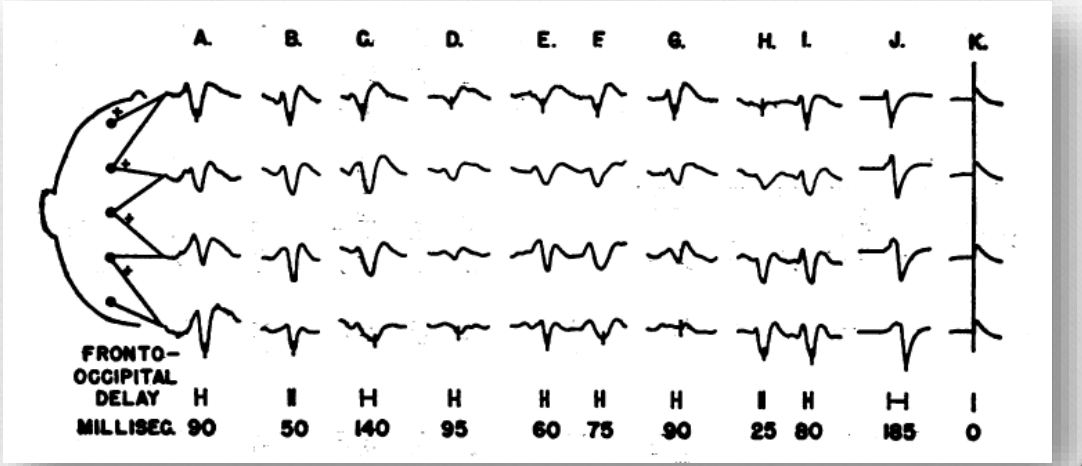
- Transient intermittent rhythmic slow waves, 1.5-4 Hz, localized mainly over frontopolar regions
- Occurs in adults, in contrast with OIRDA
- Associated with **mild to moderate diffuse encephalopathy** particularly from renal failure and hyperglycemia
- **Pathological hyperactivity occurring in diffuse gray matter disease, in both cortical and subcortical gray locations**
- Old ischemic structural brain lesions may predispose some patients to develop FIRDA during acute metabolic derangement
- Deep midline lesions were present only in a minority of the patients

  Cobb's (1945) lesions in the **epithalamus** produced "rhythmic delta activity"



Triphasic waves

- “ **The main deflection is downward, indicating a surface positive change**. The main deflection is usually preceded and followed by low-amplitude negative deflections giving the whole complex a triphasic contour”



Bickford RG and Butt HR; J Clin Invest 1955

Clinical correlates

- TWs have been described in ***a large number of medical conditions*** including
  - Metabolic encephalopathies
  - Dementia
  - Drugs (cephalosporin, lithium, levodopa, baclofen, valproic acid)
  - Paramedian thalamic infarction
  - Sepsis-associated encephalopathy
  - Hashimoto's encephalopathy
- TWs are believed to reflect abnormal activity within thalamo-cortical circuits

Kernaze DS and Bickford RG; Electroencephalogr Clin Neurophysiol 1984

- **TWs are likely to be a marker of a single variable, but rather a result of a complex interplay of metabolic, toxic, infectious, and structural cerebral abnormalities that affect thalamo-cortical circuits**

Predominant brain abnormalities:

white matter change (60%) and/or

brain atrophy (55%)

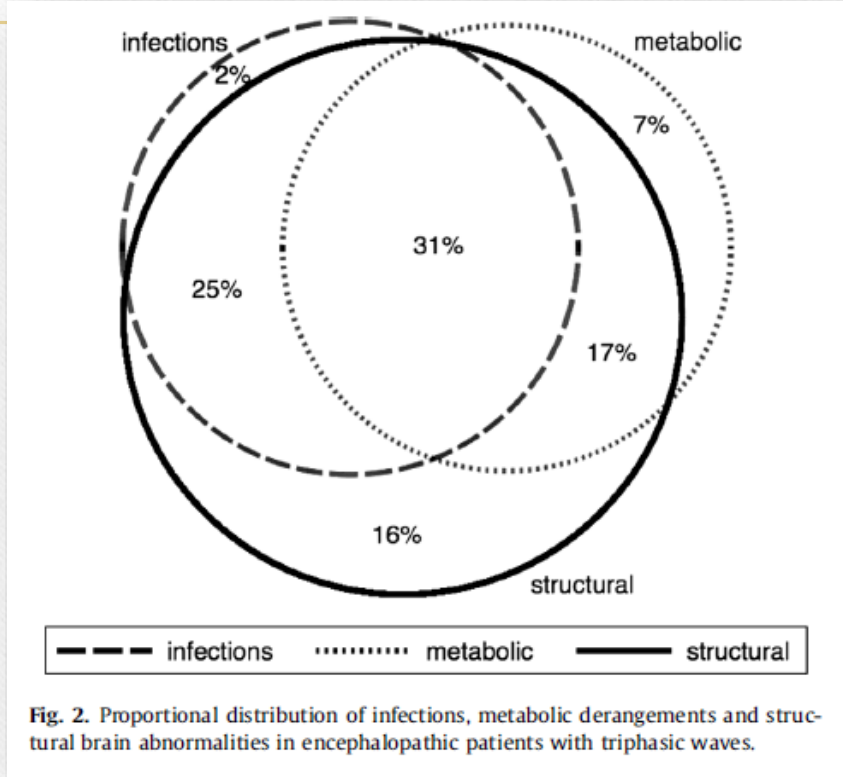


Fig. 2. Proportional distribution of infections, metabolic derangements and structural brain abnormalities in encephalopathic patients with triphasic waves.

Sutter R; Clin Neurophysiol 2013

Theta pattern

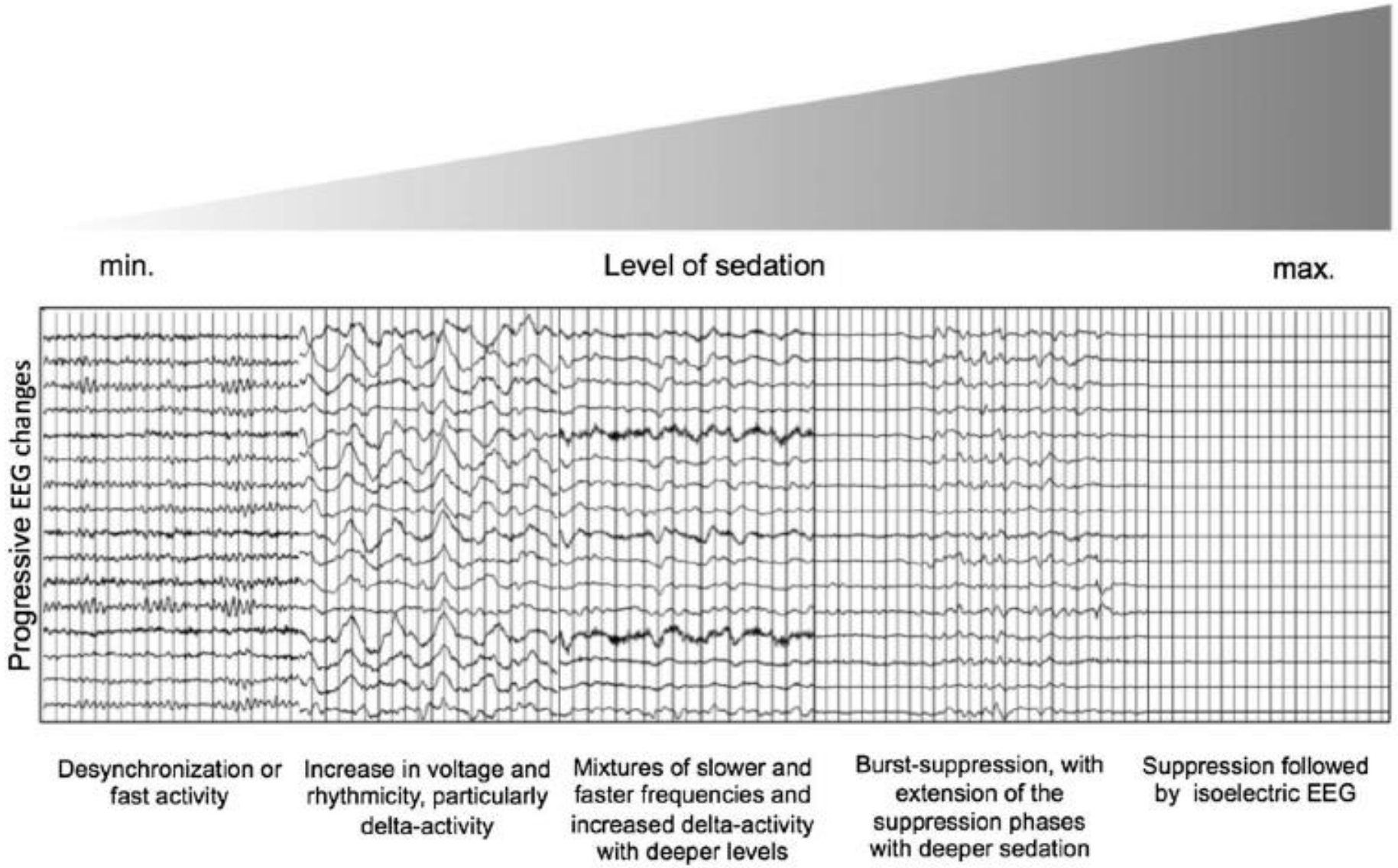
- Generalized slow background activity with a frequency of 4-7 Hz and amplitude of > 40 μV without intrusion of delta (<4 Hz) or alpha activity (8-13 Hz) for > 20% of the recording during wakefulness
- Benign theta-dominant patterns with preserved background reactivity in patients with cortical dysfunction (dementia and mild-to-moderate encephalopathy), it can be seen without background reactivity to external stimulation in coma from hypoxic-ischemic brain injury and carries a poor prognosis

