ICU EEG: Prognosis in Adults

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Disclosures

- None relevant to this presentation
- Scientific Advisory Board
  - Eisai Inc.
  - Biotie, Inc.
- Research
  - UCB Pharma
  - Acorda Therapeutics
  - Epilepsy Therapy Development Project
  - Sage Pharmaceuticals
  - NeuroPace, Inc.
  - Pfizer

Utility of EEG in Critically Ill

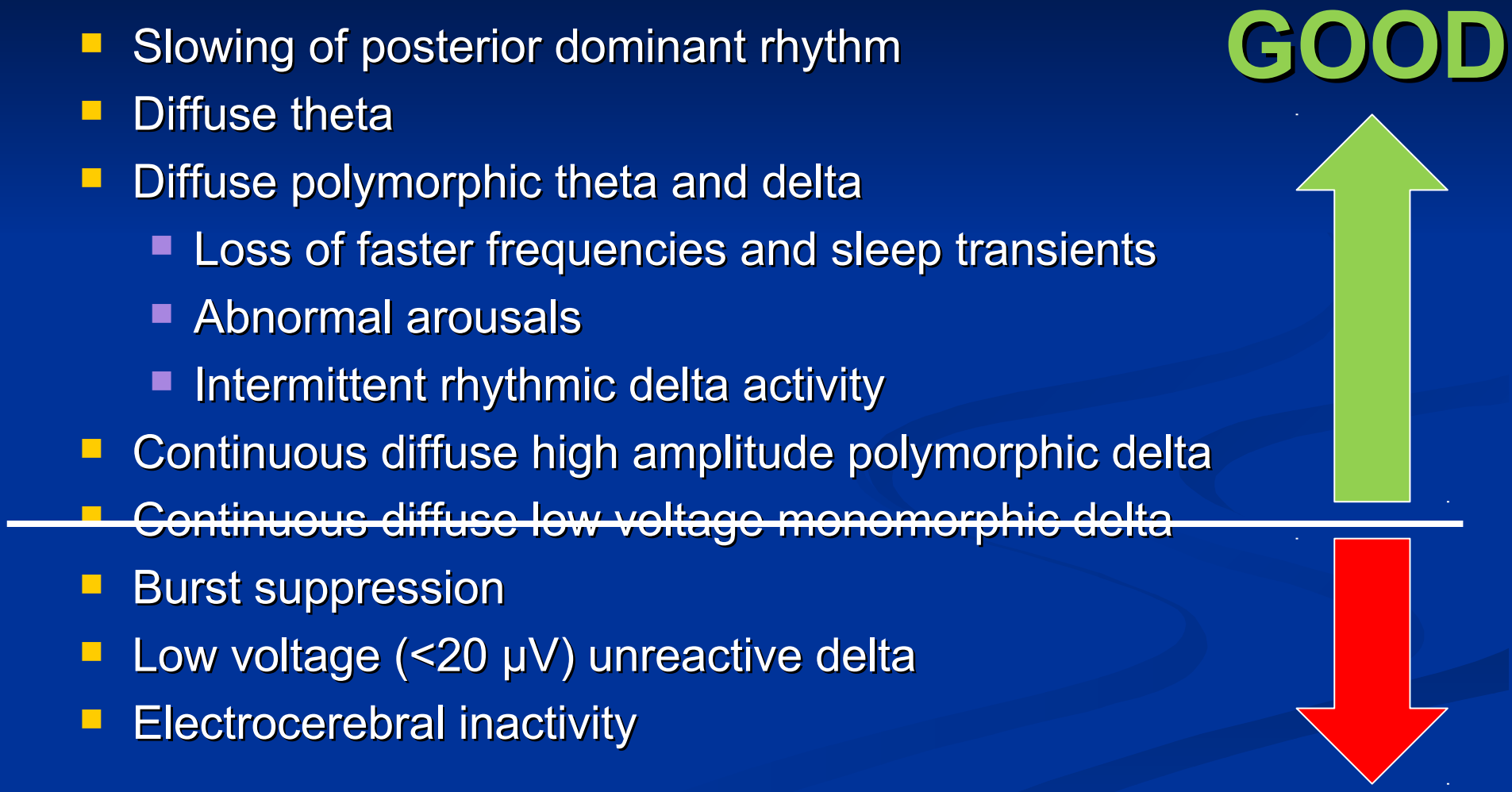
- Objectively measure severity of alteration in consciousness
- Assess neurologic function in patients who are pharmacologically paralyzed
- Narrow the differential diagnostic possibilities when combined with appropriate clinical information
- Determine if nonconvulsive seizures are cause of altered consciousness and assess response to treatment
- Follow progression / improvement with serial studies
- Provide prognostic information
- Confirm the diagnosis of brain death

Diffuse Etiologies

- Metabolic, toxic, infectious encephalopathies
- Grade or degree of abnormalities correlates fairly well with clinical status
  - EEG changes may precede or lag clinical changes
  - Serial studies may be useful
- Etiology often plays larger role than EEG pattern

Diffuse Etiologies

- Slowing of posterior dominant rhythm
- Diffuse theta
- Diffuse polymorphic theta and delta
  - Loss of faster frequencies and sleep transients
  - Abnormal arousals
  - Intermittent rhythmic delta activity
- Continuous diffuse high amplitude polymorphic delta
- ~~Continuous diffuse low voltage monomorphic delta~~
- Burst suppression
- Low voltage (<20 μV) unreactive delta
- Electrocerebral inactivity



