Coma, Post-Anoxic, Brain Death EEG

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• No disclosures
Learning Objectives

• To recognize common coma nonspecific and specific patterns

• To learn the clinical significance and common EEG patterns of post-anoxia

• To study electrocerebral inactivity (ECI) EEG technological requirements and criteria for brain death
Coma EEG

• Nonspecific patterns

• Specific patterns
Nonspecific Abnormalities

• Slowing

• Asymmetry

• Decrease in Continuity
EEG Slowing
1. Frequency
   - Frequency of the EEG parallels the degree of impairment

   - Progression of the EEG pattern in encephalopathies:
     - Frequency: alpha $\rightarrow$ theta $\rightarrow$ delta
     - Prevalence: intermittent slowing $\rightarrow$ continuous slowing
EEG Slowing
PDR Slowing
Intermittent Generalized Delta Activity (max bifrontal)
Continuous generalized theta slowing

69-year-old male with diffuse encephalopathy

Confused
Continuous Generalized delta theta slowing
Continuous generalized delta slowing, reactive

14-year-old female with encephalitis

Reactivity = changes in EEG in response to stimuli; appearance of EMG does not count!

5 days ago – onset of headache, confusion, and delirium
Now comatose
Delta Coma – No EEG Reactivity

36 yo 13 hours after head injury; no brainstem functions on exam
IRDA – Intermittent Rhythmic Delta Activities

- High voltage, regular quasi-sinusoidal waves, mostly 2-3 Hz

In encephalopathies:
- Adult: most prominent over frontal regions (FIRDA) – may be blocked by eye opening
- Children: most prominent over occipital regions (OIRDA)
RDA

Need 6 cycles to qualify as RDA
Figure. Model of Pattern Characteristics and Seizure Risk

Seizure Risk vs. Pattern Frequency, Hz

- LPD
- LPD+
- LRDA+, GPD+
- LRDA, GPD
- GRDA, GRDA+

Significant Risk
Asymmetry
Left Subdural Hematoma

70-year-old female

Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2

50 μV
1 sec
Right Frontal Abscess

9-year-old male

- $F_{P1}-F_{3}$
- $F_{3}-C_{3}$
- $C_{3}-P_{3}$
- $P_{3}-O_{1}$
- $F_{P2}-F_{4}$
- $F_{4}-C_{4}$
- $C_{4}-P_{4}$
- $P_{4}-O_{2}$
Focal Rhythmic Delta Activities (RDA)

Right SDH with right to left midline shift
Specific Patterns

- Epileptiform
- Periodic
- Coma
Generalized 3 Hz Spike and Wave Discharges in Absence Status

24-year-old female

Confused
Effect of Valium in Absence Status

24-year-old female

Confused

Inject Valium

2 mg Valium in

Feel? “Ok” Alert

CP1078578-14
Periodic and Rhythmic Patterns
Main Terms for **Rhythmic and Periodic Patterns**

- Describe with main term #1 followed by #2, with modifiers added as appropriate.

<table>
<thead>
<tr>
<th>Main term #1</th>
<th>Main term #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>(G) Generalized</td>
<td>(PDs) Periodic Discharges</td>
</tr>
<tr>
<td>(L) Lateralized</td>
<td>(RDA) Rhythmic Delta Activity</td>
</tr>
<tr>
<td>(BI) Bilateral Independent</td>
<td>(SW) (Poly)Spike-&amp;-Wave/Sharp-and-Wave</td>
</tr>
<tr>
<td>(Mf) Multifocal</td>
<td></td>
</tr>
</tbody>
</table>

*Sneak preview:*
- UI: Unilateral Independent
Main term 2: Periodic

Discharge

Interdischarge interval
Main term 2: Rhythmic

Discharge

No interdischarge interval
Main term 2: Spike-and-Wave

Alternating spike and wave

No interdischarge interval
LPDs
Lateralized Periodic Discharges (LPDs)
Lateralized Periodic Discharges (LPDs)
BIPDs (previously BIPLLEDs)
GPDs – Clinical Context

GPDs occur most commonly in comatose patients following:

• Acute, severe cerebral anoxia
• Creutzfelt-Jakob disease
• Metabolic and toxic encephalopathy (with triphasic morphology; “Triphasic waves”)
• Medicine (cephalosporin, such as cefepime)
Generalized Periodic Discharges (GPDs)
GPDs with Triphasic Morphology ("Triphasic wave")

Triphasic waves: Morphology
• 2 electronegative waves
• Separated by a positive wave of high amplitude
• Total duration: 300-500ms
• Occur in semi-rhythmic trains at 1.5-2.5/s
• Associated with PDR slowing