Theta/delta pattern

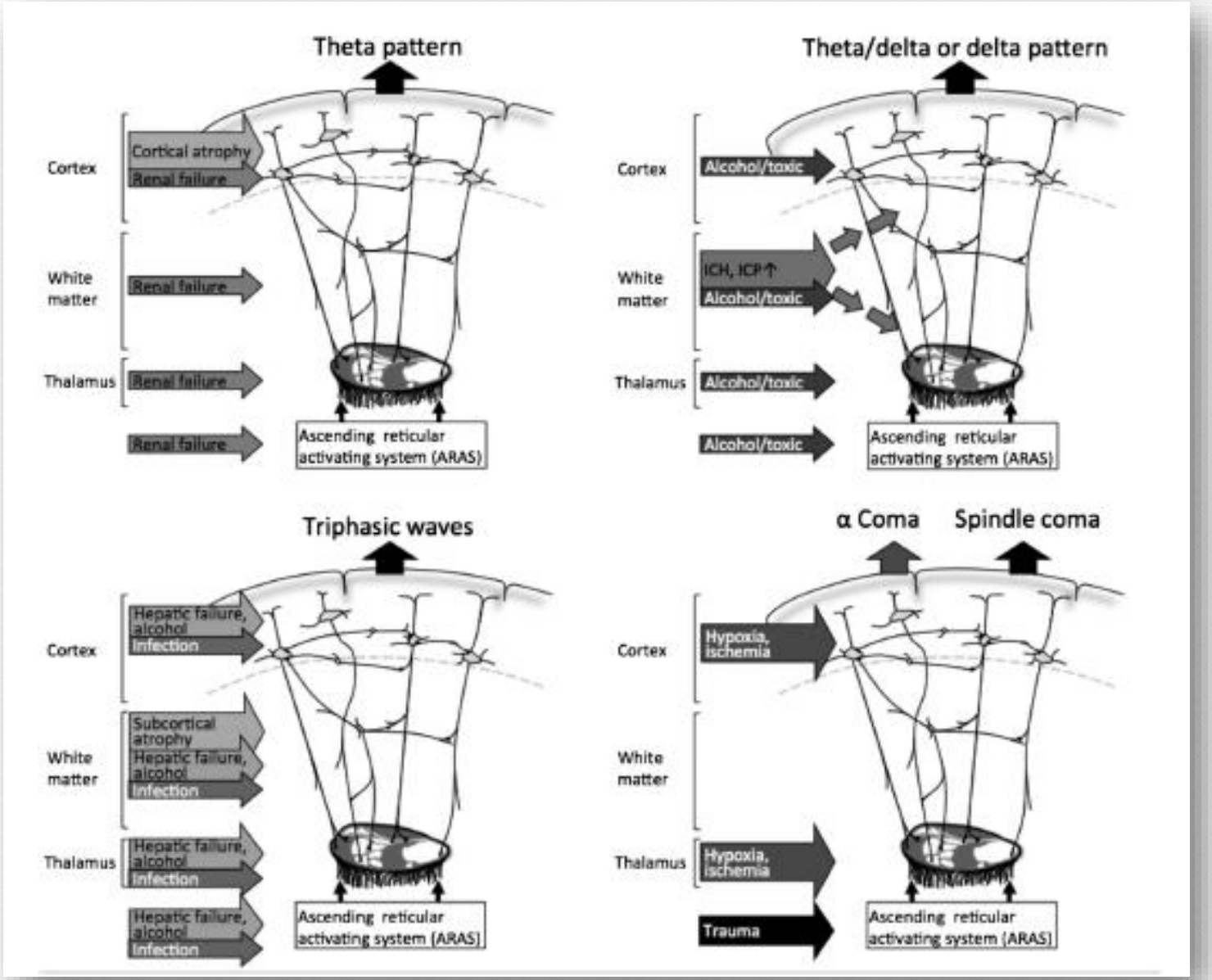
- Generalized slow background activity of 4-7 Hz and amplitude of > 80 μV with intrusion of alpha activity for < 20% of the recording during wakefulness and intermixed with delta activity in 20-50% during drowsiness or arousal

Polymorphic high-voltage delta pattern

- Generalized slow background activity of <4 Hz and amplitude of > 80 μV with intrusion of theta or alpha activity for <20% of the recording during drowsiness or arousal
- Usually arises in more advanced states of encephalopathy as well as in coma and is predominantly reflected over the anterior regions but then tends to appear more diffusely as coma deepens
- Predominant structural abnormalities involve large areas of the subcortical white matter; however, severe metabolic derangements may also produces similar patterns and focal or unilateral delta activity usually associated with focal subcortical brain lesions

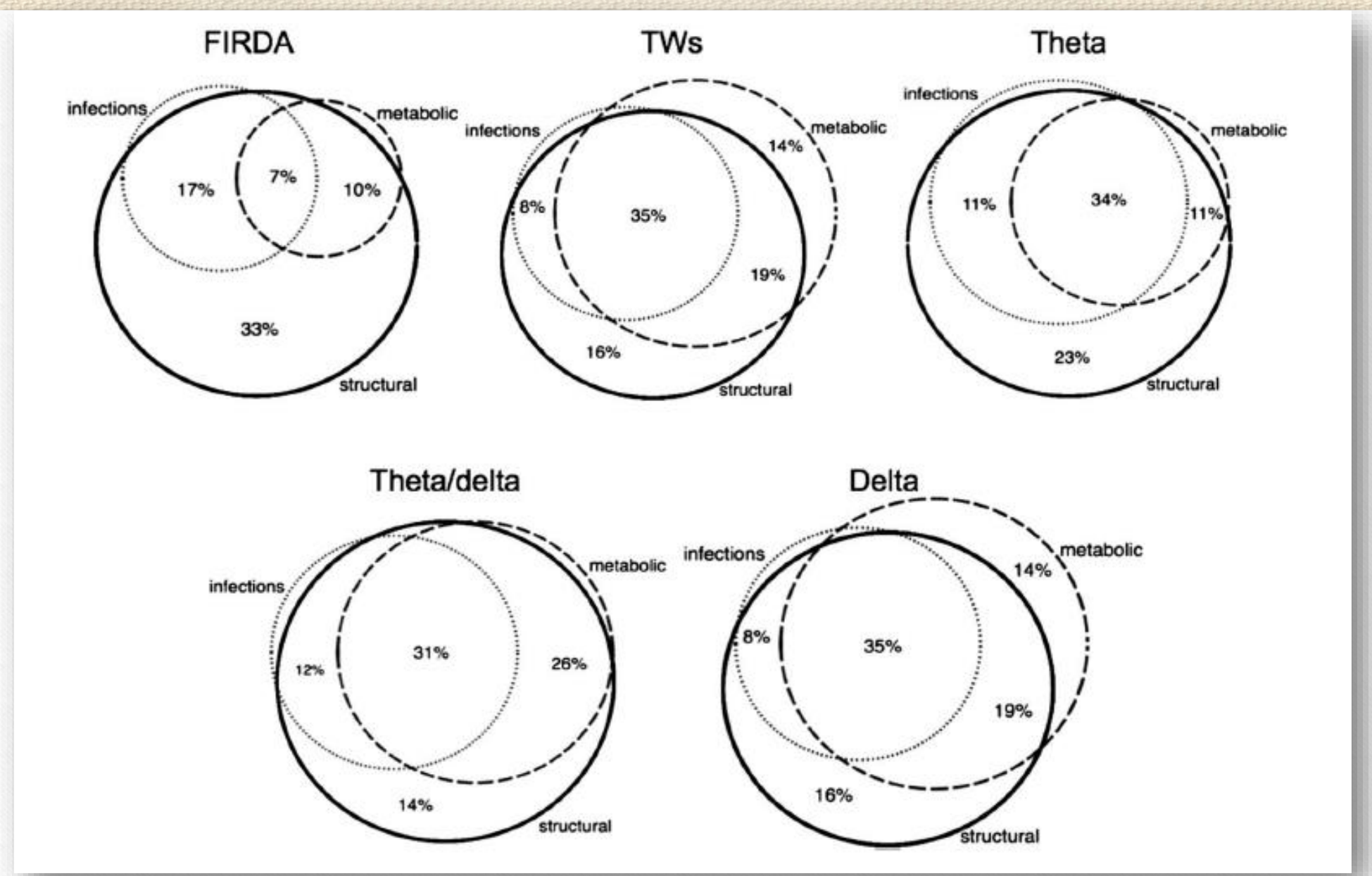


Sutter R et al; J Clin Neurophysiol 2015



Etiologies of specific EEG patterns in encephalopathy. Intracerebral hemorrhage (ICH) and increased intracranial pressure (ICP)

Kaplan PW and Sutter R; J Clin Neurophysiol 2013



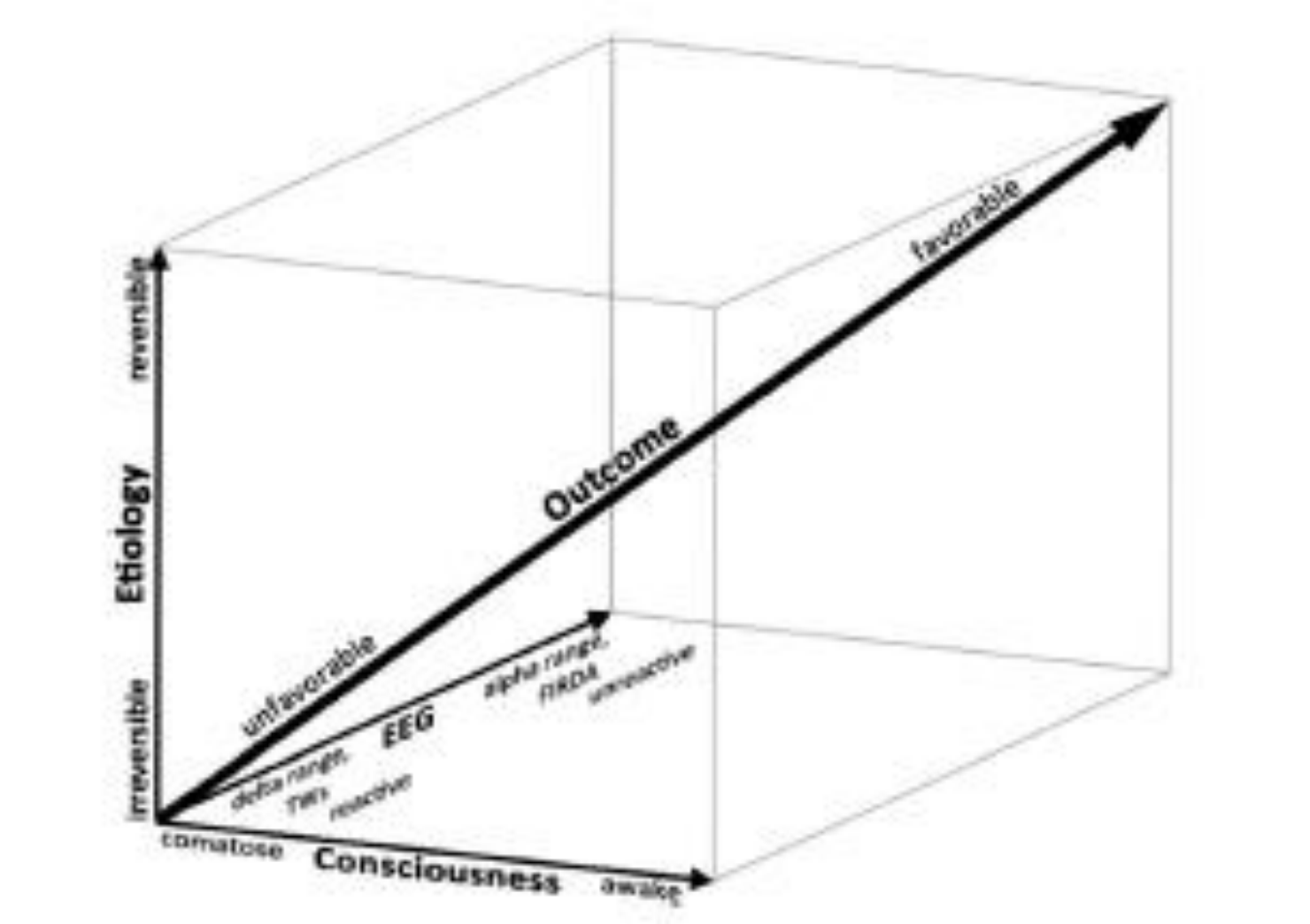
Sutter R and Kaplan PW; J Clin Neurophysiol 2013