Classification System

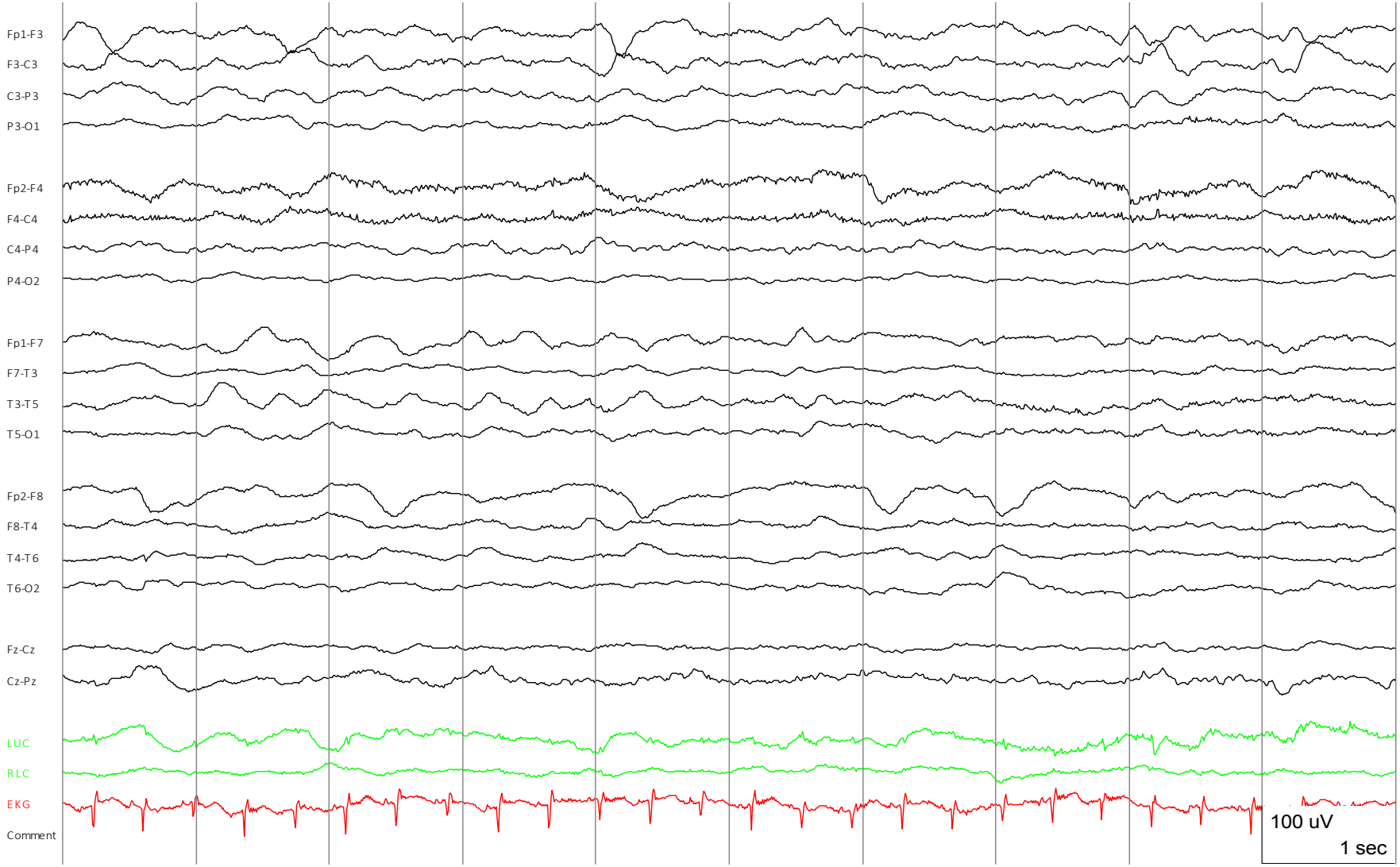
Gr	Synek	Scollo-Lavizzari	Young
I	Regular alpha, some theta	Normal alpha	Delta-theta > 50% of record
II	Predominant theta	Alpha, theta/delta	Triphasic waves
III	Widespread delta, spindle coma	Theta/delta, no alpha	Burst suppression
IV	Burst-suppression, alpha coma, theta coma, delta coma ≤ 20 μV	Delta, low voltage; burst-suppression, PEDs, alpha coma	Alpha / theta / spindle coma, unreactive
V	ECI ≤ 2 μV	Very low to ECI	Epileptiform activity
VI			Suppression ≤ 10μV

Synek VM. J Clin Neurophysiol. 1988; 5: 161-74
Scollo-Lavizzari G, et al. Eur Neurol. 1987; 26: 161-70
Young GB, et al. Can J Neurol Sci 1997;24:320-325

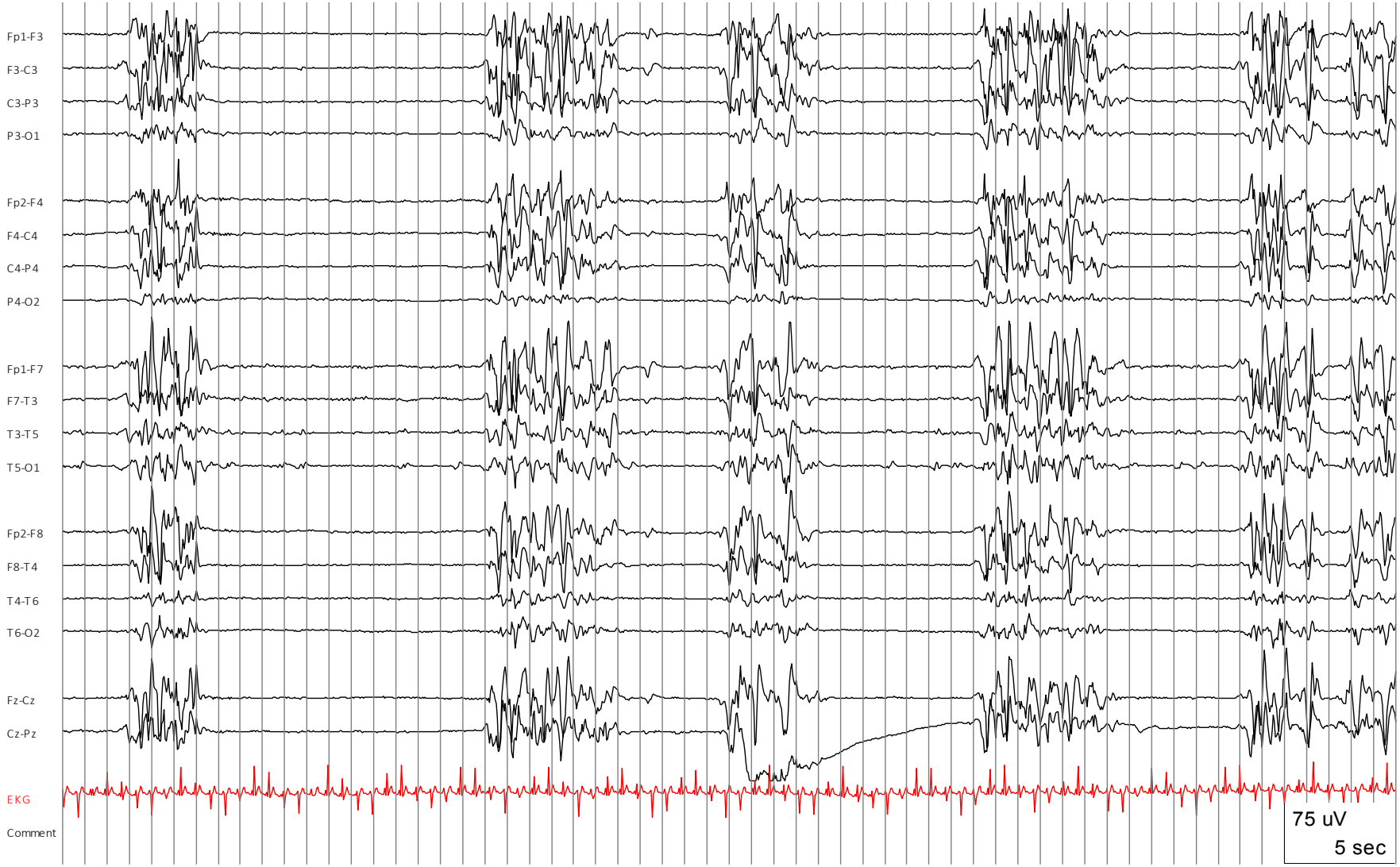
Synek: Prediction of Outcome after Cardiac Arrest