Triphasic waves: Localization
• Maximum in the frontal and fronto-temporal regions
• Bilaterally synchronous
GPDs with Triphasic Morphology ("Triphasic wave")

• Classic finding in: hepatic encephalopathy, other metabolic encephalopathies

• Progression in hepatic encephalopathy:
  • initially just shows increased slowing
  • As encephalopathy progresses toward coma, there is development of triphasic waves

• NOTE: GPDs with triphasic morphology carry the same seizure risk as GPDs without triphasic morphology!!
GPDs with Triphasic Morphology

[Fp1-F3, F3-C3, C3-P3, P3-O1, Fp2-F4, F4-C4, C4-P4, P4-O2]

1 sec

70 µV
Generalized Periodic Discharges with Triphasic Morphology

Foreman et. al. Clinical Neurophy 2016
Generalized Periodic Discharges: Clinical Significance of Triphasic Morphology

No difference in seizure risk!

Foreman et. al. Clinical Neurophy 2016
Creutzfeld Jakob Disease (CJD)

• Slow (i.e. 2.5 Hz or below) spike and wave
• Periodicity may vary
• Sometimes triphasic-like in character
Creutzfeld-Jakob Disease

48-year-old male

Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
What about this EEG?

Ventilator artifacts every 4.5 sec
Summary: Modifiers

- Prevalence
- Duration
- Frequency
- Phases
- Sharpness
- Amplitude
- Polarity
- Stimulus-Induced (SI)
- Evolving OR Fluctuating
- Plus (+)
Modifiers, cont’d: Fluctuating

At least 3 changes, <1 min apart, in:
- Frequency (by $\geq 0.5$/s),
- Morphology, or
- Location (by $\geq 1$ standard inter-electrode distance),
  but *not qualifying as evolving*.

- Includes patterns alternating from $1 \rightarrow 1.5 \rightarrow 1 \rightarrow 1.5$ Hz; spreading in and out of a single electrode repeatedly; or alternating between 2 morphologies repeatedly.

- *Would not qualify as fluctuating:*
  $2$/s for 30s $\rightarrow 1.5$/s for 30s $\rightarrow 2$/s for 3 min $\rightarrow 1.5$/s for 30s $\rightarrow 2$/s for 5 min. *(Changes are too far apart, i.e. $>1$ minute).*

- *Would qualify as fluctuating:*
  $2$/s for 10 s $\rightarrow 2.5$/s for 30s $\rightarrow 2$/s for 5s $\rightarrow 2.5$/s for 5s.
Modifiers, cont’d: **Plus**

Additional feature which renders the pattern more ictal-appearing than the same pattern without the plus:

- How to specify:
  - +F superimposed fast activity (theta or faster; for PDs or RDA)
  - +R superimposed rhythmic or quasi rhythmic delta activity (for PDs only)
  - +S “frequent” superimposed sharp waves/spikes (frequent = >1/10s but not periodic and not SW), or sharply contoured (for RDA only)

- If both subtypes apply, PDs can have “+FR” and RDA can have “+FS”.
- Does not apply to SW.
Figure. Model of Pattern Characteristics and Seizure Risk

