MAYO CLINIC | School of Continuous Professional Development

MAYO CLINIC

ELECTROMYOGRAPHY (EMG), ELECTROENCEPHALOGRAPHY (EEG), AND NEUROPHYSIOLOGY IN CLINICAL PRACTICE

February 19-25, 2023
Ritz-Carlton Amelia Island
Amelia Island, FL

MAYO CLINIC | School of Continuous Professional Development

EEG IN PROGNOSTICATION OF ANOXIC BRAIN INJURY

Jeffrey W Britton, MD
Chair, Division of Epilepsy
Professor of Neurology, Mayo Clinic Rochester

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Inventor's agreement – SEER Medical

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

All relevant financial relationships have been mitigated.

All Images in the presentation are used with permission

OBJECTIVES

- Identify EEG findings portending poor prognosis in anoxic brain injury
- Diagnose EEG findings associated with good prognosis in anoxic brain injury
- Describe the effects of targeted temperature management (TTM) therapy on the EEG

LEARNING OBJECTIVES

This lecture will help the learner to:

- Identify EEG findings portending poor prognosis in anoxic brain injury
- Diagnose EEG findings associated with good prognosis in anoxic brain injury
- Describe the effects of targeted temperature management (TTM) therapy on the EEG

OUTLINE

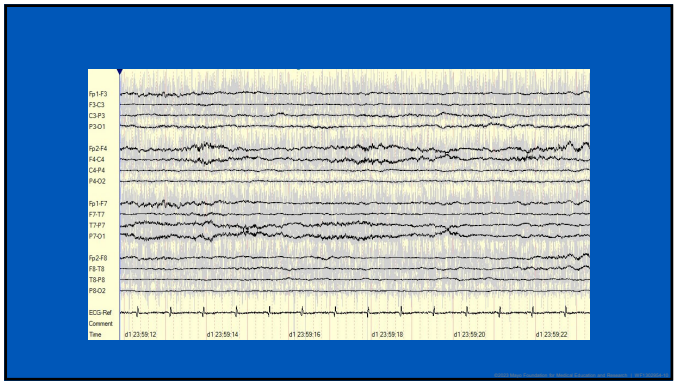
1. Cases
2. Epidemiology/prognosis of anoxic brain injury and targeted temperature management (TTM)
3. Prognostic tools for anoxic brain injury
4. Clinical exam/non-EEG factors in prognosis
5. EEG findings of prognostic significance

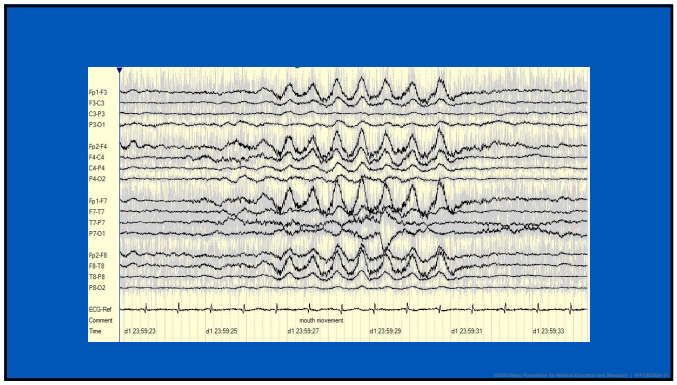
CASE 1

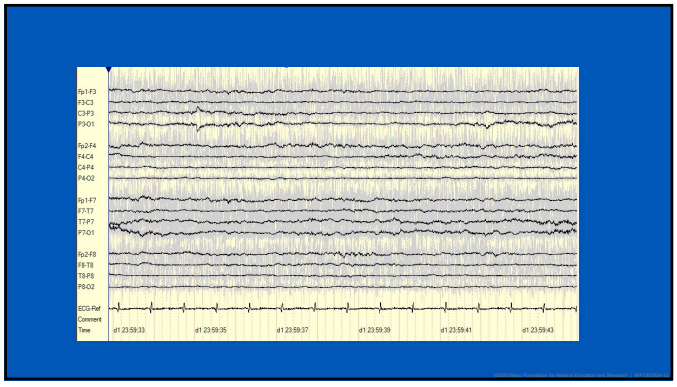
- 48 yoF, DM, hyperlipidemia, HOCM, nephrotic syndrome, OSA admitted post cardiac arrest
- Developed angina, then hours later acute arrest
- CPR, EMS found her to be in PEA, then VTach, cardioverted, timing of ROSC unknown
- TTM initiated, comatose since arrest