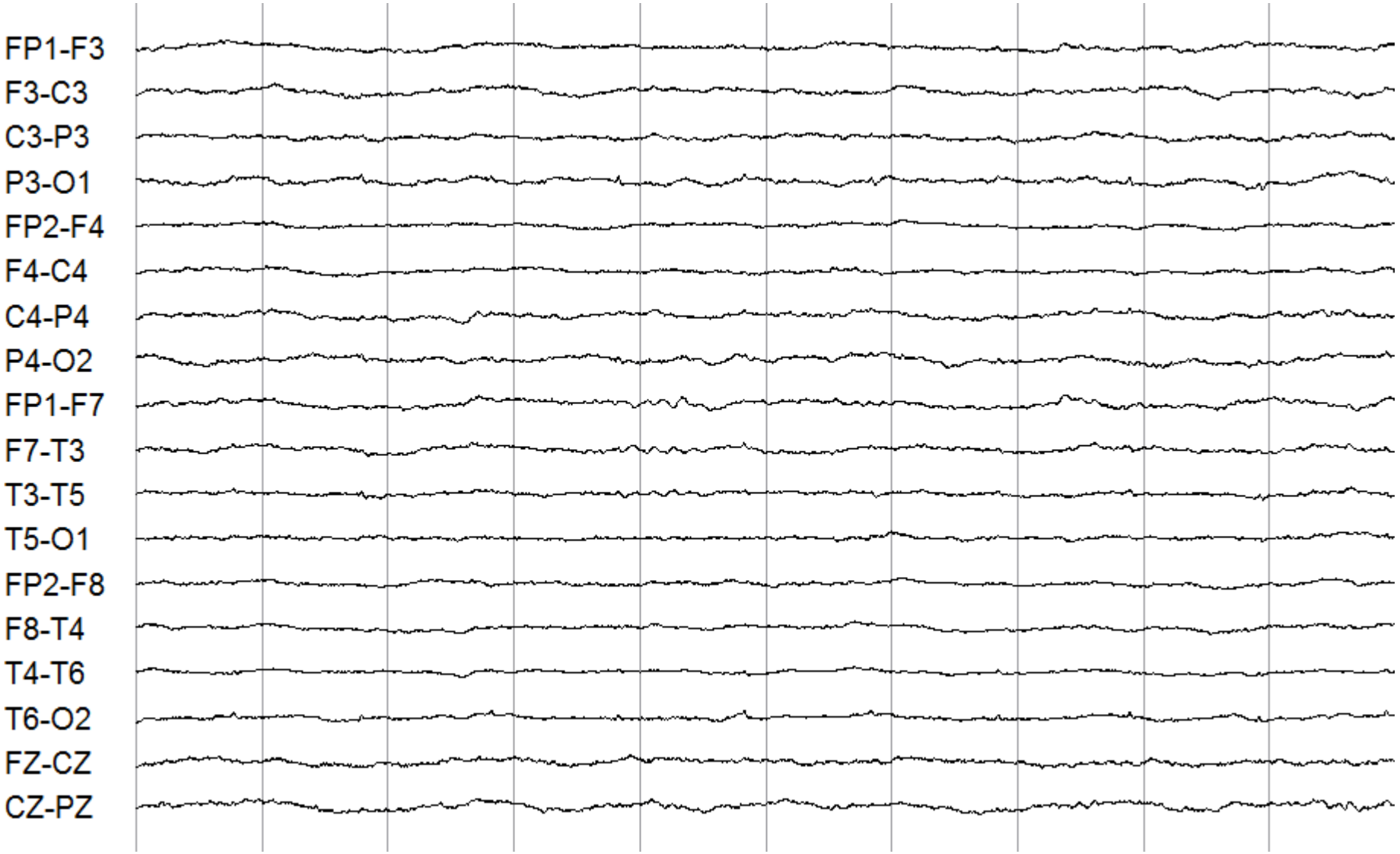
- Good Outcome
  - Grade 1 48/61 79%
  - Grade 2 45/88 51%
  - Grade 3 11/43 26%
  - Grade 4 0/138 0%
  - Grade 5 0/70 0%