Clinical and imaging correlates of EEG patterns in encephalopathic patients (154 hospitalized patients)

	Imaging correlates	OR	Multivariate analysis *p*-value	Outcome
Theta	Brain atrophy	2.6	0.02	
Theta/delta	Intracerebral hemorrhages	6.8	0.005	Unfavorable (OR 2.5, p =0.033)
FIRDA	Past CVA	2.7	0.004	Favorable (OR 4.8, *p* = 0.004)
TWs	Liver failure multi-organ failure	6 4	0.004 0.039	Death (OR 4.5. *p* = 0.005)
Delta	Alcohol/drug abuse with or without intoxication HIV infection	3.8 9	0.003 0.004	

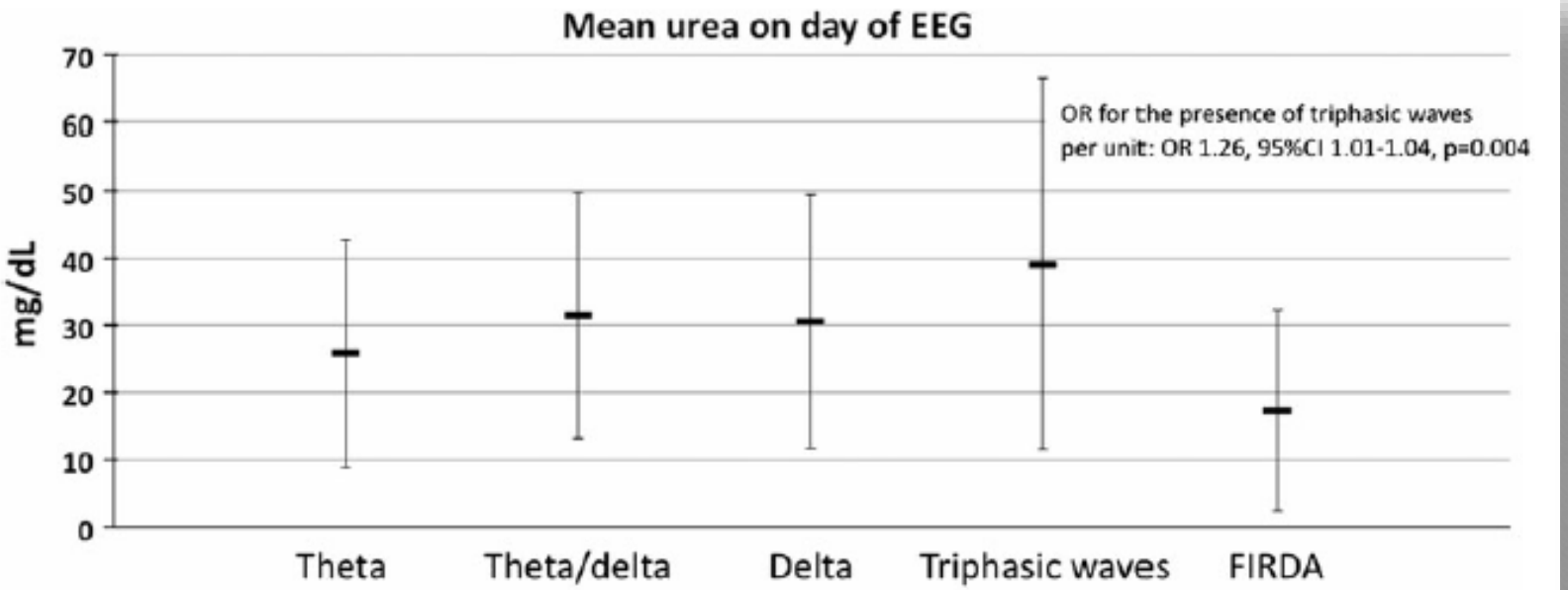
At discharge: GCS 1-3: unfavorable; GCS >3 : favorable outcome

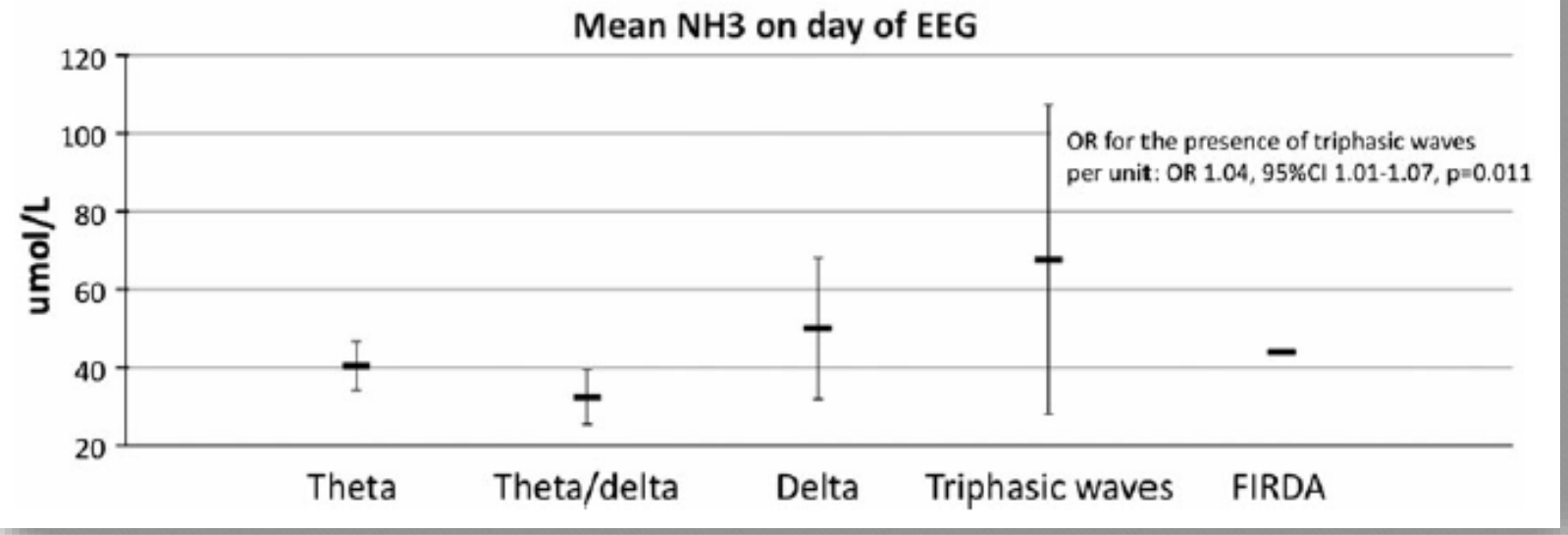
Sutter R et al; J Neurol 2013

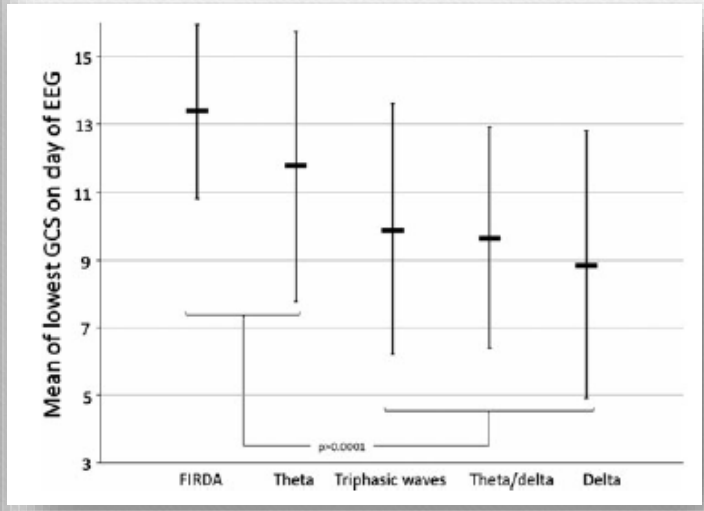


Proposed diagram for prognostication of outcome in encephalopathy

Kaplan PW and Sutter R; J Clin Neurophysiol 2013







Sutter R et al; J Neurol 2013

Reactivity of the background activity

- A variety of forms of reactivity
  - an increase or decrease in amplitude
  - an increase or decrease in frequency
- EEG responsiveness (EEG change after sensory stimulation) is associated with greater chance of recovery than lack of reactivity
- Reactivity should be tested in all comatose patients, unless contraindicated because of concerns regarding raised intracranial pressure

Young GB et al; J Clin Neurophysiol 1999

Bedside testing for EEG reactivity

- **Auditory reactivity**: clapping or shouting in the patient's ears
- **Somatosensory stimulation**: applying pressure to the nail bed of each hand and to the supraorbital nerve above the medial third of the eyebrow
- **Passive eye opening**: is recommended in suspected alpha coma

Young GB et al; J Clin Neurophysiol 2000

- The most valid and reliable data on the predictive value of EEG background reactivity in coma comes from patients with hypoxic-ischemic brain injury after cardiac arrest, where the absence of EEG reactivity is highly predictive of poor outcome and death

Table 3 EEG Reactivity and Outcome of Patients

	No. of patients with no awareness	No. of patients with awareness
No. of patients with reactivity	1	10
No. of patients with no reactivity	17	1

No reactivity EEG:
Sensitivity of 90% (95% CI 0.57-1) for not regaining awareness

Specificity of 94% (95% CI 0.7-1)

The lack of reactivity implies widespread damage to the ARAS

Thenayan et al; J Crit Care 2010

- There is weak evidence for the predictive value of unreactive EEG in patients with nonhypoxic encephalopathy

Sutter R and Kaplan PW; Clin EEG and Neurosci 2015
Rossetti AO et al; Ann Neurol 2010

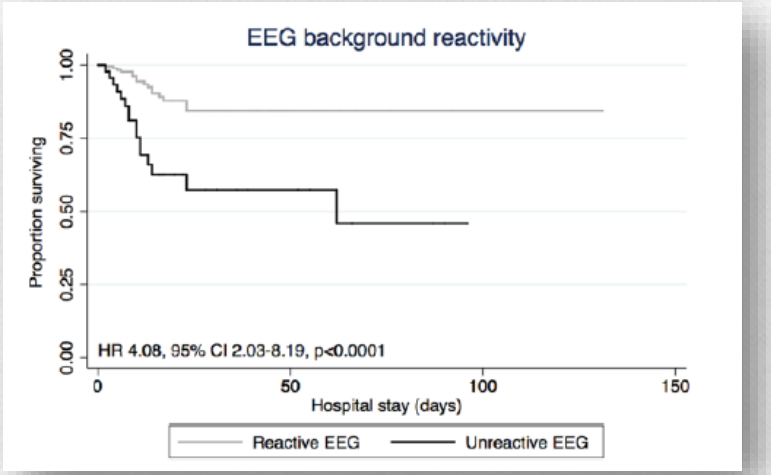
Table 3. Poisson Regression Analyzes of Coma and Nonreactive EEG Background Activity for Prediction of Death.