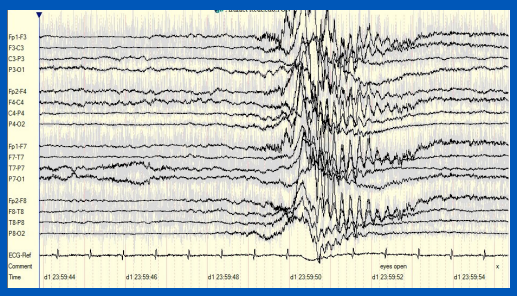
CASE 1 (EXAM)

- Intermittent sucking, periodic upward eye deviation
- Minimal pupillary response
- Corneal, oculocephalic reflexes absent
- Spontaneously breathing over vent, but no gag or cough response
- No response to voice, noxious stimuli


Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F7
F7-T7
T7-P7
P7-O1
Fp2-F8
F8-T8
T8-P8
P8-O2
ECG-Ref
Comment
Time
d1 23:59:12
d1 23:59:14
d1 23:59:16
d1 23:59:18
d1 23:59:20
d1 23:59:22


Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F7
F7-T7
T7-P7
P7-O1
Fp2-F8
F8-T8
T8-P8
P8-O2
ECG-Ref
Comment
mouth movement
Time
d1 23:59:23
d1 23:59:25
d1 23:59:27
d1 23:59:29
d1 23:59:31
d1 23:59:33

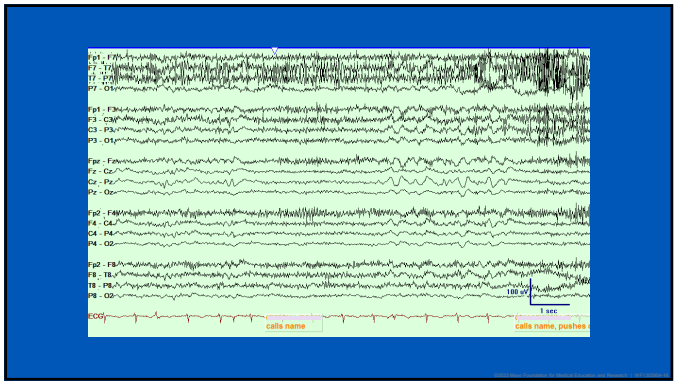

Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F7
F7-T7
T7-P7
P7-O1
Fp2-F8
F8-T8
T8-P8
P8-O2
ECG-Ref
Comment
Time
d1 23:59:33
d1 23:59:35
d1 23:59:37
d1 23:59:39
d1 23:59:41
d1 23:59:43

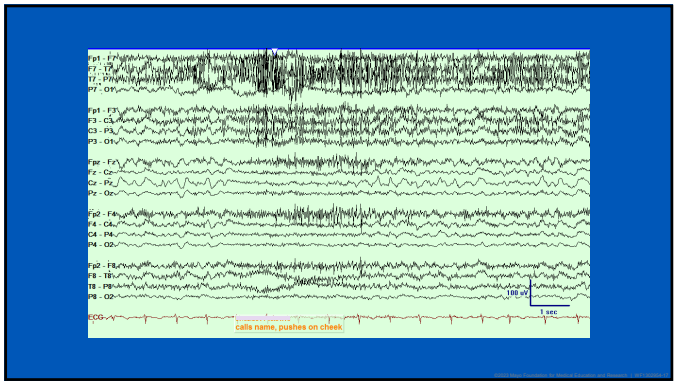


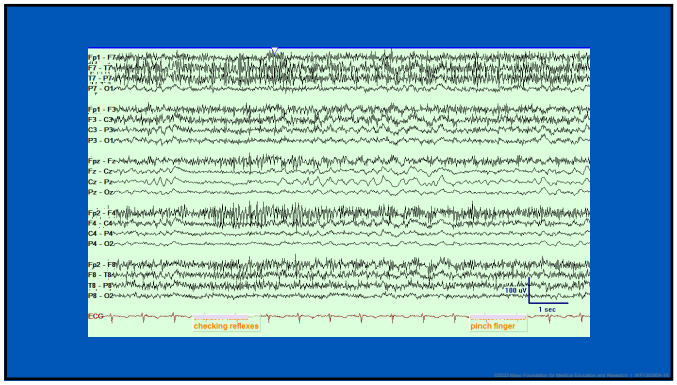
PROGNOSIS?

