The Ictal-Interictal Continuum

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Disclosures

• Demos Publishing – Royalties
Objectives

• Apply standardized critical care EEG terminology to identify ictal interictal continuum patterns

• Become familiar with common clinical correlates that are associated with IIC patterns

• Learn management strategies for how to approach patterns along the IIC

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Evolution in our Understanding of ICU EEG Patterns

Stage I: Definitions

Stage II: Clinical Correlates

Stage III: Management

2005

Seizures/Status

Periodic/Rhythmic

IIC

2021
The Critical Care EEG Spectrum

Sporadic epileptiform discharges

Any PD, SW or RDA (except GRDA)

GRDA

Stimulus-induced

Triphasic morphology

B(I)RDs

INTERICTAL

<0.5 Hz

1 Hz

2.5 Hz

3.0+ Hz

No “Plus”

“Plus” (+F, R, S)

Static

Fluctuating

Evolving

Ictal Interictal Continuum

Periodic and Rhythmic Patterns

Electrographic Seizure(s)

Response to Treatment Clinical Correlate

Electroclinical Seizure(s)

Haider, LaRoche, Hirsch 2018

GCSE

NCSE

NCSz
Periodic and Rhythmic Patterns: Association with Seizures

Rodriguez et al, JAMA Neurology, 2017
Ictal Interictal Continuum (IIC)  
ACNS Standardized Definition

1. Any PD or SW pattern $> 1.0$ Hz and $\leq 2.5$ Hz

2. Any PD or SW pattern $> 0.5$ Hz and $\leq 1$ Hz and **plus modifier or fluctuation**

3. LRDA $> 1$ Hz and **plus modifier or fluctuation**

❖ Pattern must be at least 10 seconds

❖ Does not qualify as electrographic seizure or status

❖ EEG Term, synonymous ‘possible’ seizure but **NOT** a clinical diagnosis

JCN Feb, 2021
71 yo found by family confused
Right Subdural Hematoma, INR 15
71 yo found by family confused
Right Subdural Hematoma, INR 15

2.5 Hz Lateralized Periodic Discharges, Plus Electrographic Status Epilepticus
>20% of 1 hour epoch
Few Hours Later...

Propofol, Levetiracetam
Few Hours Later...
Propofol, Levetiracetam
Few Hours Later...
Propofol, Levetiracetam

Lateralized Periodic Discharges, Evolving Electrographic Seizures
<20% of 1 hour epoch
More Propofol, Levetiracetam Add Valproate

Electrographic Status, Resolving Not IIC

Burst Suppression with Highly Epileptiform Bursts
1 – 1.5 Hz Lateralized Periodic Discharges < 10 seconds, not IIC
71 yo female GTC x 3
Intubated
Levetiracetam, Propofol
Right Gaze Deviation

1.5 Hz Lateralized Periodic Discharges
Electroclinical Status Epilepticus
Add Valproate
No Right Gaze Deviation
Levetiracetam, Propofol, Valproate

1.5 Hz Lateralized Spike Wave
IIC = Possible Electrographic Status
Add Lacosamide
Levetiracetam, Propofol, Valproate, Lacosamide

Clinical Scenario: Acute Neurological Injury, Clinical Seizures

< 1.0 Hz Lateralized Periodic Discharges Not IIC
67 yo female
Gradual right hemiparesis, “speech” problems

Angioplasty with thrombectomy
Day #2, somnolent, unable to extubate
Day #2, somnolent, unable to extubate
Day #2, somnolent, unable to extubate

Lateralized Periodic Discharges
Fluctuating vs. Evolving? > 2.5 Hz?
Start Propofol, Load Valproate

EEG Improvement
No Clinical Change
Next day, Off Propofol

Clinical Scenario: Acute neurological injury, No clinical seizures, Positive ASD Challenge = Electrographic seizures

Continued EEG Improvement
Definite Clinical Improvement
85 yo admitted for pneumonia
Day #3: Persistent confusion

1.5 – 2 Hz Generalized Periodic Discharges (GPDs)
Triphasic morphology
IIC = Possible Electrographic Status
5 min after Lorazepam 2 mg: Awake, Follows Commands

Clinical Scenario: Toxic metabolic disturbance, Positive treatment trial

Clinical and EEG improvement = Electroclinical Status Epilepticus
42 yo male with renal cell carcinoma and confusion

1.5 Hz Generalized Periodic Discharges
Triphasic Morphology
5 Minutes after Lorazepam 1 mg

Resolution of GPDs/ IIC

No Clinical Improvement,
Possible Electrographic Status
1 hour after Lorazepam, IIC Returns

Add Fosphenytoin
During Dialysis, 1 Hour after Fosphenytoin

Resolution of GPDs/IIC
No Clinical Improvement,
Possible Electrographic Status
Response to anticonvulsant trials in patients with triphasic waves

- 3 institutions (Yale, Columbia, MGH), retrospective, N=64
  - 72% had metabolic derangement or infection
- Response: resolution of EEG and unequivocal improvement in encephalopathy
  - immediate (<2 hours), delayed or possible
- ASD: Lorazepam, levetiracetam, phenytoin