Severe Diffuse Slowing & Attenuation

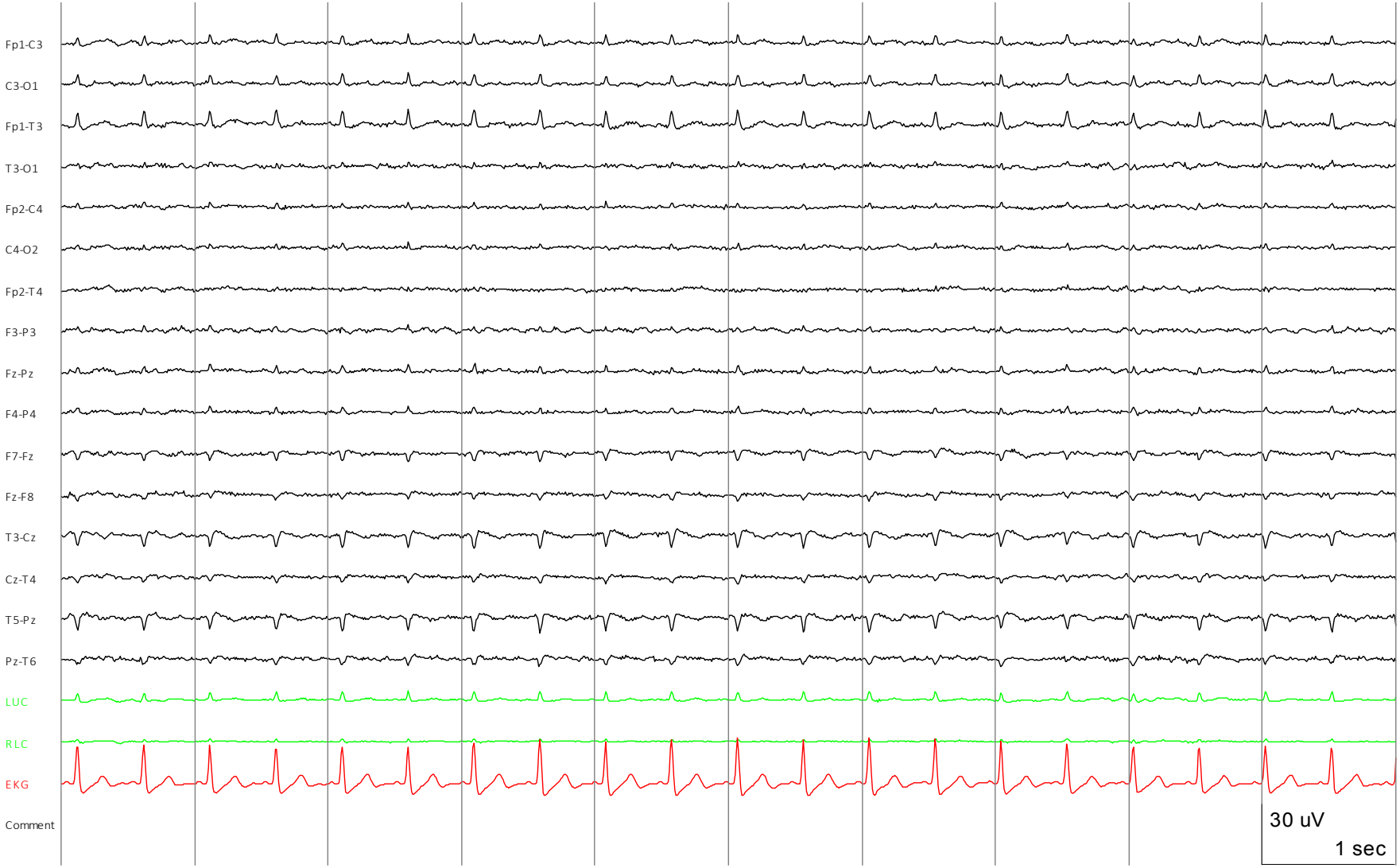


Burst Suppression: Barbiturate-Induced




FP1-F3
F3-C3
C3-P3
P3-O1
FP2-F4
F4-C4
C4-P4
P4-O2
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
FZ-CZ
CZ-PZ

Electrocerebral Inactivity, ECI Montage



2 uV/mm

Focal Structural Etiologies

- Cause coma from herniation and compression/distortion of brainstem and diencephalon
- Focal asymmetries
  - Polymorphic delta activity: Subcortical white matter
  - Attenuation of faster frequencies: Cortex
  - Intermittent rhythmic delta activity: Deep gray matter structures
- May not be clear which hemisphere is more severely affected
  - Slower frequencies and lower voltages

Other Etiologies

- Brainstem lesions
  - Exception to relationship between EEG and clinical exam
  - Patient may be deeply comatose
  - Cortex (and therefore EEG) may be relatively unaffected
    - Locked-in syndrome
- Psychogenic coma, catatonia
  - EEG is normal