CASE 2

- 76 M, out of hospital VFib arrest, resuscitated then arrested again, ROSC 22 min
- Pulmonary contusion resulting in difficulty with oxygenation
- TTM instituted with target temp 33^0
- Exam – opened eyes to voice, visually fixated on others, moving 4 limbs spontaneously


Fp1 - F7
F7 - T7
T7 - P7
P7 - O1
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
Fpz - Fz
Fz - Cz
Cz - Pz
Pz - Oz
Fp2 - F4
F4 - C4
C4 - P4
P4 - O2
Fp2 - F8
F8 - T8
T8 - P8
P8 - O2
100 uV
1 sec
ECG
calls name
calls name, pushes


Fp1 - F7
F7 - T7
T7 - P7
P7 - O1
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
Fpz - Fz
Fz - Cz
Cz - Pz
Pz - Oz
Fp2 - F4
F4 - C4
C4 - P4
P4 - O2
Fp2 - F8
F8 - T8
T8 - P8
P8 - O2
100 uV
1 sec
ECG
calls name, pushes on cheek


Fp1 - F7
F7 - T7
T7 - P7
P7 - O1
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
Fpz - Fz
Fz - Cz
Cz - Pz
Pz - Oz
Fp2 - F4
F4 - C4
C4 - P4
P4 - O2
Fp2 - F8
F8 - T8
T8 - P8
P8 - O2
100 uV
1 sec
ECG
checking reflexes
pinch finger

PROGNOSIS?

EPIDEMIOLOGY OF CARDIAC ARREST

- US: Incidence ~76/10^5 per yr; 326,200 persons/yr
- 50-60% of cardiac arrests are unwitnessed
- Survival rates following cardiac arrest
  - all (witnessed and not) - 10.6%
  - witnessed arrest - 31.4%
  - shockable rhythm - 33%
  - asystole, PEA - <10%

Mozaffarian et al. Circulation 2015; 131:434-41

EFFICACY OF TTM FOLLOWING CARDIAC ARREST

		Mortality	P =	Good outcome	Odds ratio or p-value
Bernard et al. NEJM 2002; 346:557-63					
- VF only, μ = 68 yrs	Hypothermia	51%	0.14	49%	5.25 (1.5-18.8; p= 0.011)
- ROSC μ = 26 min	Normothermia	68%		26%	
Hozer et al. NEJM 2002; 346: 549-56					
- VF only, μ = 59 yrs	Hypothermia	41%	0.02	55%	1.4 (1.1-1.8; p= 0.009)
- ROSC μ = 21-22 min	Normothermia	55%		39%	
Nielsen et al. NEJM 2013; 369:2197-206					
- VF+, μ = 64 yrs	T=33^0	50%	0.51	46%	p = 0.78
- ROSC = 25 min	T=36^0	48%		48%	

VF = ventricular fibrillation, ROSC = return of spontaneous circulation, red font = statistically sign values

CLINICAL EXAM IN ANOXIC BRAIN INJURY

- Clinical signs of poor prognostic significance
  - Absent pupillary response
  - Absent corneal, oculocephalic responses
  - Extensor or absent motor response
  - Myoclonus

CLINICAL EXAM IN ANOXIC BRAIN INJURY

Prognostic value of clinical signs

- Specific when abnormal - low false positive rate (FPR) for poor prognosis
- However, modest predictive values (PV) for good prognosis (moderate false negative rates)
- Exam may be affected by TTM therapy, sedation