	Univariable Analyses			Multivariable Analyses[a]		
Death	RR	95% CI	*P* Value[b]	RR	95% CI	*P* Value[b]
Age	1.02	1.00-1.04	.060	1.02	1.00-1.04	**.020**
Intracranial hemorrhage	2.48	1.30-4.74	**.006**	2.31	1.25-4.27	**.008**
Coma (GCS ≤8)	3.20	1.69-6.06	**<.0001**	2.28	1.20-4.35	**.012**
Nonreactive EEG background activity	4.61	2.49-8.54	**<.0001**	3.74	2.02-6.91	**<.0001**

Abbreviations: 95% CI, 95% confidence interval; EEG, electroencephalography; GCS, Glasgow Coma Scale; RR, relative risk.
[a]The multivariable model includes all variables that were significant in the univariable comparisons between survivors and nonsurvivors (Tables 1 and 2).
[b]Boldfaced *P* values are considered significant.

In acute nonhypoxic encephalopathy
Univariate analysis: older age, intracranial hemorrhage, coma (GCS ≤ 8), and **nonreactive EEG background activity** were independently associated with death

Multivariate analysis: only nonreactive EEG background activity was associated with death



Sutter R and Kaplan PW; Clin EEG and Neurosci 2015

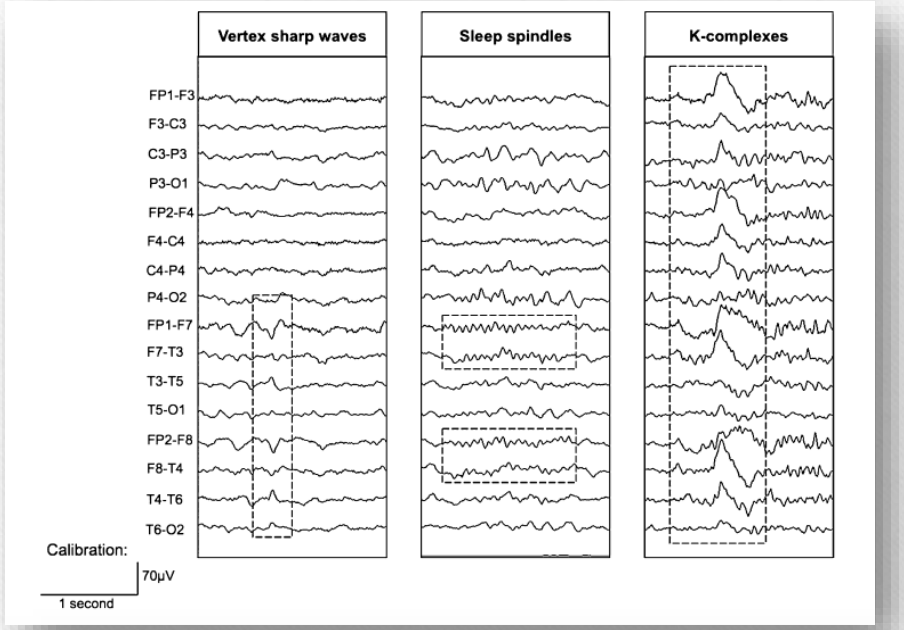


Table 4 Logistic regression analyses of electroencephalographic characteristics for prediction of good outcome (GOS 5)

	Crude			Adjusted[a]		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Vertex sharp-waves	2.53	1.12–5.74	**0.026**	2.11	0.89–4.99	0.088
K-complexes	3.40	1.47–7.85	**0.004**	2.79	1.16–6.69	**0.022**
Sleep spindles	1.57	0.69–3.55	0.281	1.25	0.53–2.95	0.615

GOS, Glasgow Outcome Scale. Bold *P* values are considered significant.
[a]Adjusted for the confounders age and septic shock (i.e. variables with significant differences between patients with and without sleep elements; Table 3).

Whilst EEG sleep elements were detected more frequently in patients favorable outcome, **only K- complexes were significantly and independently associated with good outcome** in ICU patients with acute encephalopathy

Each sleep element comes from a different cerebral source and may carry some distinct prognostic value

K-complexes: correspond to signal in primary sensory cortex

Sutter R et al; Clin Eur J Neurol 2014

EEG patterns in post cardiac arrest

10 yo girl with coma after cardiac arrest

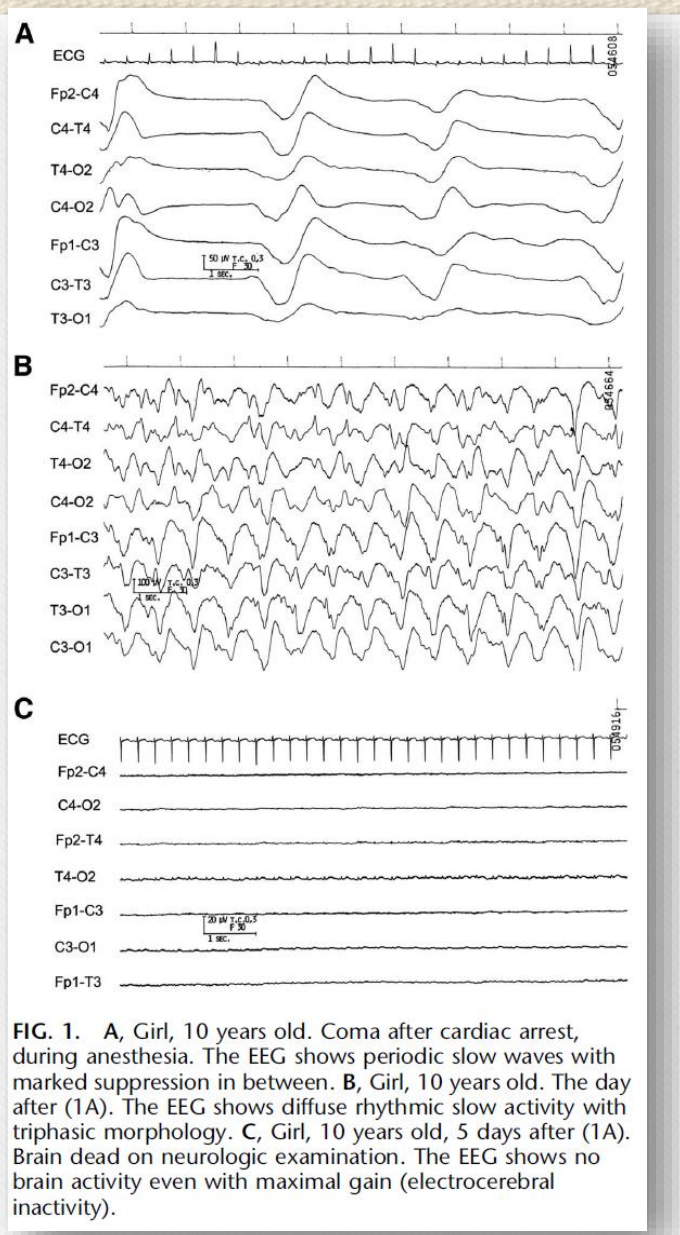


FIG. 1. **A**, Girl, 10 years old. Coma after cardiac arrest, during anesthesia. The EEG shows periodic slow waves with marked suppression in between. **B**, Girl, 10 years old. The day after (1A). The EEG shows diffuse rhythmic slow activity with triphasic morphology. **C**, Girl, 10 years old, 5 days after (1A). Brain dead on neurologic examination. The EEG shows no brain activity even with maximal gain (electrocerebral inactivity).

The day of cardiac arrest

The day after

5 days after

The temporal dynamic changes of EEG pattern over time in patients with post cardiac arrest

Bauer G et al; J Clin Neurophysoiol 2013

Malignant EEG patterns in post cardiac arrest

- Generalized low voltage EEG
- Burst suppression
- Alpha and theta coma
- Generalized periodic discharges

Thenayan et al; J Crit Care 2010
Fugate JE et al; Ann Neurol 2010

Table 3 Predictive values of (combinations of) clinical and neurophysiologic measures

	Time since cardiac arrest, h	Predicted outcome	Specificity	Sensitivity	PPV	NPV
Favorable EEG pattern	12	Good	95 (87-99)	54 (42-65)	92 (80-98)	65 (55-74)
Unfavorable EEG pattern	24	Poor	100 (95-100)	28 (21-35)	100 (91-100)	54 (48-61)
Absent pupillary light responses	48	Poor	100 (97-100)	17 (12-25)	100 (86-100)	52 (45-58)
Absent SSEP	72	Poor	100 (90-100)	44 (34-54)	100 (92-100)	39 (29-50)
Unfavorable EEG pattern at 24 h, absent pupillary light responses at 48 h, or absent SSEP at 72 h		Poor	100 (97-100)	50 (41-58)	100 (95-100)	63 (56-70)

EEG within 24 hours is a robust contributor to prediction of poor or good outcome of comatose patients after cardiac arrest, despite the use of mild therapeutic hypothermia and sedative medication

Rapid recovery toward continuous patterns within 12 h is strongly associated with a good neurological outcome

Hofmeijer J et al; Neurology 2015

Table 1 Malignant EEG patterns are II to V

Category	Subcategory
Benign	
I. Delta/theta >50% of recording (not theta coma)	A. With reactivity B. Without reactivity
Malignant	
II. Triphasic waves	
III. Burst-suppression pattern	A. With epileptiform activity B. Without epileptiform activity
IV. Alpha/theta/spindle pattern coma (no reactivity)	
V. Suppression (generalized)	A. <20 but >10 μV B. <10 μV

Table 2 EEG Patterns and Patient Outcomes

	No. of patients with no awareness	No. of patients with awareness
No. of patients with malignant EEG pattern	17	4
No. of patients with benign EEG pattern	1	7