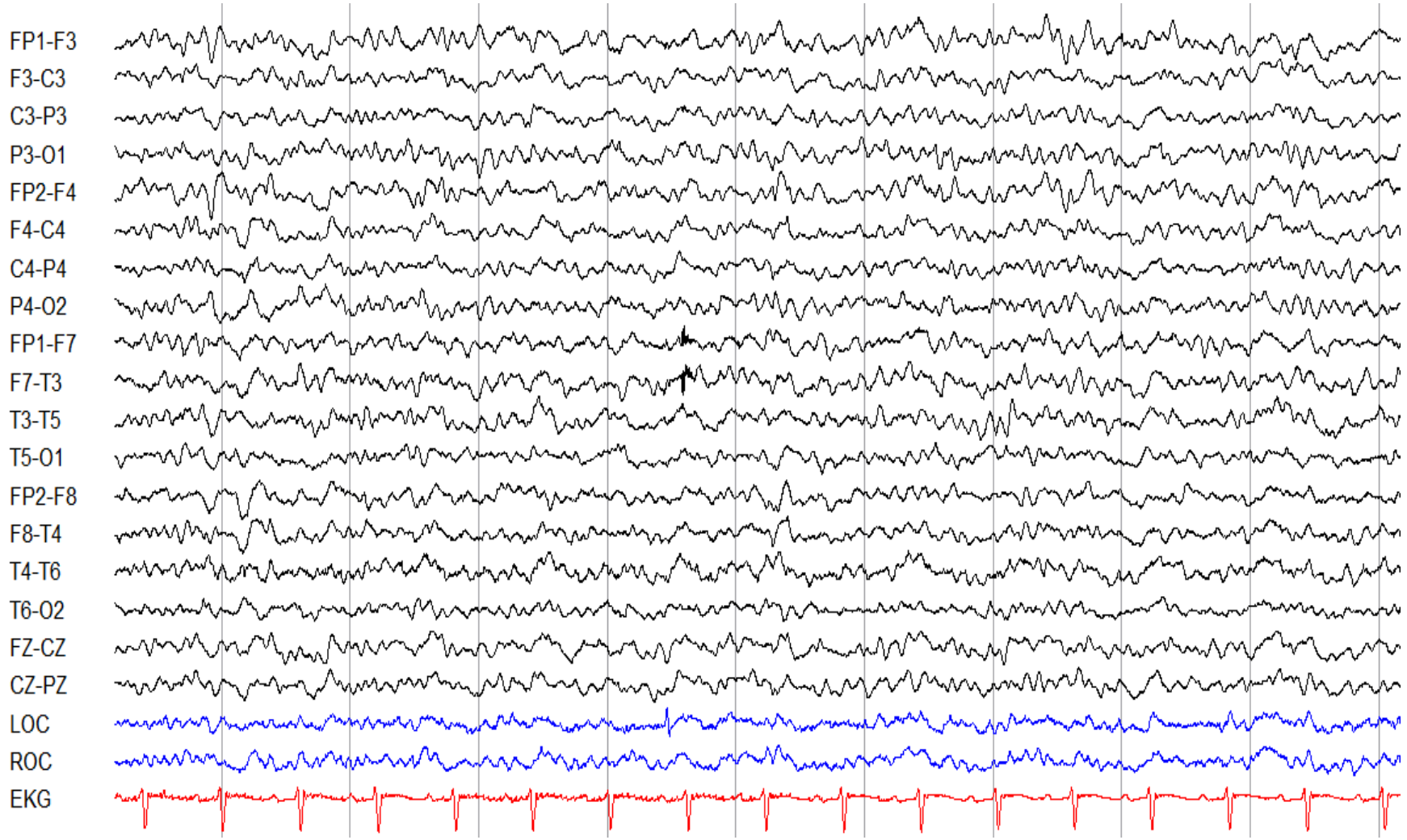
Reactivity

- EEG change in response to sensory stimulation
  - Auditory
  - Visual
  - Somatosensory
- Light coma
  - Generalized high voltage delta bursts
- Deeper coma
  - Diffuse attenuation
- Deep coma
  - No reactivity; poorer prognosis

Specific Coma Patterns

Alpha Coma

- Diffuse alpha frequency activity, 8-13Hz
  - Often frontally dominant
  - Invariant
  - Unreactive
- Transient pattern, evolves to other patterns
- Etiology
  - Anoxia
  - Brainstem strokes
  - Traumatic brain injury
  - Drug intoxication (benzodiazepines, tricyclic antidepressants)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C4-P4
P4-O2
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
FZ-CZ
CZ-PZ
LOC
ROC
EKG

Alpha Coma and Prognosis

- Meta-analysis, 335 cases
- Etiology predicts outcome

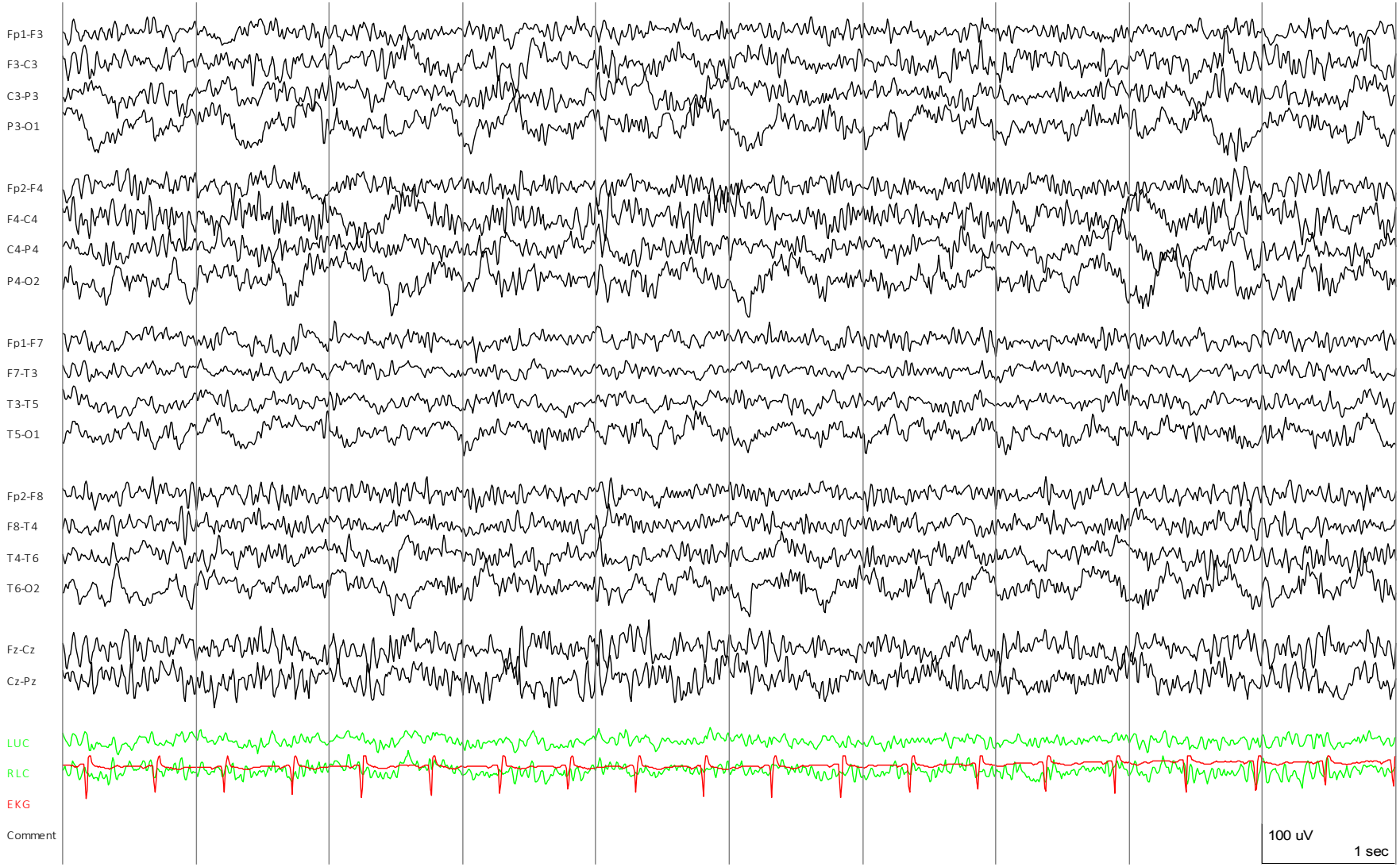
Etiology	Mortality
Anoxia	88%
Brainstem infarct	90%
Drug intoxication	8%