CLINICAL EXAM

- Absent pupillary response
  - False positive rate (FPR) at 72 hrs = 0.5% (CI 0-2) first 24 hrs
  - with TTM ~ 8%
  - *Reactive pupillary response @72hrs – predictive value for good outcome = only 61% (CI 50-71)*
- Absent corneal response
  - FPR @ 72 hrs = 5% (CI 0-25); (sedatives, NM blockade)
  - *Intact corneal reflexes @ 72 hrs – PV for good outcome = 62% (CI 52-72)*

Rossetti, Rabinstein, Oddo. Lancet Neurol 2016; 15:597-609

CLINICAL EXAM IN ANOXIC BRAIN INJURY AND TTM

- Absent or extensor response to pain
  - *susceptible to NM blockade, sedative, opiate effects, each of which prolonged by hypothermia, renal/hepatic co-morbidities*
  - FPRs of absent or extensor response ~ 24% (CI 6-48)
- *Flexor or preserved localizing response PV for good outcome 81% (CI 66-91)*

Rossetti, Rabinstein, Oddo. Lancet Neurol 2016; 15:597-609

CLINICAL EXAM IN ANOXIC BRAIN INJURY

- *Post-anoxia myoclonus (PAM)*
  - prognosis not uniformly bad
- Type and characteristics of PAM are important[1]
  - *Generalized myoclonus*, poor prognosis FPR = 0 (CI 0-3)
  - *Brief twitches face/trunk* poor prognosis FPR = 11% (CI 3-26)

1. Rossetti, Rabinstein, Oddo. Lancet Neurol 2016; 15:597-609; 2. Seder et al. Crit Care Med 2015; 43:965–972; 3. Elmer et al. Ann Neurol 2016; 175-84; 4. Hofmeijer et al. Clin Neurophysiol 2014;125:947–954

CLINICAL EXAM IN ANOXIC BRAIN INJURY

- EEG findings add prognostic value in PAM
  - *Good outcome rate in PAM overall = 9%[2]*
  - *Without epileptiform EEG = 15%*
  - *With epileptiform EEG = 2%[2]*

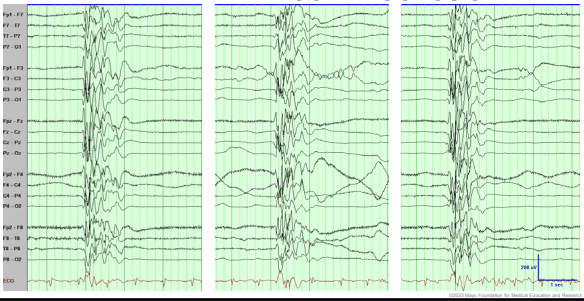
1. Rossetti, Rabinstein, Oddo. Lancet Neurol 2016; 15:597-609; 2. Seder et al. Crit Care Med 2015; 43:965–972; 3. Elmer et al. Ann Neurol 2016; 175-84; 4. Hofmeijer et al. Clin Neurophysiol 2014;125:947–954

EEG - PROGNOSIS IN POSTANOXIC MYOCLONUS

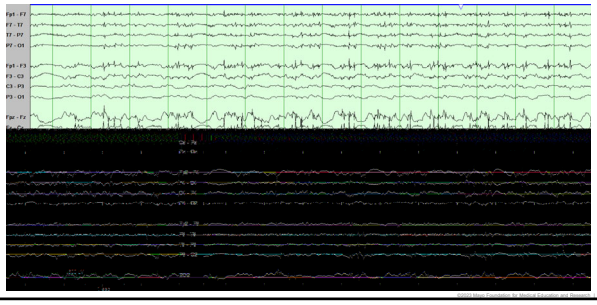
- EEG background and features helpful[3]
  - *Continuous background = good, vs burst suppression*[3]
  - *Narrow vertex spikes linked with myoclonic jerks = good, vs large uniform polyspike discharges*[3] *(aka "identical bursts")*[4]
  - *suppression ratio (proportion of each epoch that shows ≥0.5 seconds of <3μV amplitude) – lower ratio good, higher ratio bad*[3]

1. Rossetti, Rabinstein, Oddo. Lancet Neurol 2016; 15:597-609; 2. Seder et al. Crit Care Med 2015; 43:965–972; 3. Elmer et al. Ann Neurol 2016; 175-84; 4. Hofmeijer et al. Clin Neurophysiol 2014;125:947–954