Generalized suppression (< 10 uV) or **burst suppression with epileptiform activity** are indicators of failure to gain awareness after cardiac arrest

Thenayan et al; J Crit Care 2010

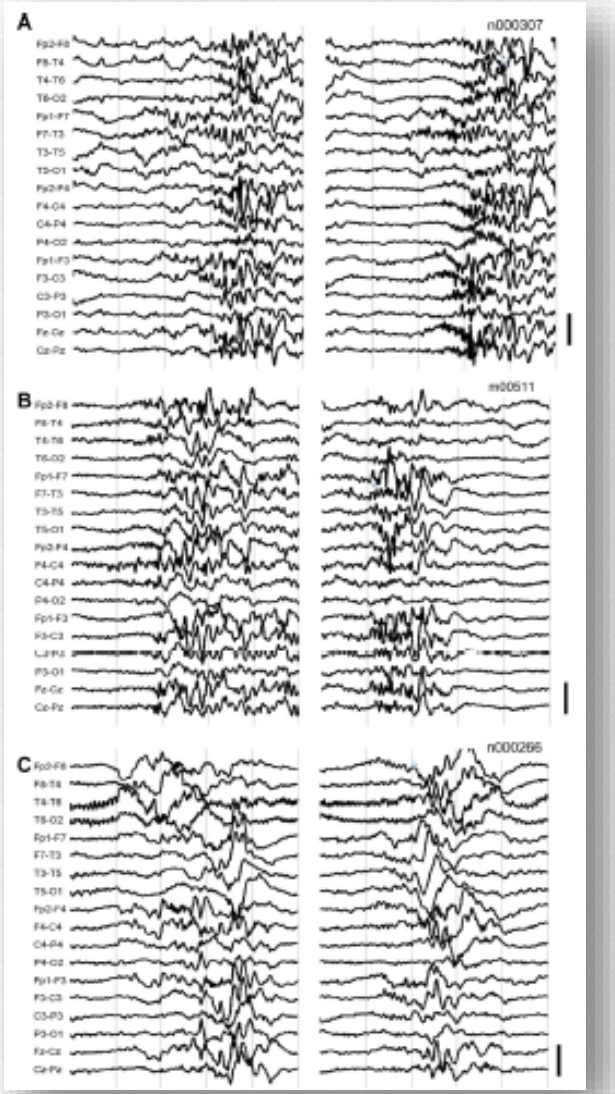
TABLE 1. Summary of the Relevant EEG Features in Comatose Patients After Cardiac Arrest, and Their Prognosis Significance

EEG Feature	Prognosis Significance	Accuracy
Continuous background	Regaining consciousness	100% specificity in NT (Rundgren et al., 2006)
	Good outcome (CPC 1–2)	0.91 PPV in TH (Rundgren et al., 2010)
		100% specificity (Cloostermans et al., 2012)
Burst-suppression	Mortality	100% specificity in TH (Rundgren et al., 2010; Sadaka et al., 2014)
	Poor outcome (GOS 1–3)	100% specificity at any time (Sivaraju et al., In press)
Burst-suppression with identical bursts	Poor outcome (CPC 3–5)	100% specificity (Cloostermans et al., 2012)
Isoelectric or low voltage	Death	100% specificity (Hofmeijer et al., 2014)
No reactivity	No awareness recovery	94% specificity (Thenayan et al., 2010)
	Mortality	93% specificity in NT (Rossetti et al., 2010*a*)
		100% specificity in NT (Tsetsou et al., 2013)
Status epilepticus	Poor outcome (CPC 3–5)	94% specificity (Legriel et al., 2013)
		100% specificity (Rittenberger et al., 2012)
	Mortality	92% specificity (Rossetti et al., 2007)
Epileptiform transients	Poor outcome (CPC 3–5)	100% specificity (Rossetti et al., 2012)

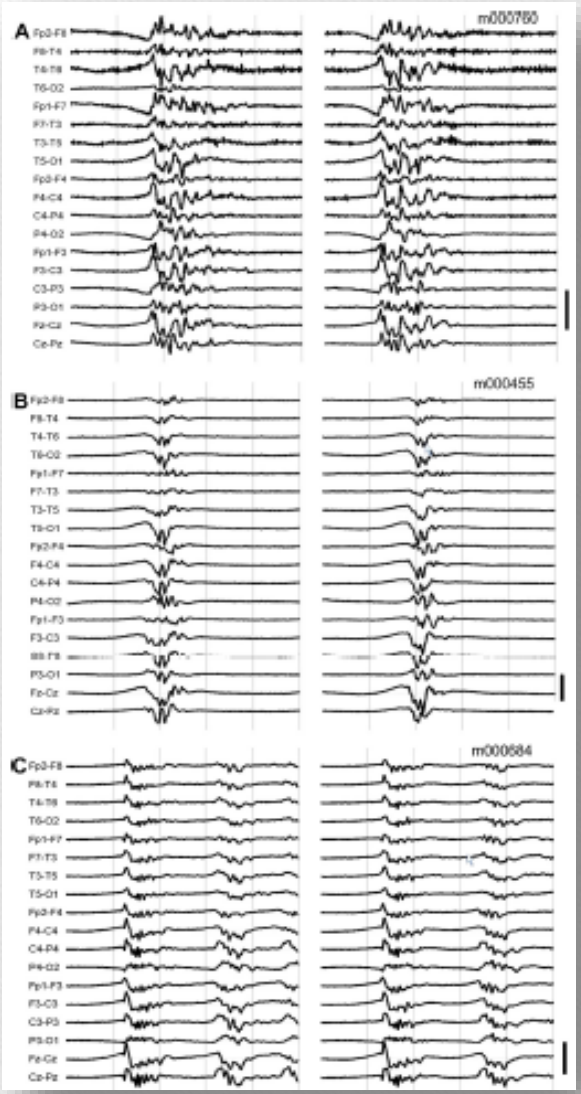
CPC, cerebral performance category; GOS, Glasgow Outcome Score; NT, normothermia; PPV, positive predictive value; TH, therapeutic hypothermia.

Juan E et al; J Clin Neurophysiol 2015

BS without identical bursts



BS with identical bursts



Hofmeijer J et al; Clin Neurophysiol 2014

Ictal-interictal continuum (IIC) EEG patterns

IIC EEG patterns

- **Rhythmic delta activity (RDA):** LRDA, GRDA
- **Periodic discharges (PDs):** LPD, GPD, BiPD, MfPD
- **Spike or sharp wave discharges (SW)**

Periodic lateralized epileptiform discharges (PLEDs)

- PLEDs are highly associated with seizures
- Incidence of seizures in the acute setting of PLEDs to be 58-100%
- PLEDs were associated with an **acute process** and occurred early during the course of illness
- PLEDs have been associated with focal destructive lesions

✓ Acute infarction (most common)
✓ Infections
✓ Hematomas
✓ Tumors

Combined pre-existing structural lesion with a metabolic disturbance

PLEDs can be also seen after status epilepticus in patients with chronic epilepsy

Pohlmann-Eden et al; J Clin Neurophysiol 1996, Garcia-Morales I et al; J Clin Neurophysiol 2002

PLEDs

- **Associated clinical seizures**: repetitive focal motor seizures or epilepsia partialis continua
- Repetitive confusional states due to complex partial status epilepticus were also in some patients with PLEDs
- The prognosis of patients with PLEDs is largely determined by the underlying disease process. Acute stroke appears to be associated with the worst prognosis, with mortality rates ranging from 28.8% to 53%

PLEDs-proper versus PLEDs-plus

- **PLEDs-plus**: required an accompanying low amplitude rhythmic discharge
- **Higher rate of seizure in PLEDs-plus**
  - 74% of the 50 patients with PLEDs-plus
  - 6% of the 34 patients with solely PLEDs-proper

Reiher J et al; Electroencephalogr Clin Neurophysiol 1991

Bilateral independent PLEDs (BIPLEDs)

- Bilateral asynchronous PLEDs
- Highly associated with seizures (78%) (18 patients)
- BIPLEDs were typically related to acute structural lesions with or without metabolic disturbance

De la Paz and Brenner ; Arch Neurol 1981

Table 1.—Causative Disorders

Diagnosis	No. of Patients PLEDs*	BIPLEDs*
Stroke (recent)	15	1
Seizure disorder		
Chronic	10	4
Recent onset	4	1
Anoxic encephalopathy	3	5
CNS infection	2	5
Tumor	5	0
Craniotomy (recent)	3	0
Hepatic encephalopathy	1	1
Eclampsia	1	0
Hypertensive encephalopathy	0	1
Hypoglycemic encephalopathy	1	0
Total	**45**	**18**

Etiology

- ✓ Anoxic encephalopathy
- ✓ CNS infection
- ✓ Chronic epilepsy

Table 2.—Clinical Features

	No. of Patients PLEDs* (N = 45)	BIPLEDs* (N = 18)
Seizures		
Focal	26	4
Generalized	6	8
Both	5	2
Focal neurologic deficits	37	2
Coma	11	13

De la Paz and Brenner ; Arch Neurol 1981

BIPLEDs: more GTCs, more severe clinical state (coma)

The clinical state and prognosis with BIPLEDs may be worse than with PLEDs; however, it should be kept in mind that this conclusion is based on small numbers of reported cases

Generalized periodic epileptiform discharges (GPEDs)

- Generalized, synchronous, periodic or near periodic complexes that occupied at least 50% of a standard 20 minute EEG
- Periodic sharp, slow, and triphasic-like waves, and combinations thereof
- Excluded suppression-burst complexes, triphasic waves, FIRDA

Husain AM et al; J Clin Neurophysiol 1999

Etiologies

- Anoxia and toxic-metabolic encephalopathy (40%)
- Primary neurologic process (32%)
- Toxic-metabolic encephalopathy (28%)

Husain AM et al; J Clin Neurophysiol 1999

GPEDs

- **Relationship to status epilepticus:**

  8 (32%) out of 25 patients met criteria for SE

- **Prognosis**:

  Nine patients (36%) were alive at the time of discharge, whereas 16 of 25 (64%) had died

Husain AM et al; J Clin Neurophysiol 1999

GPEDs

- The ictal significance of GPEDs post cardiac arrest is under debate
  - whether this EEG pattern represent irriverible hypoxic brain damage (thereby futile to treat)

or

  - potentially nonconvulsive status epilepticus (thereby potentially treatable)

Prognostic significance of GPEDs

Table 2
Clinical data, EEG, and neuroimaging studies among survivors.