Kaplan PW, et al. Clin Neurophysiol. 1999; 110: 205-13

Beta Coma

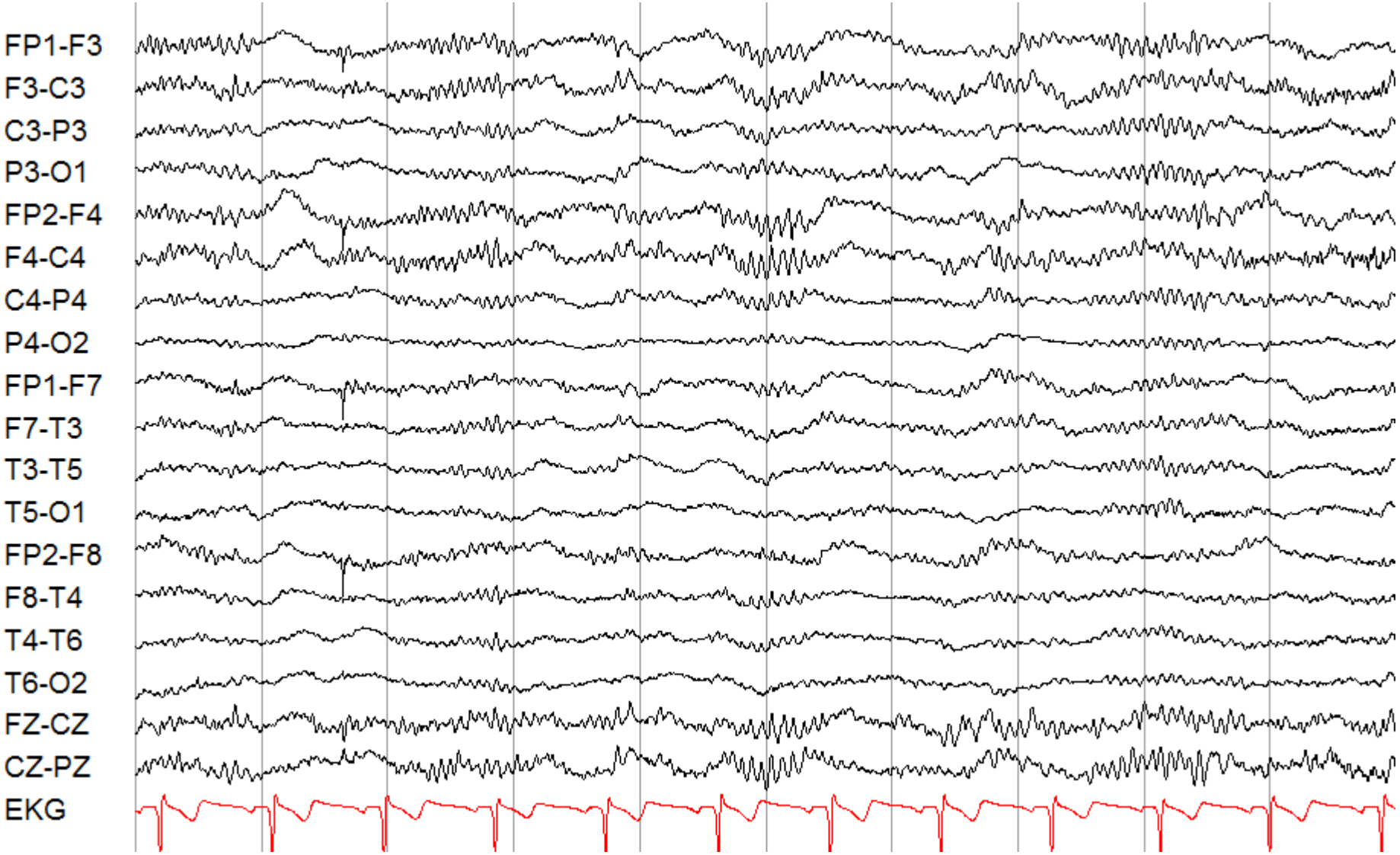
- High amplitude (>30 μV) diffuse 12-16 Hz activity
  - Often frontally maximal
  - Unreactive
- Etiologies
  - Drug intoxication
  - Anesthesia
- Prognosis usually determined by etiology rather than EEG pattern