Seizure Risk

Pattern Frequency, Hz

LPD+
LPD
LRDA+, GPD+
LRDA, GPD
GRDA, GRDA+

Significant Risk

Rodriguez Ruiz et al. JAMA Neurol 2017
# Prevalence Matters

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Number of Sessions w/o Seizures</th>
<th>Number of Sessions with Seizures</th>
<th>Odds Ratio (95% CI)</th>
<th>FDR-adjusted p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GRDA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rare/Occasional</td>
<td>348 (86%)</td>
<td>55 (14%)</td>
<td>1.23 (0.86-1.71)</td>
<td>0.35</td>
</tr>
<tr>
<td>Frequent</td>
<td>317 (88%)</td>
<td>43 (12%)</td>
<td>1.11 (0.75-1.61)</td>
<td>0.66</td>
</tr>
<tr>
<td>Abundant/Continuous</td>
<td>109 (84%)</td>
<td>129 (20%)</td>
<td>1.42 (0.79-2.42)</td>
<td>0.31</td>
</tr>
<tr>
<td>Not Recorded</td>
<td>31 (89%)</td>
<td>4 (11%)</td>
<td>1.46 (0.39-4.11)</td>
<td>0.60</td>
</tr>
<tr>
<td><strong>LRDA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rare/Occasional</td>
<td>159 (79%)</td>
<td>42 (21%)</td>
<td>1.91 (1.25-2.86)</td>
<td>0.006</td>
</tr>
<tr>
<td>Frequent</td>
<td>89 (68%)</td>
<td>42 (32%)</td>
<td>2.75 (1.72-4.36)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Abundant/Continuous</td>
<td>43 (67%)</td>
<td>21 (33%)</td>
<td>3.69 (1.92-6.87)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Not Recorded</td>
<td>6 (43%)</td>
<td>8 (57%)</td>
<td>5.79 (1.43-24.09)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>GPD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rare/Occasional</td>
<td>172 (92%)</td>
<td>15 (8%)</td>
<td>0.54 (0.28-0.97)</td>
<td>0.10</td>
</tr>
<tr>
<td>Frequent</td>
<td>185 (85%)</td>
<td>32 (15%)</td>
<td>1.49 (0.94-2.29)</td>
<td>0.14</td>
</tr>
<tr>
<td>Abundant/Continuous</td>
<td>202 (77%)</td>
<td>61 (23%)</td>
<td>2.90 (2.00-4.16)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Not Recorded</td>
<td>27 (93%)</td>
<td>2 (7%)</td>
<td>0.78 (0.12-2.84)</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>LPD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rare/Occasional</td>
<td>127 (65%)</td>
<td>68 (35%)</td>
<td>6.26 (4.43-8.80)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Frequent</td>
<td>142 (63%)</td>
<td>85 (37%)</td>
<td>7.44 (5.35-10.31)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Abundant/Continuous</td>
<td>167 (46%)</td>
<td>194 (54%)</td>
<td>12.47 (9.61-16.22)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Not Recorded</td>
<td>13 (68%)</td>
<td>6 (32%)</td>
<td>6.56 (2.13-18.05)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*eTable 3. Rodriguez Ruiz et al. 2017*
Stimulus-Induced – doesn’t seem to matter

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Number of Sessions/Total Sessions with Seizures</th>
<th>% of Sessions with Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRDA – No SI</td>
<td>95/770</td>
<td>12%</td>
</tr>
<tr>
<td>GRDA – SI</td>
<td>27/157</td>
<td>17%</td>
</tr>
<tr>
<td>LRDA – No SI</td>
<td>102/356</td>
<td>28%</td>
</tr>
<tr>
<td>LRDA – SI</td>
<td>11/54</td>
<td>20%</td>
</tr>
<tr>
<td>GPD – No SI</td>
<td>89/569</td>
<td>17%</td>
</tr>
<tr>
<td>GPD – SI</td>
<td>21/127</td>
<td>17%</td>
</tr>
<tr>
<td>LPD – No SI</td>
<td>323/701</td>
<td>49%</td>
</tr>
<tr>
<td>LPD – SI</td>
<td>30/101</td>
<td>30%</td>
</tr>
<tr>
<td>BiPD – No SI</td>
<td>28/93</td>
<td>36%</td>
</tr>
</tbody>
</table>
Coma EEG – Burst suppression
Burst suppression

Burst suppression conditions:
- Severe anoxic encephalopathies
- Acute intoxication with drugs depressing central nervous system
- Severe hypothermia
- Anesthesia
Anoxic Brain Injury and Myoclonic Status
Epidemiology

- 300,000 out of hospital and 200,000 in hospital cardiopulmonary arrest annually in the US
- 40-50% are witnessed
- 17-49% attain return to spontaneous circulation (ROSC)
- Withdrawal of life-sustaining treatment remains the most common cause of death in patients who have poor outcome
- Out of 4265 subjects hospitalized after out of hospital cardiac arrest, 33% had withdrawal of life sustaining treatment within 72 hours after admission because of perceived poor neurological prognosis

Mozaffarian et. Al. Circulation 2015
Phung et al. Am J Hosp Palliat Care 2018
Elmer et al. Resuscitation 2016

• Targeted Temperature Management (TTM)/Therapeutic hypothermia (TH): 72 hours after return to normothermia

• No TTM: 72 hours after cardiac arrest
When to get an EEG

• Start CEEG during TH/TTM
  • Provide prognostic information
  • Monitor for subclinical seizures and NCSE
Postanoxic Refractory Status Epilepticus

• Seen in 9-35% of patients
• Can be associated with clinical motor seizures (myoclonic, clonic, or tonic clonic)
What to look for in EEG?