BURST-SUPPRESSION WITH IDENTICAL BURSTS IN PATIENT WITH PAM – POOR PROGNOSIS



NARROW MIDLINE SPIKES IN PATIENT WITH PAM – ASSOCIATED WITH MORE FAVORABLE

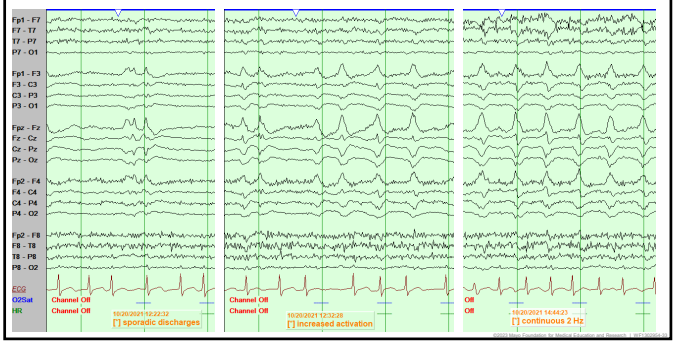


EEG in prognosis of anoxic brain injury

EEG IN ANOXIC BRAIN INJURY AND TTM

- A number of individual EEG findings have been found to have prognostic significance, however:
  - EEG findings often occur in combination
  - EEG evolves post anoxic insult
  - TTM can alter EEG
    - Sedatives, opiate direct effects
    - TTM also affects elimination of sedatives, opiates
    - Hypothermia can affect EEG

EVOLUTION OF ABNORMALITIES IN ANOXIC BRAIN INJURY



EEG SEVERITY SCALE – POST ANOXIA

Grade 1	Anesthetic pattern Theta slowing	Reactive background Continuous background
Grade 2	Diffuse or focal delta slowing Stimulus-induced rhythmic, periodic and ictal-like discharges (SIRPIDS) Discontinuous - episodic low amplitude events (ELAEs)	Spindle coma Interictal epileptiform discharges Triphasic waves FIRDA, OIRDA, TIRDA Lateralized periodic discharges (LPDs)
Grade 3	Burst-suppression pattern Low voltage/suppression (≤ 10 μV) Alpha/theta coma, other invariant pattern	Seizure discharges Non-reactive background Generalized periodic discharges (GPDs) Status epilepticus

Crepeau et al. Neurology 2013; 80: 339-44

EEG FINDINGS PORTENDING POOR PROGNOSIS

	EEG finding	Odds ratio
Good outcome	Grade 1 (during hypo- and normo- thermia) *0 of 13 with Grade 1 had poor outcome*	0 (0-0.5)
Poor outcome	Grade 3 (during hypo- and normo-thermia) *16 of 16 with Grade 3 had poor outcome*	49.6 (8.5-284.7)
	Seizures *5 of 5 with seizures had poor outcome*	∞ (64.4 - ∞)
	Non-reactive background *11 of 13 had poor outcome*	17.05 (3.22-90.3)
	Epileptiform discharges present *16 of 23 had poor outcome*	11.89 (3.22-43.9)

Crepeau et al. Neurology 2013; 80: 339-44

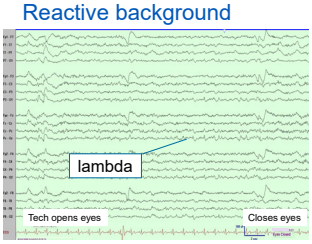
EEG SEVERITY AND PROGNOSIS IN ANOXIC BRAIN INJURY

Benign	Malignant	Highly malignant
Continuous background	Discontinuous background (10-49% of record suppressed)	Suppression-burst (>50% of record suppressed)
Reactivity present	No reactivity other than (SIRPIDs)	Severe suppression (amplitude < 10μV)
Variable background	Abundant rhythmic or periodic discharges	
	Low voltage (amplitude < 20 μV)	

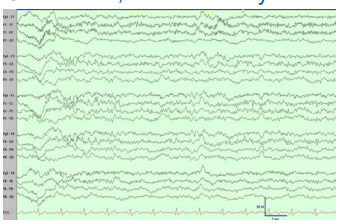
Adapted from: Westhall, Rossetti et al. BMC Neurol 2014; 14:159. Hirsch et al, JCN 2013;30:1-27