Diffuse Beta, Barbiturate-Induced



Spindle Coma

- Diffuse exaggerated 12-14 Hz sleep spindles
  - Resembles stage 2 or 3 (N2 or N3) sleep
    - May show some stage changes (vertex waves, K complexes)
    - No REM
  - Little or no reactivity to external stimuli
- Etiologies
  - Traumatic brain injury
  - Anoxia
  - Brainstem lesions
  - Drug intoxication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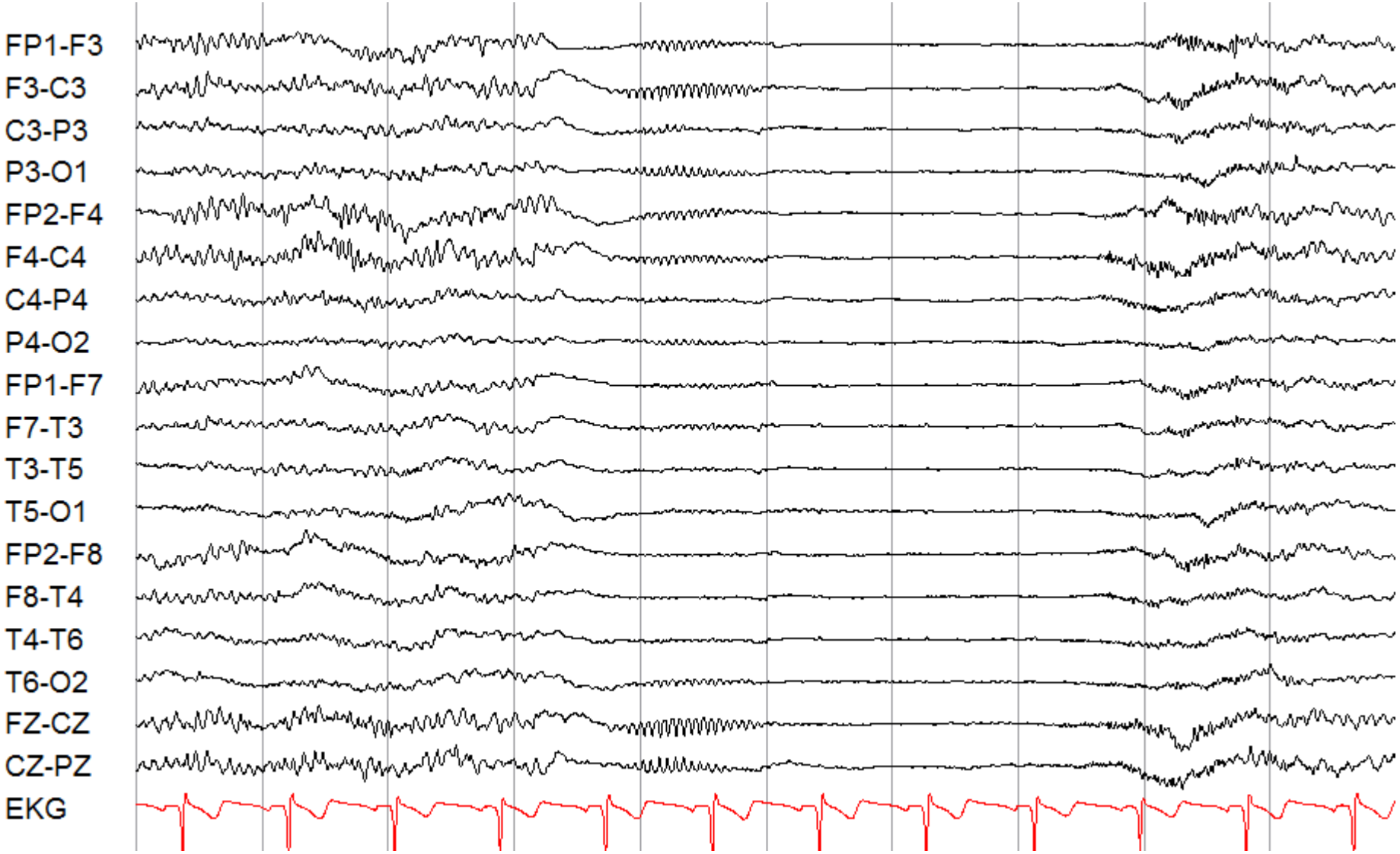
F8-T4
T4-T6
T6-O2
FZ-CZ
CZ-PZ
EKG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T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
FZ-CZ
CZ-PZ
EKG

Spindle Coma and Prognosis

- Etiology plays a role
- Overall better prognosis than alpha coma, mortality 23%
- Presence of normal sleep tranisents suggests that cortex and diencephalon are more intact

Etiology	Mortality
Structural / brainstem	73%
Hypoxia	33%
Trauma	15%
Drug intoxication	0%

Kaplan PW, et al. Clin Neurophysiol. 2000; 111: 584-90

Subarachnoid Hemorrhage

- 116 / 756 SAH patients with CEEG and 3 mo mRS
  - 88% poor grade SAH (Hunt & Hess ≥ 3)
  - Overall 3 month outcome
    - 69% moderate-severely disabled or dead
    - 34% dead
  - Multivariate analysis
    - Poor admission Hunt & Hess grade (OR 7.0)
    - Older age (OR 1.0 per year > 65)
    - Intraventricular hemorrhage (OR 2.6)
    - No effect of delayed cerebral ischemia

Claassen J et al. Neurocrit Care 2006;4:103-112
Dennis LJ et al.. Neurosurgery 2002;51:1136-1143

CEEG Risk Factors in SAH

EEG Finding	Poor outcome With RF (%)	Poor outcome Without RF (%)	OR	95% CI
Lateralized periodic discharges	91	66	18.8	1.6 - 214.6
Any periodic discharges	90	63	9.0	1.7 - 49.0
Absent sleep, 1st 24 hrs	74	29	10.4	1.4 - 78.1
Absent sleep, entire EEG	89	47	4.3	1.1 - 17.2
Absent reactivity, n = 9 *	100	0	-	-
NCSE within 24 hrs, n = 4 *	100	0	-	-
NCSE, entire EEG, n = 12	92	8	-	-
GPEDs or BiPLEDs, n = 17 *	100	0	-	-

* = Specificity and PPV for poor outcome = 100

Claassen J et al. Neurocrit Care 2006;4:103-112
Dennis LJ et al.. Neurosurgery 2002;51:1136-1143

Intracerebral Hemorrhage

- Predictors of poor outcome
  - Generalized periodic discharges
  - Lateralized periodic discharges
  - Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs)

Claassen J et al. Neurology 2007;69:1356-1365
Vespa PM et al. Neurology 2003;60:1441-1446

Cardiac Arrest

- Therapeutic hypothermia
  - 4 randomized clinical trials
  - Comatose patients within 6 hrs of arrest
  - Ventricular fibrillation or pulseless ventricular tachycardia
  - Mild TH (32-34º C) for 24 hrs
  - Decreased mortality by 20%
  - Decreased poor neurologic outcome by 27%

Cheung KW et al. Can J Emergency Med. 2006;8:329-337

Cardiac Arrest

- AAN Practice Parameter: Prediction of outcome in comatose survivors after cardiopulmonary resuscitation

Clinical factor	Timing	Level
Absent pupillary response	3 days	A
Absent corneal reflexes	3 days	A
Absent motor responses	3 days	A
Myoclonic status epilepticus	24 hrs	B
Serum NSE > 33µg/L	1-3 days	B
Bilateral absent cortical SSEP	3 days	B

Wijdicks EF et a;. Neurology 2006;67:203-210

Cardiac Arrest

- AAN Practice Parameter: Prediction of outcome in comatose survivors after cardiopulmonary resuscitation