- Background
- EEG Reactivity (not just EMG/muscle)
- Epileptiform discharges
- Seizures/Status
**EEG Severity Scale – Post-Anoxia in TH era**

**Table 1: EEG grading system for cEEG findings following cardiac arrest**

<table>
<thead>
<tr>
<th>Mild (grade 1)</th>
<th>Moderate (grade 2)</th>
<th>Severe (grade 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excess beta</td>
<td>Diffuse or focal delta slowing</td>
<td>Burst suppression pattern</td>
</tr>
<tr>
<td>Theta slowing</td>
<td>SIRPIDS</td>
<td>Low voltage output pattern ($\leq 10 \mu V$)</td>
</tr>
<tr>
<td>Anesthetic pattern</td>
<td>ELAE</td>
<td>Alpha/theta coma</td>
</tr>
<tr>
<td>Spindle coma</td>
<td></td>
<td>Focal or generalized seizures</td>
</tr>
<tr>
<td>Interictal epileptiform discharges</td>
<td>Nonreactive to stimuli</td>
<td></td>
</tr>
<tr>
<td>Generalized triphasic waves</td>
<td>GPED</td>
<td>Status epilepticus</td>
</tr>
<tr>
<td>FIRDA, TIRDA, OIRDA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLED</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Crepeau et al. Neurology 2013*
EEG Reactivity

• Reactive EEG:
  • Specificity: 73% for good outcome
  • Sensitivity: 82% for good outcome

• Absent reactivity:
  • Specificity: 82% for poor outcome
  • Sensitivity: 73% for poor outcome

• AHA: Absence of EEG reactivity is a poor prognostic marker

Admiraal et al. An Neurol 2019
<table>
<thead>
<tr>
<th></th>
<th>Good outcome, n (%)</th>
<th>Poor outcome, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (at TH)</td>
<td>6 (18.18)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Grade 3 (at TH)</td>
<td>2 (6.06)</td>
<td>16 (75.19)</td>
</tr>
<tr>
<td>Grade 1 (at NT)</td>
<td>13 (40.63)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Grade 3 (at NT)</td>
<td>0 (0)</td>
<td>16 (84.21)</td>
</tr>
<tr>
<td>Seizures (any time) vs no seizures</td>
<td>0 (0)</td>
<td>5 (23.81)</td>
</tr>
<tr>
<td>Nonreactive (any time) vs reactive</td>
<td>2 (6.06)</td>
<td>11 (52.38)</td>
</tr>
<tr>
<td>Epileptiform discharges (any time) vs no epileptiform abnormalities</td>
<td>7 (21.21)</td>
<td>16 (76.19)</td>
</tr>
<tr>
<td>Episodic low-amplitude events (any time) vs no ELAE</td>
<td>21 (63.63)</td>
<td>5 (23.81)</td>
</tr>
<tr>
<td>Improved grade</td>
<td>8 (25)</td>
<td>1 (5.26)</td>
</tr>
<tr>
<td>Worsened grade</td>
<td>1 (3.13)</td>
<td>3 (15.79)</td>
</tr>
</tbody>
</table>
Myoclonic Status ≠ Bad outcome

- 9-11.9% had good neurological outcome

Mikhaeil-Demo et al. Resuscitation 2017
Sedar et al. Crit Care Med 2015
Dhakar et al. Resuscitation 2018
Pattern 1: Post-anoxic EEG with early myoclonus

Post arrest day 0

Post arrest day 1

Pattern 2

Pattern 2: 4/8 survived
Pattern 1: 0/48 survived

Post arrest day 0

Post arrest day 30
 Burst-suppression with identical bursts: A distinct EEG pattern with poor outcome in postanoxic coma

Jeannette Hofmeijer a,b,*, Marleen C. Tjepkema-Cloostermans a,c, Michel J.A.M. van Putten a,c

a Clinical Neurophysiology, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands
b Department of Neurology, Rijnstate Hospital, Arnhem, The Netherlands
c Department of Clinical Neurophysiology, Medisch Spectrum Twente, The Netherlands
Burst suppression with Identical Burst (BS-IB)
Burst suppression – Identical Bursts

• Burst-suppression with identical bursts was always bilateral synchronous, amplitudes were higher

• All 20 patients (100%) with identical bursts after cardiac arrest had a poor outcome vs. 10 (36%) without
Coma Patterns

- Spindle
- Alpha
- Beta
- Theta
Spindle Coma

• Comatose patients with EEG contain features of stage II sleep – spindle like activity

• Conditions:
  • **Propofol**
  • Lesions between the pontomesencephalic junction and the thalamus
  • nonprogressive conditions such as a post-traumatic or post-encephalitis encephalopathy

• Prognosis: **good**
Spindle Coma Pattern Following Head Trauma

39-year-old male

Stuporous since head injury 5 days ago
Beta Coma

• High-amplitude beta activity (>30uV) in comatose patients

• Conditions:
  • Drug intoxication (benzo, barbiturates)
  • Acute brainstem lesions
Drug Overdosage