Age	Gender	EEG	Reactivity	Imaging	Myoclonus	Seizure	AED	CPC at discharge
38	F	BiPLEDs	No	HI (CT)	No	No	No	4
56	M	GPEDs	No	HI (MRI)	No	Yes	Yes LEV	4
55	M	GPEDs	Yes	No HI (MRI)	Yes	Yes	Yes LEV, VPA, PHT, Clon, Thiop	CPC 1–3
61	M	GPEDs	No	HI (CT)	Yes	Yes	Yes PHT, VPA	4
66	M	GPEDs	Yes	No HI (MRI)	No	No	Yes	3
52	F	GPEDs	Yes	No HI (MRI)	No	Yes	Yes PHT, LEV	4
49	M	GPEDs	No	HI (CT)	No	Yes	Yes	4
68	M	GPEDs	Yes	No HI (CT)	No	Yes	No	4
40	M	BiPLEDs	No	HI (MRI)	Yes	No	Yes PHT, LEV	4
87	M	BiPLEDs	Yes	No HI (MRI)	No	No	No	4

F — female, M — male, HI — hypoxic injury, LEV — levetiracetam, VPA — sodium valproate, PHT — phenytoin, Clon — clonazepam, Thiop — thiopentone.

36 postcardiac patients with hypoxic encephalopathy; 24 with GPEDs, 12 with BIPLEDs; **10/36 pts survived**

- GPEDs carry a **grave clinical prognosis** following cardiac arrest

Robeiro A et al; Epilepsy & Behav 2015

Table 1
Clinical findings, neuroimaging studies and outcome of the 14 patients with BiPLEDs and GPEDs and HE.

Pt	Age (year)	Sex	Type of PED	Diagnosis	MR/CT (abnormal)	Localization: Cortical +	Mental status: Coma +	Clinical seizures at onset	SE	AED therapy	Death
1	23	M	BiPLED	Laceration myocardial	+					PRO, PHT	+
2	67	F	BiPLED	Heroin overdose	+		Focal	+		PRO	+
3	72	F	BiPLED	Myocardial infarction	+					PRO, PHT	+
4	74	F	BiPLED	Myocardial infarction	+	Subcortical				PRO, PHT, DZP	+
5	83	F	BiPLED	Cardiogenic shock	+					PRO, CNZ, PHT, LEV, VPA	+
6	85	M	BiPLED	Ventricular tachycardia	NI[a]					PRO, PHT, VPA, CNZ	+
7	71	M	BiPLED	Myocardial infarction	+			+		PRO, GBP	+
8	75	F	BiPLED	Laceration myocardial	?	?				PB, PHT	+
9	26	M	GPED	Carbon monoxide poisoning	+	Subcortical		+	+	PRO, CNZ	+
10	51	M	GPED	Myocardial infarction	+		Focal	+		PRO	+
11	76	F	GPED	Bithalamic stroke	+					PRO	+
12	71	M	GPED	Respiratory failure	+	Subcortical			+	PRO	+
13	37	M	GPED	Ventricular tachycardia	NI[a]					PRO	+
14	54	F	GPED	Ventricular tachycardia	+					PRO	+

(?) Not performed; SE, status epilepticus; PRO, propofol; PHT, phenytoin; DZP, diazepam; CNZ, clonazepam; LEV, levetiracetam; VPA, valproate; PB, phenobarbital; GBP, gabapentine.

[a] CT head normal.

52 patients with hypoxic encephalopathy: 14 patients had either GPEDs (6 pts) or BiPLEDs (8 pts);

All 14 pts were comatose and died

Aggressive treatment of patients may not be warranted when these EEG patterns are seen after anoxic brain injury

San-Juan OD et al; Seizure 2009

Prognostic significance of GPEDs

- **GPDs on a suppressed background pattern** are strongly associated with a **poor outcome**, whereas patients with GPDs on a continuous, normal amplitude background may occur

Bauer G et al; J Clin Neurophysoiol 2013

Pathophysiology of GPDs

- The glutamatergic synapse of excitatory pyramidal cells to inhibitory interneurons is relatively sensitive to hypoxia
- Selective synaptic failure or neuronal damage of inhibitory interneuron, leading to disinhibition of excitatory pyramidal cells, presumably plays a critical role

Van Putten and Hofmeijer J et al; Epilepsy & Behav 2015

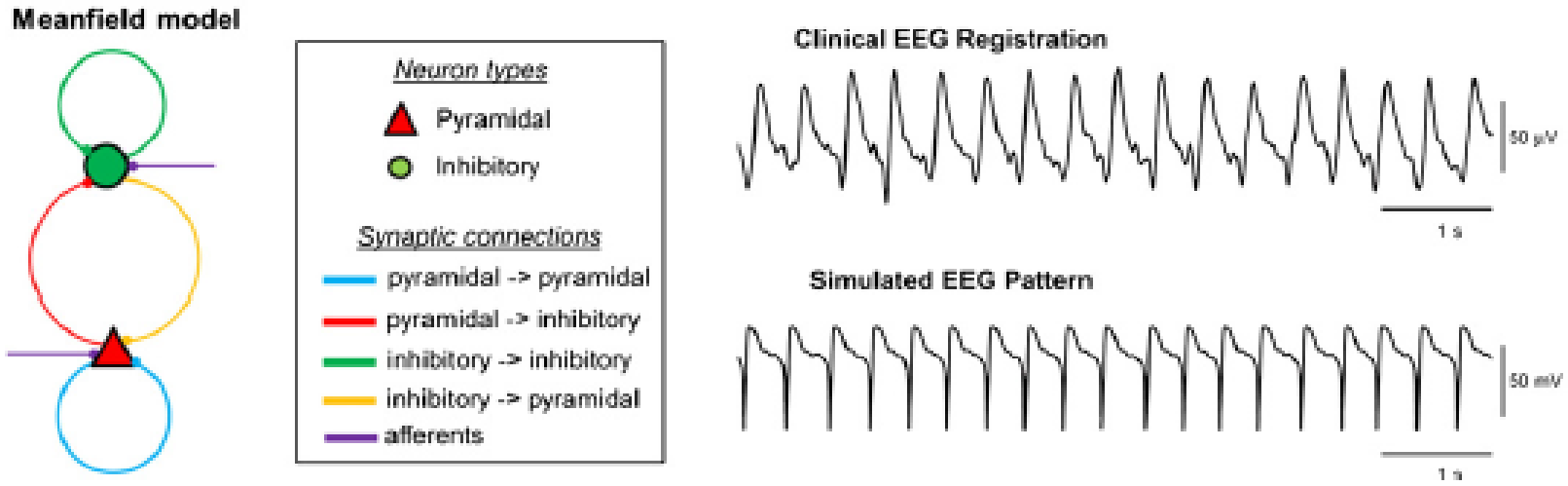


Fig. 2. (Left) Meanfield model used to simulate generalized periodic discharges (GPDs). Pyramidal cells receive both excitatory afferent input and, with a brief delay, inhibitory input from the same presynaptic source (feed-forward inhibition). (Right) Top panel: EEG recording from a patient after cardiac arrest showing GPDs. Bottom panel: simulated EEG showing GPDs. In this simulation, the number of synapses from pyramidal cells to interneurons was selectively reduced to 90%, while the number of other synapses was unchanged. The dominant frequency is similar (~2.5 Hz).
Illustration slightly modified from [32].

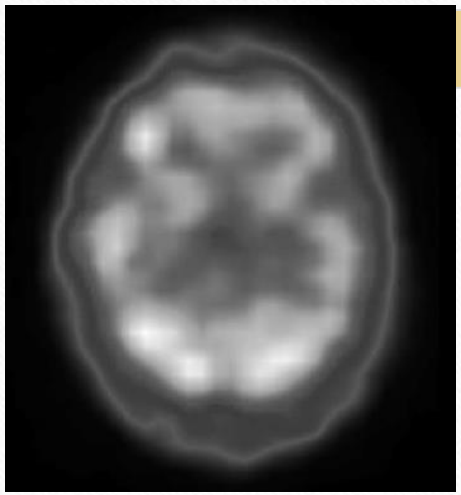
Van Putten and Hofmeijer J et al; Epilepsy & Behav 2015

SIRPIDs (Stimulus-Induced Rhythmic, Periodic, or Ictal Discharges)

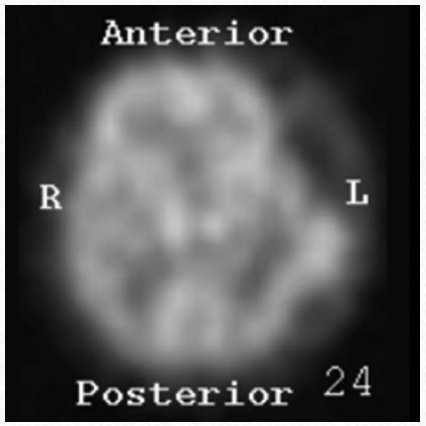
- SIRPIDs are commonly elicited by stimulation in critically ill (stuporous or comatose), encephalopathic patients
- Pathophysiology of SIRPIDs is unknown
- The relationship between clinical seizures and SIRPIDs is unclear, although some association is found between SIRPIDs and clinical status epilepticus
- Whether these discharges contribute to neuronal injury or altered mental status is uncertain

SPECT–Negative SIRPIDs Argues Against Treatment as Seizures

Steven R. Zeiler, Lisa C. Turtzo,† and Peter W. Kaplan‡*



Zieler SR et.al; J Clin Neurophysiol 2011



SPECT-Negative SIRPIDs: Less Aggressive Neurointensive Care?