EEG finding	Timing	Level
Generalized suppression ≤ 20μV	Any	C
Burst-suppression	Any	C
GPEDs on flat background	Any	C

Wijdicks EF et a;. Neurology 2006;67:203-210

Predictors of Poor Outcome: No TH

- Myoclonic status epilepticus
  - EEG usually shows burst suppression and/or GPDs
  - Rare (<5%) with good cognitive outcome
    - Usually treated with high-dose cIV-AEDs
    - Preserved brainstem reflexes
    - Intact cortical SSEP responses
    - Reactive EEG background

Predictors of Poor Outcome: No TH

- Background EEG
  - Burst-suppression
  - Discontinuity
  - Generalized voltage attenuation (< 20μV)
  - Alpha / theta / spindle coma without reactivity
- Lack of reactivity
- Periodic discharges
  - Generalized periodic discharges on attenuated background

EEG after Cardiac Arrest: No TH

- Sensitivity 94%
- Specificity 63%
  - 4 patients with malignant recovered awareness

Benign	Malignant
Delta / theta > 50% of recording, with or without reactivity	Triphasic waves
	Burst-suppression, with or without epileptiform activity
	Alpha / theta / spindle coma, without reactivity
	Generalized suppressioin

Thenayan EA et al. J Crit Care 2010;25:300-304

Predictors of Outcome after Cardiac Arrest: No TH

- Meta-analysis of 50 studies
- 2828 adult patients, comatose after cardiac arrest
- Outcomes assessed by Cerebral Performance Category (CPC)
  - CPC 4-5 vs. 1-3
  - CPC 3-5 vs. 1-2
  - Variable timing: hospital discharge to 12 mos

Sandroni C, Cavallaro F, Callaway CW, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: A systematic review and meta-analysis. Part 1: Patients not treated with therapeutic hypothermia. Resuscitation 2013.

Predictors of Outcome after Cardiac Arrest: No TH

Finding	Timing	Sensitivity	FPR	95% CI	Quality
Myoclonus, n=471	24-48 hrs	9	0	0-3	Low
Bilateral absent SSEP, n = 293	24-72 hrs	45-46%	0	0-9	Low
Absent pupillary response, n = 382	72 hrs	18	0	0-8	Low
NSE, S-100B	Variable	--	--		Very low

Sandroni C, Cavallaro F, Callaway CW, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: A systematic review and meta-analysis. Part 1: Patients not treated with therapeutic hypothermia. Resuscitation 2013.

Predictors of Outcome after Cardiac Arrest: No TH

EEG Finding	Timing	Sensitivity	FPR	95% CI	Quality
Grade III-V (Edgren), n=46	24 hrs	36	0	0-22	Very low
Grade IV-V (Synek), n=40	≤ 48 hrs	42	0	0-19	Very low
Grade IV-V (Bassetti), n=59	≤ 72 hrs	42	0	0-24	Very low
Low voltage EEG, ≤ 20 μV, n=355	24-72 hrs	28	0	0-6	Low
Alpha coma			--		

Sandroni C, Cavallaro F, Callaway CW, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: A systematic review and meta-analysis. Part 1: Patients not treated with therapeutic hypothermia. Resuscitation 2013.

Predictors of Poor Outcome: TH

- Background EEG
  - Burst-suppression
  - Discontinuity
  - Generalized voltage attenuation (< 10μV)
  - Lack of reactivity
- Periodic discharges
  - Generalized periodic discharges on attenuated background

Predictors of Poor Outcome: TH

- Prospective, 111 adult survivors of cardiac arrest
- Unreactive EEG background strong predictor of mortality and poor long-term neurologic recovery (FP = 7%)
- Motor response to pain (FP = 24%)
- 2+ risk factors = specificity 1.0; PPV 1.0
  - Bilaterally absent cortical SSEP
  - Unreactive EEG
  - Early myoclonus
  - Incomplete recovery of brainstem reflexes

Rossetti AO et al. Ann Neurol 2010;67:301-307

Predictors of Outcome after Cardiac Arrest: TH

- Meta-analysis of 37 studies
- 2403 adult patients, comatose after cardiac arrest
- Outcomes assessed by Cerebral Performance Category (CPC)
  - CPC 4-5 vs. 1-3
  - CPC 3-5 vs. 1-2
  - Variable timing: hospital discharge to 12 mos

Sandroni C, Cavallaro F, Callaway CW, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: A systematic review and meta-analysis. Part 2: Patients treated with therapeutic hypothermia. Resuscitation 2013.

Predictors of Outcome after Cardiac Arrest: TH

Finding	Timing	Sensitivity	FPR	95% CI	Quality
Bilateral absent SSEP	During TH	28	0	0-2	Moderate
Bilateral absent SSEP	After TH	42	0	0-4	Low
Absent pupillary + absent corneal + motor response ≤ extension, n = 103	72 hrs	15	0	0-8	Very low
NSE, S-100B	Variable	--	--		Very low

Sandroni C, Cavallaro F, Callaway CW, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: A systematic review and meta-analysis. Part 2: Patients treated with therapeutic hypothermia. Resuscitation 2013.

Predictors of Outcome after Cardiac Arrest: TH

EEG Finding	Timing	Sensitivity	FPR	95% CI	Quality
Burst-suppression	During TH	37	0	0-5	Low
Burst-suppression	After TH	18	0	0-5	Low
Status epilepticus from burst-suppression	Any time	42	0	0-5	Low
Nonreactive background	After TH	62	0	0-3	Low

Sandroni C, Cavallaro F, Callaway CW, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: A systematic review and meta-analysis. Part 2: Patients treated with therapeutic hypothermia. Resuscitation 2013.

Confounders

- Sedating medications
  - Propofol, midazolam, pentobarbital
- Presence of multiple etiologies (e.g. post-arrest + hepatic or renal failure)
- Artifact
  - Shivering / EMG
  - Electrode artifact

Conclusion

- Use EEG for patients with altered mental status
  - Objective measure for encephalopathy
  - Narrow differential diagnosis when etiology unknown
- Serial or continuous studies may be helpful
- EEG can help with prognostication when etiology is known
  - Better at predicting poor outcome
- Early inaccurate prognostication may result in self-fulfilling prophecy: early withdrawal of care
- Large prospective studies needed to determine prognostic value of CEEG across multiple etiologies and severity of illness