EEG IN ANOXIC BRAIN INJURY – "BENIGN"

Reactive background

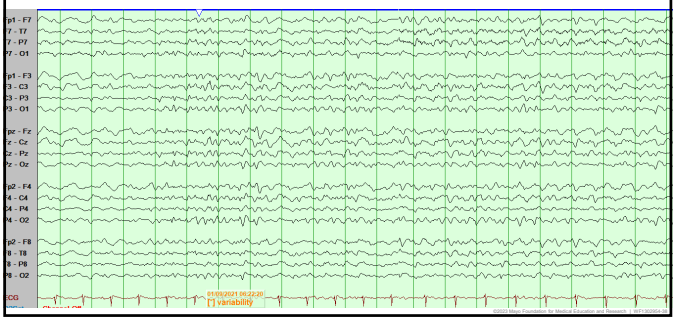


Continuous, with variability



Westhall et al. Neurology 2016; 86: 1482-90

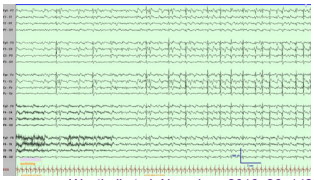
BACKGROUND VARIABILITY



EEG IN ANOXIC BRAIN INJURY – "MALIGNANT" (AS OPPOSED TO "HIGHLY MALIGNANT")

Mildly discontinuous record (suppressed segments <50% of background)

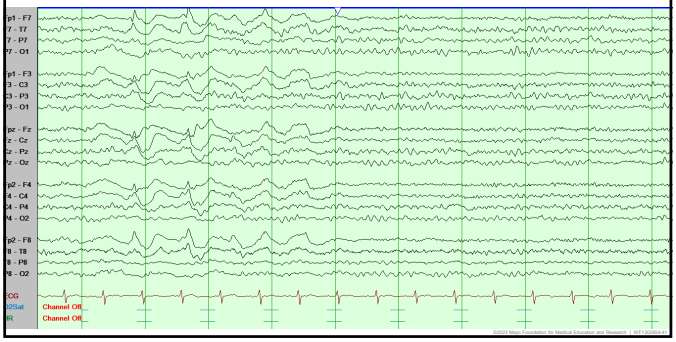
Abnl reactivity (SIRPIDs), abundant (not continuous) generalized periodic discharges (GPDs)



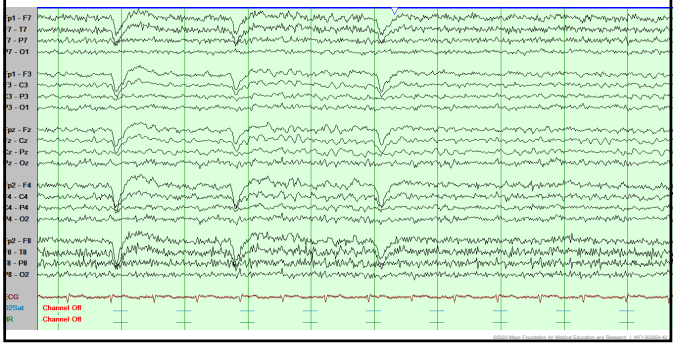
Westhall et al. Neurology 2016; 86: 1482-90

DISCONTINUITY

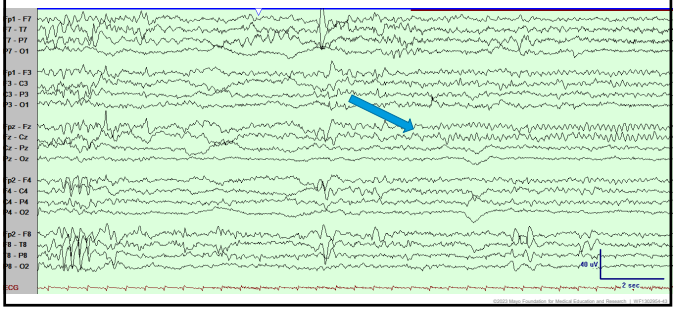
BIFRONTAL SHARP WAVES AND ALPHA COMA



THETA COMA

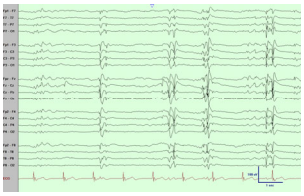


MULTIFOCAL SHARP WAVES AND FOCAL SEIZURE (ONSET FZ-F3)