Christina C. Smith, William O. Tatum,† Vivek Gupta,‡ Robert A. Pooley,§ and William D. Freeman*†*

Smith CC et.al; J Clin Neurophysiol 2014

- However, the pace of technological advances that now allows long-term recording of video-EEG has not been matched by that of increased understanding of the pathophysiology that creates the myriad of ambiguous but potentially ictal patterns, their clinical implications, or how aggressively to treat them

Chong DJ and Hirsch LJ et al; J Clin Neurophysiol 2005

EEG patterns and their correlation with NCS/NCSE

EEG patterns	Do NOT reflect NCSE NOT TREATED	Reflect NCSE Should be TREATED	BORDERLINE Of NCSE in coma One additional criteria is needed to diagnose NCSE
❖ **Classical coma patterm** - Diffuse polymorphic delta activity - Spindle coma - Alpha/theta coma - Low votage - Burst suppression	× × × × ×		
❖ Ictal patterns with typical spatiotemporal evolution ❖ Epileptiform discharges > 2.5 Hz in comatose patients		× ×	
❖ GPDs or LPDs < 2.5 Hz ❖ Rhythmic discharges (RDs) > 0.5 Hz			× ×

Trinka U and Leitinger M; Epilepsy & Behav 2015

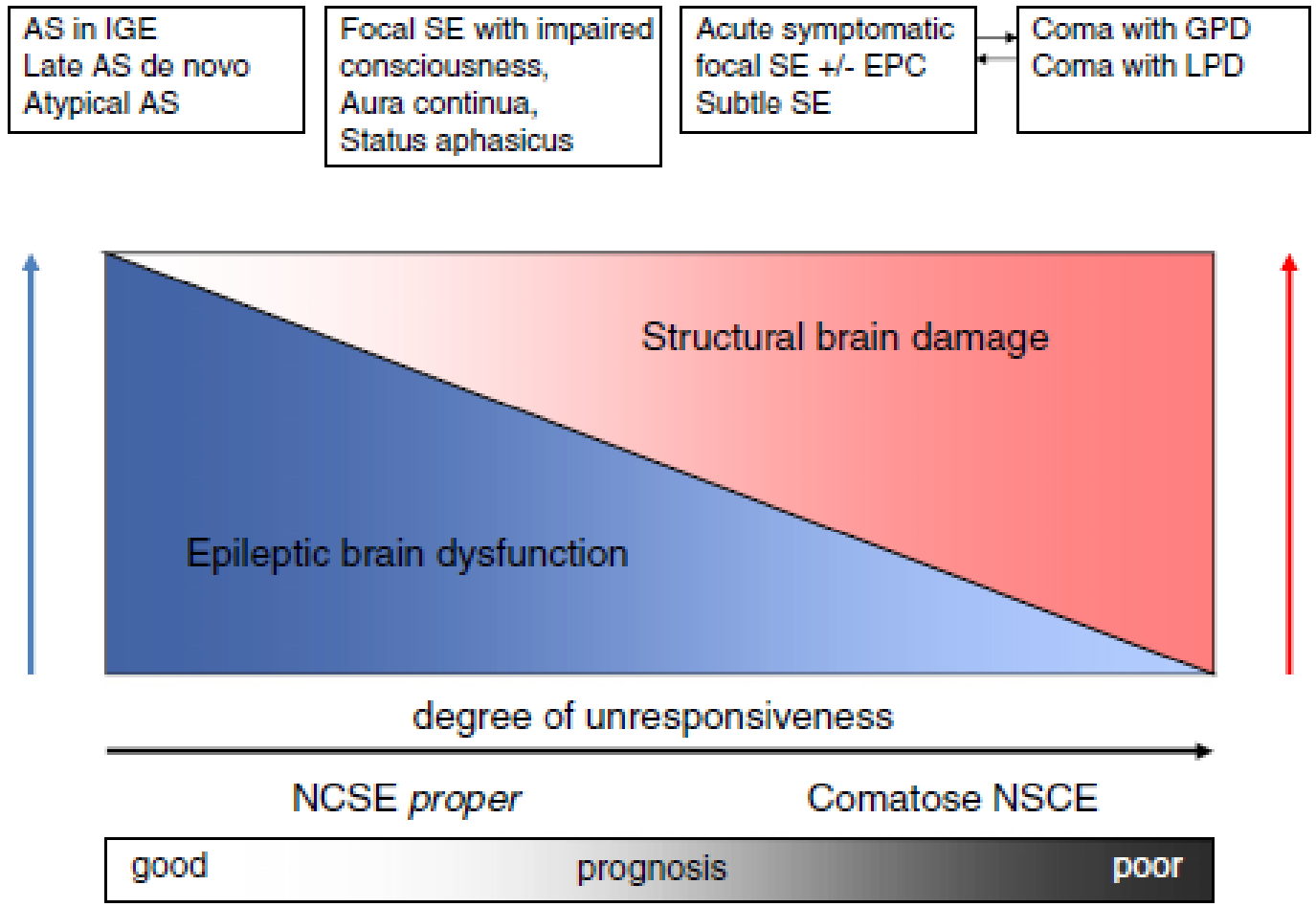


Fig. 2. The relationship of the depth of coma and the contribution of the epileptic activity during nonconvulsive status epilepticus (modified from 14, Fig. 11). Abbreviations: AS: absence status epilepticus, EPC: epilepsia partialis continua, GPDs: generalized periodic discharges, IGE: idiopathic generalized epilepsy, LPDs: lateralized periodic discharges, NCSE: nonconvulsive status epilepticus.

Trinka U and Leitinger M; Epilepsy & Behav 2015

Coma with epileptiform discharges (Coma-EDs)

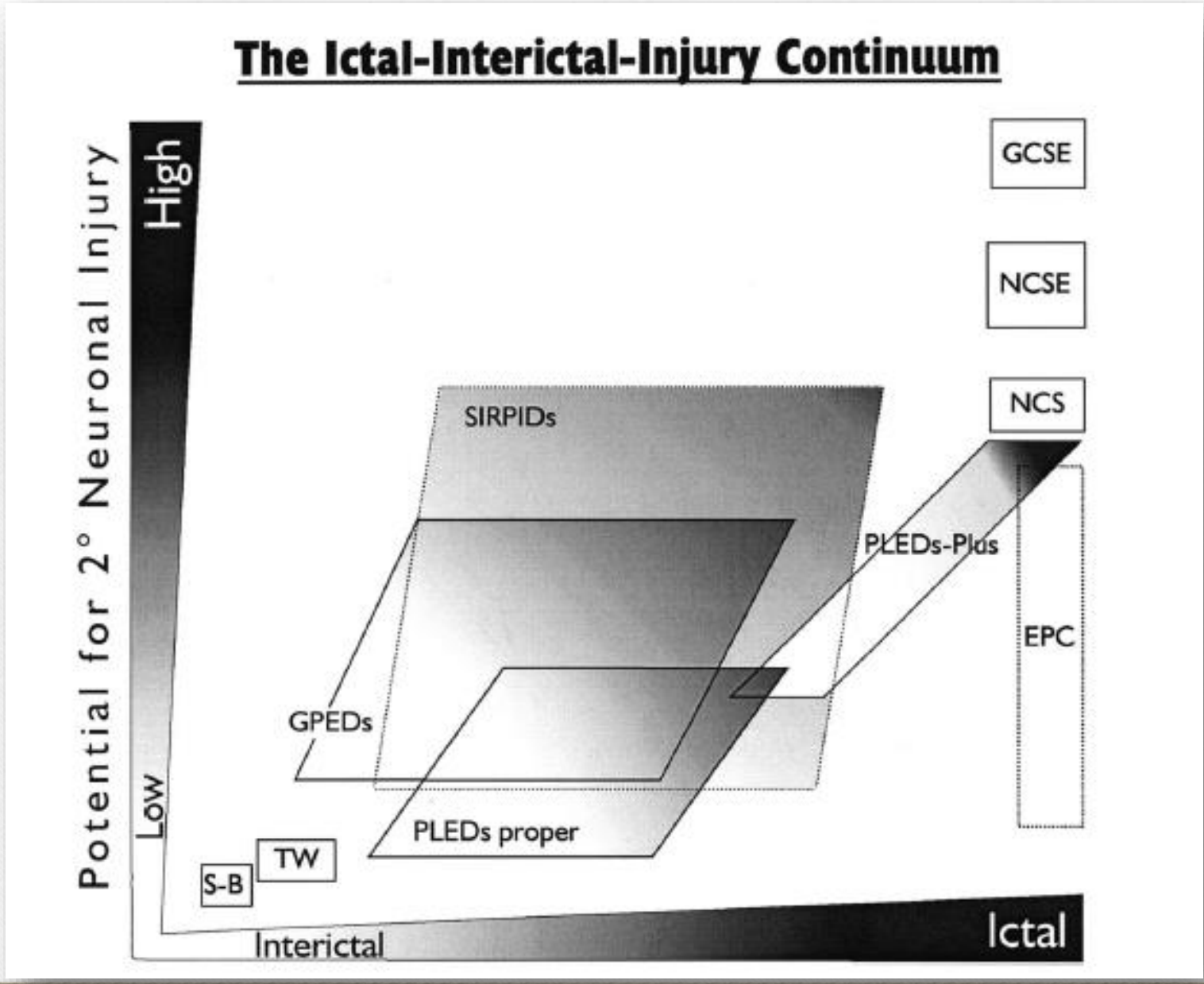
- Prior deciding treat or not treat the observed EEG patterns, clinician has to answer the following questions

1) Is the coma caused by SE or by the underlying brain condition itself?
2) To what degree does the epileptic activity contribute to the depth of coma?
3) Dose the ongoing epileptic activity worsen the prognosis?

TABLE 1. EEG and Clinical Characteristics of the Periodic Discharges

			GPEDs	
	PLEDs	**BIPLEDs**	**PSIDDs**	**PLIDDs**
Inter-discharge interval	Typical: 0.5 to 4 s, up to 8 s	Typical: 0.5 to 4 s, up to 8 s	0.5–4 s	4–30 s
Topography	Lateralized (contralateral spread common)	Independently lateralized	Diffuse	Diffuse
Rate of focal or tonic-clonic seizures	High, approximately 80%	Typically lower than in PLEDs but still high	Variable/unclear but not rare	Rare
Associated myoclonus	Rare	Rare	Common with CJD but often not time-locked	Common with SSPE, time-locked
Mental status	Altered	Altered	Altered	Variable
Outcome*	Variable*	Variable*	Variable*	Variable*
Morphology/other characteristics	Morphology variable. Associated with EPC	Morphology variable	Sharp waves, spikes, polyspikes, or sharply-contoured delta waves	Variable; often complex, stereotyped, polyphasic bursts, lasting 0.5–3 s
Etiology	Acute structural lesion: Infarct, ICH, tumor, infection; occasionally no lesion. After SE. Increased risk with metabolic disturbance. **HSE**	Anoxia, bilateral acute lesions. Occasionally unilateral or no lesion apparent. **HSE**	Metabolic encephalopathy, anoxia. NCSE. After SE. Lithium, baclofen, **CJD**	Toxins (PCP, ketamine barbiturates, anesthetics), anoxia **SSPE**

Chong DJ and Hirsch LJ et al; J Clin Neurophysiol 2005



Chong DJ and Hirsch LJ et al; J Clin Neurophysiol 2005

- Periodicity was thought to have been caused by disconnection of the cortex from subcortical structures, usually secondary to a large white matter lesion

Cobb W and Hill D; Brain 1950

- The majority of the patients (64.7%) had lesions of cortical gray and subcortical white matters

Gurer G et al; Clin EEG Neurosci 2004

American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 Version

- No uniformly accepted nomenclature for EEG patterns frequently encountered in critically ill patients
- No consensus on which patterns are associated with ongoing neuronal injury, which patterns need to be treated, or how aggressively to treat them

Hirsch LJ et al; J Clin Neurophysiol 2013

Proposed nomenclature

A. Rhythmic or periodic patterns

B. Minimal time epochs to be reported. Documented separately

- First 30 minutes
- Each 24 hour period

C. Quantification and categorization of sporadic (non-rhythmic and non-periodic) epileptiform discharges (includes sharp waves and spikes)

D. Background EEG

Hirsch LJ et al; J Clin Neurophysiol 2013

Rhythmic or periodic patterns

- Main term 1
  - Generalized (G)
  - Lateralized (L) (further specify whether unilateral or bilateral asymmetric)
  - Bilateral independent (BI)
  - Multifocal (Mf)

- Main term 2

➢ Periodic discharges (PDs): presence of inter-discharge interval

➢ Rhythmic delta activity (RDA)

➢ Spike-and-wave or sharp-and-wave (SW)

No interval between consecutive waveforms

TABLE 1. New Terms for Older Terms

OLD Term		NEW Term
Triphasic waves, most of record	=	continuous 2/s GPDs (with triphasic morphology)
PLEDs	=	LPDs
BIPLEDs	=	BIPDs
GPEDs/PEDs	=	GPDs
FIRDA	=	Occasional frontally predominant brief 2/s GRDA (if 1-10% of record)
PLEDS+	=	LPDs+
SIRPIDs* w/ focal evolving RDA	=	SI-Evolving LRDA
Lateralized seizure, delta frequency	=	Evolving LRDA
Semirhythmic delta	=	Quasi-RDA

*SIRPIDs = stimulus-induced rhythmic, periodic or ictal discharges.