16-year-old female

Comatose

1 sec 40 μV
Anesthetic Pattern

30-year-old female

- \( F_{P1} - F_3 \)
- \( F_3 - C_3 \)
- \( C_3 - P_3 \)
- \( P_3 - O_1 \)
- \( F_{P2} - F_4 \)
- \( F_4 - C_4 \)
- \( C_4 - P_4 \)
- \( P_4 - O_2 \)

Scale: 1 sec, 70 \( \mu V \)
Theta/Delta Coma

• Delta or theta activity as prominent EEG background activity in comatose patients

• Conditions:
  • Diffuse encephalopathies of diverse etiologies

• Prognosis:
  • Potentially reversible EEG pattern
  • Depends on reversibility of the underlying cause
Theta Coma Post Cardiac Arrest

31-year-old male

Cardiac arrest
Comatose with decerebrate posturing

50 μV
1 sec
Alpha Coma

Causes of genuine alpha coma:
- Post-hypoxia, brainstem lesions - generally poor outcome
- Drug overdose (rare, and often with better outcome)

Post-hypoxic alpha coma:
- Widespread
- Unreactive
**Alpha Coma**

- **57-year-old male**

<table>
<thead>
<tr>
<th>Channel</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$F_{P1}-F_3$</td>
<td></td>
</tr>
<tr>
<td>$F_3-C_3$</td>
<td></td>
</tr>
<tr>
<td>$C_3-P_3$</td>
<td></td>
</tr>
<tr>
<td>$P_3-O_1$</td>
<td></td>
</tr>
<tr>
<td>$F_{P2}-F_4$</td>
<td></td>
</tr>
<tr>
<td>$F_4-C_4$</td>
<td></td>
</tr>
<tr>
<td>$C_4-P_4$</td>
<td></td>
</tr>
<tr>
<td>$P_4-O_2$</td>
<td></td>
</tr>
</tbody>
</table>

Comatose
Autopsy – brain stem infarction

![Graph: EEG waveforms with annotations](image)
Summary - Coma EEG Pattern: Favorable Prognosis

- Reactivity
- Variability
- Improving EEG
Spontaneous Variability of the EEG in a Comatose Patient

52-year-old male

Cardiac arrest 6 hr prior to EEG

50 µV
1 sec
Reactivity of the EEG in a Comatose Patient

52-year-old male

Call patient’s name

Call patient’s name
Summary - Coma EEG Pattern: Unfavorable Prognosis

- No reactivity
- No variability
- Progressive suppression
Cerebral Death
Brain Death

- Brain death exists when there is no cerebral or brainstem function

- Electroencephalographic inactivity (EEG) is NOT synonymous with brain death
Role of EEG in Brain Death Evaluation

- EEG is supportive evidence
- Helpful when clinical exam is difficult or not definitive
- Easier than blood flow studies
- ECI is NOT synonymous with brain death

Recording the EEG:
- Demonstration of ECI is extremely difficult
- Requires well-trained, experienced, and persistent technologists
ACNS Guidelines: Cerebral Death

Minimal Requirements
• At least 8 scalp electrodes
• Interelectrode distances of at least 10 cm
• Impedance between 100 and 10,000 ohms
• Integrity of entire recording system must be tested
• Recording at a sensitivity of 2 µV
• High frequency filter should not be below 30 Hz and the low frequencies filter should not be above 1 Hz
• Demonstratable nonreactivity to somatosensory, visual, and auditory stimuli
Electrocerebral Inactivity

- No EEG activity over 2 microvolts
- No reactivity to strong and thorough tactile, auditory, visual stimuli
- Other causes (hypothermia, drug intoxication) must be excluded

• **When in doubt, repeat EEG**
Electrocerebral Inactivity

61-year-old male

Post cardiac arrest

1 sec 50 μV
ECI

30-year-old male

F<sub>P1</sub>-C<sub>3</sub>
C<sub>3</sub>-O<sub>1</sub>
F<sub>P2</sub>-C<sub>4</sub>
C<sub>4</sub>-O<sub>2</sub>
F<sub>P1</sub>-T<sub>3</sub>
T<sub>3</sub>-O<sub>1</sub>
F<sub>P2</sub>-T<sub>4</sub>
T<sub>4</sub>-O<sub>2</sub>
ECG

1 sec  20 µV
ECI Recording (Elimination of EMG Artifact)

23-year-old male

Following 20 mg Atracurium Besylate (Tracrium)

<table>
<thead>
<tr>
<th>Fp2-T4</th>
<th>T4-O2</th>
<th>F4-A1</th>
<th>C4-</th>
<th>O2-</th>
<th>Hand</th>
</tr>
</thead>
</table>

20 μV
Questions