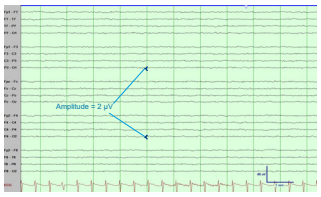


EEG IN ANOXIC BRAIN INJURY – "HIGHLY MALIGNANT"

Suppression-burst (>50% of record suppressed)



Severe suppression (amplitude < 10μV)



Westhall et al. Neurology 2016; 86: 1482-90

EEG AND POOR OUTCOME – POST TTM

Pattern type	No. (%) (n=103)	Sensitivity	Specificity	False positives (had good prognosis)
≥1 Highly malignant	37%	50%	100%	0
≥1 Malignant feature	86%	99%	48%	14
≥2 Malignant feature	57%	76%	96%	1
Malignant periodic/ rhythmic discharges	32%	43%	100%	0
Malignant background	69%	82%	74%	7

Adapted from: Westhall et al. Neurology 2016; 86: 1482-90

BENIGN EEG AND GOOD OUTCOME

- 14 “benign” EEG
  - 13 had good outcome - *specific*
- Benign EEG seen in 48% (CI 31-66%) with good outcome
  - 1% (CI 0-7%) with poor outcome – *limited sensitivity*
- Benign AND reactive EEG = 0% (CI 0-7%) with poor outcome
  - Constituted 30% (CI 16-49%) with good outcome – *limited sensitivity, good specificity*

Westhall et al. Neurology 2016; 86: 1482-90

APPLICATION OF EEG SCALE AND OTHER FACTORS FOR ANOXIC INJURY

- Collaboration CHUV, UNIL (Lausanne) *(n=260)*, Mayo *(n=97)*
- Prospective and retrospective review EEGs post cardiac arrest: “early” (during TTM) and “late” (post TTM)
- Also, clinical exam, SEPs, NSE
- V fib and nonshockable arrests included
- Outcome measures: CPC 1-2 “good”, mortality

EEG MALIGNANCY SCALE/OTHER FACTORS: PROGNOSIS POST ANOXIC BI

Factor	P value
Good outcome	
EEG reactivity “early” (during TTM)	<0.001
EEG continuous “early”	<0.001
Motor Glasgow Coma ≥ 3	<0.001
Mortality	
EEG non-reactive “early”	<0.001
EEG epileptiform “early”	<0.001
EEG non-reactive “late” (post TTM)	0.001

Derived from: Rossetti et al. Critical Care Medicine 2017; 45(7): p e674–e682

SUMMARY – EEG AND PROGNOSIS POST ANOXIC INJURY

- Several clinical factors are as important as EEG
  - Pupillary response, corneals and oculocephalics, motor response, PAM, type of arrest
- EEG has reasonable prognostic accuracy for good and bad outcome when clearly benign and highly malignant findings are present
- EEG background likely more important than individual patterns such as periodic discharges, in isolation

SUMMARY – EEG AND PROGNOSIS POST ANOXIC INJURY

- EEG findings associated with <u>good</u> prognosis:
  - *reactive and continuous background*
  - *Lack of malignant or highly malignant abnormalities*
- EEG findings associated with <u>poor</u> prognosis:
  - *Suppression of amplitude < 10 μV*
  - *Significant discontinuity (>50% record suppressed)*
  - *<u>></u>2 malignant features in same record*
  - *Abundant periodic discharges and seizures*

OUTCOME OF TWO CASES

Case 1: episodic eye opening mouth movements

- Poor prognostics:
  - clinical - PEA arrest, PAM
  - EEG - severe suppression, severe discontinuity, burst suppression
- Support withdrawn, patient died

Case 2:

- Good prognostics:
  - Clinical - shockable rhythm, no PAM, able to track
  - EEG - reactivity, variability and no discontinuity
- Dismissed from hospital, became independent, continued driving

MAYO CLINIC | School of Continuous Professional Development

THANK YOU FOR YOUR ATTENTION!