Hirsch LJ et al; J Clin Neurophysiol 2013

Ictal EEG patterns and criteria for nonconvulsive status epilepticus in comatose patients

Table 1 *Criteria for seizure*

Guideline: To qualify at least *one* of primary criteria 1–3 *and* *one or more* of secondary criteria, with discharges >10 seconds

Primary criteria

1. Repetitive generalized or focal spikes, sharp waves, spike-and-wave or sharp-and-slow wave complexes at >3/second.
2. Repetitive generalized or focal spikes, sharp waves, spike-and-wave or sharp-and-slow wave complexes at <3/second *and* secondary criterion #4.
3. Sequential rhythmic waves and secondary criteria 1, 2 *and* 3 with or without 4.

Secondary criteria

1. Incrementing onset: increase in voltage and/or increase or slowing of frequency.
2. Decrementing offset: decrease in voltage or frequency.
3. Post-discharge slowing or voltage attenuation.
4. Significant improvement in clinical state or baseline EEG after anti-epileptic drug.

Young's criteria for seizure

Young GB et al; Neurology 1996

TABLE 2. Criteria for Non-Convulsive Seizure

Any pattern lasting at least 10 seconds satisfying any one of the following 3 primary criteria:

Primary Criteria:

1. Repetitive generalized or focal spikes, sharp-waves, spike-and-wave or sharp-and-slow wave complexes at ≥3/sec.
2. Repetitive generalized or focal spikes, sharp waves, spike-and-wave or sharp-and-slow wave complexes at <3/sec and the secondary criterion.
3. Sequential rhythmic, periodic, or quasi-periodic waves at ≥1/sec and unequivocal evolution in frequency (gradually increasing or decreasing by at least 1/sec, e.g. from 2 to 3/sec), morphology, or location (gradual spread into or out of a region involving at least 2 electrodes). Evolution in amplitude alone is not sufficient. Change in sharpness without other change in morphology is not adequate to satisfy evolution in morphology.

Secondary criterion:

Significant improvement in clinical state or appearance of previously-absent normal EEG patterns (such as a posterior dominant rhythm) temporally coupled to acute administration of a rapidly-acting AED. Resolution of the "epileptiform" discharges leaving diffuse slowing without clinical improvement and without appearance of previously-absent normal EEG patterns would not satisfy the secondary criterion.

AED = antiepileptic drug;
Modified from (Young et al. 1996).

Chong DJ and Hirsch LJ et al; J Clin Neurophysiol 2005

Table 2
The Salzburg Consensus Criteria for nonconvulsive status epilepticus (SCNC) [1].

Patients without known epileptic encephalopathy

- EDs > 2.5 Hz, or
- EDs ≤ 2.5 Hz or rhythmic delta/theta activity (>0.5 Hz) AND one of the following:
  - EEG and clinical improvement after IV AEDs*, or
  - Subtle clinical ictal phenomena, or
  - Typical spatiotemporal evolution**

Patients with known epileptic encephalopathy

- Increase in prominence or frequency when compared with baseline with observable change in clinical state
- Improvement of clinical and EEG features with IV AEDs*

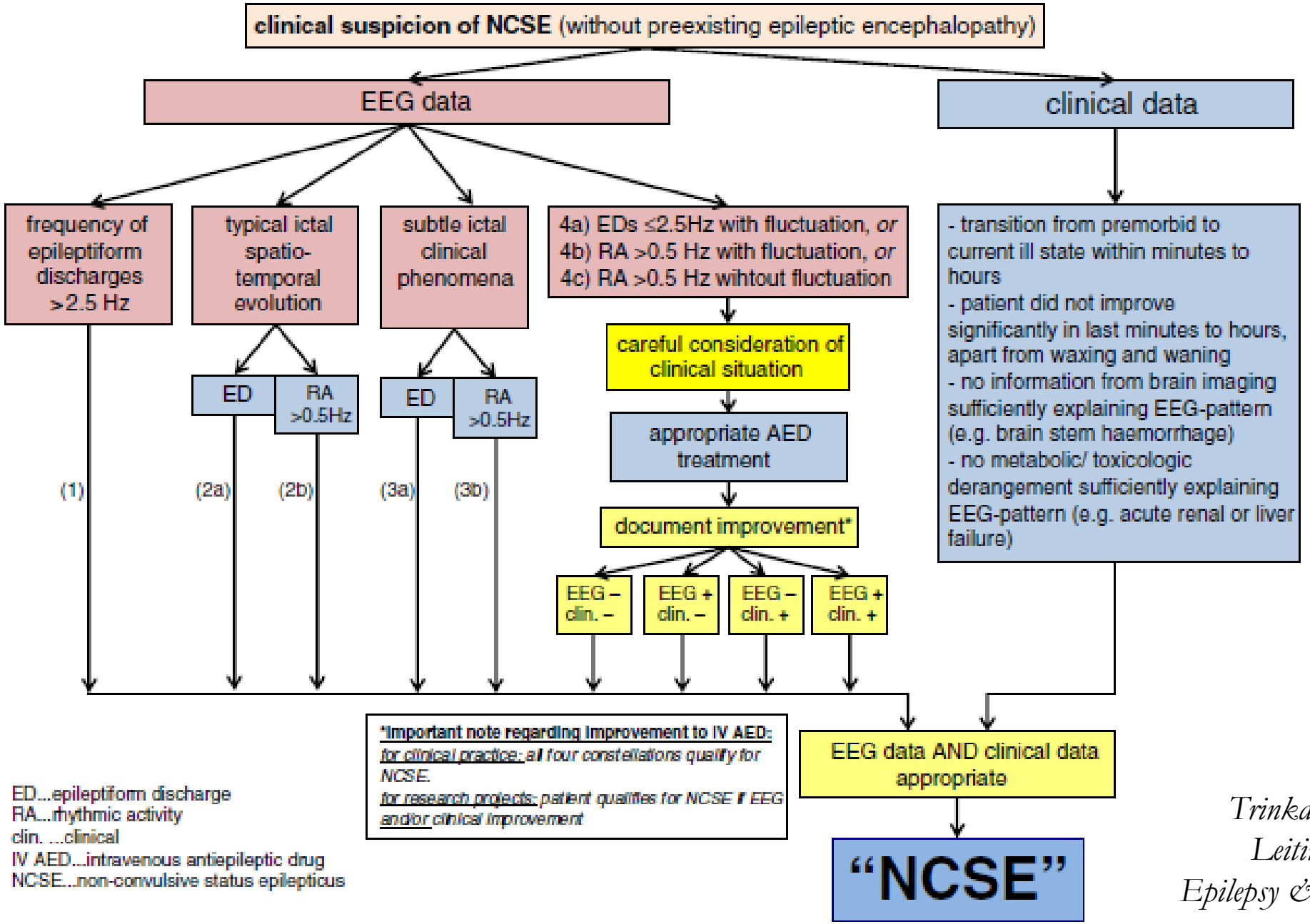
*If EEG improvement without clinical improvement, or if fluctuation without definite evolution, this should be considered **possible NCSE**.

**Incrementing onset (increase in voltage and change in frequency), or evolution in pattern (change in frequency >1 Hz or change in location), or decrementing termination (voltage or frequency)

EDs: epileptiform discharges (spikes, polyspikes, sharp waves, and sharp-and-slow-wave complexes)

IV AEDs: intravenous antiepileptic drugs

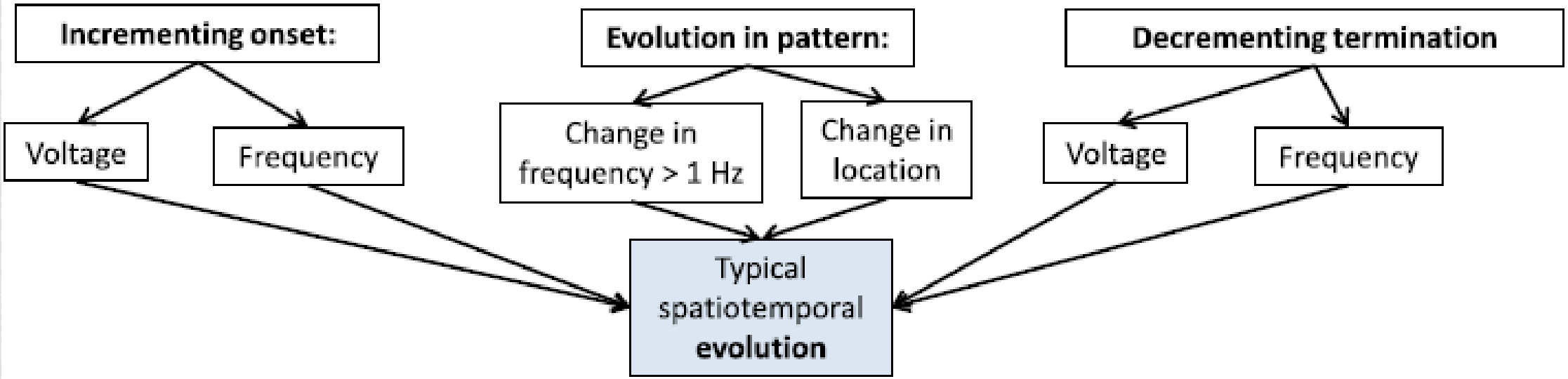
Trinka U and Leitinger M; Epilepsy & Behav 2015



Trinka U and Leitinger M; Epilepsy & Behav 2015

Fig. 12. Algorithm for diagnosis of nonconvulsive status epilepticus with the modified Salzburg Consensus Criteria for NCSE (mSCNC) (see text for further details) [152].

EEG: typical ictal spatiotemporal evolution



Trinka U and Leitinger M; Epilepsy & Behav 2015

Thank you for your attention