Benzo trial: Positive in 10/53 (19%, all immediate)

Non benzo ASDs: Positive in 19/45 (42%: 7% immediate, 20% delayed, 15% possible)
  - Overall 34% definite response and 11% possible
  - No difference in metabolic status of responders vs non-responders

O’Rourke et al. Neurocrit Care 2015
57 yo comatose female
Influenza, Pseudomonas: Cefepime

1.2 Hz Generalized Periodic Discharges, Triphasic IIC
Cefepime Stopped

IIC resolved without treatment
Toxic metabolic/ Cefepime
68 yo with Crohn’s disease admitted for bowel perforation, EEG for persistent confusion

2.56 Hz Lateralized Periodic Discharges
Electrographic Status Epilepticus
Lorazepam 1 mg - “I had an aneurysm several years ago and seizures”

EEG and Clinical Improvement
Electroclinical Status Epilepticus
Lacosamide load
1 Hour Later...

1.5 to 2 Hz Lateralized Periodic Discharges
IIC = Possible Electrographic Status Epilepticus

Lorazepam 1 mg
Lorazepam 1 mg - Obtunded

Possible Electroclinical Status Epilepticus
EEG improvement without clinical change
1 Hour Later...

2.51 Hz Lateralized Periodic Discharges
Electrographic Status Epilepticus

Fosphenytoin Load
Fosphenytoin Load

EEG Improvement following anti seizure medication
Still very somnolent
Possible Electroclinical Status Epilepticus
Next Day

Persistent EEG Improvement
Arousable, follows some commands
Electroclinical Status Epilepticus – Delayed Clinical
Beware of the Self-Fulfilling Prophecy

- Patient is confused → EEG shows IIC
- Lorazepam treatment trial → EEG transiently ‘improves’ but patient more somnolent
- Patient loaded with non sedating ASD → EEG unchanged, still IIC, patient still very somnolent, confused
- Patient loaded with another non sedating ASD → EEG still IIC, patient still very somnolent, confused
- Patient transferred to ICU for intubation, start anesthetic → EEG burst suppression
55 yo with Posterior Reversible Encephalopathy Syndrome and Confusion

1 Hz Lateralized Periodic Discharges
Not IIC
### 2HELP52B - Seizure risk score and time based stratification

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
</tr>
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<tbody>
<tr>
<td>2H: &gt; 2Hz pattern (except GRDA)</td>
<td>1</td>
</tr>
<tr>
<td>E: Epileptiform discharges, sporadic</td>
<td>1</td>
</tr>
<tr>
<td>L: Lateralized (LPD, BIPD, LRDA)</td>
<td>1</td>
</tr>
<tr>
<td>P: Plus features</td>
<td>1</td>
</tr>
<tr>
<td>S: history of Seizure</td>
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<tr>
<td>2B: Brief rhythmic discharges</td>
<td>2</td>
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### Total Score | Seizure Risk | Recommended EEG Duration
---|---|---
0 (Low) | 3.1% | 1 Hour
1 (Medium) | 12.0% | 12 Hours
≥2 (High) | 26.6% | At least 24 Hours

*Score based on 1st hour of EEG

Struck et al, JAMA Neurology, Jan 2020

Based on retrospective database of >2000 pts across 6 centers
55 yo with Posterior Reversible Encephalopathy Syndrome and Confusion

1 Hz Lateralized Periodic Discharges
Not IIC

No Acute Treatment but continue EEG

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55 yo with Posterior Reversible Encephalopathy Syndrome and Confusion

58 minutes after onset of the recording
55 yo with Posterior Reversible Encephalopathy Syndrome and Confusion
55 yo with Posterior Reversible Encephalopathy Syndrome and Confusion
55 yo with Posterior Reversible Encephalopathy Syndrome and Confusion

Electrographic Seizure Evolution
71 yo GCSE, Lorazepam, Levetiracetam
CT unremarkable, CSF Normal

<0.5 Hz Lateralized Periodic Discharges, Plus Not IIC
71 yo GCSE, Lorazepam, Levetiracetam
CT unremarkable, CSF Normal

Brief Ictal-Appearing Rhythmic Discharges, (BIRDs)
Not IIC
71 yo GCSE, Lorazepam, Levetiracetam
CT unremarkable, CSF Normal

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2HELP2S2B- 5
Continue cEEG at least 24 Hours
44 yo female, intubated for drug overdose
Day #3 Weaning Propofol, still confused

2 Hz Generalized Rhythmic Delta Activity, Plus Sharp
NOT IIC, 2HELPS2B= 0
Next day, propofol off.....transferred out of ICU

GRDA resolved
Anesthetic Withdrawal
Approach to Initial Management (not always treatment)

• Review History
  – Prior seizures
  – Acute focal lesion
  – Toxic/metabolic dysfunction

• Medication List
  – Look for medications associated with periodic patterns (GPDs) Cefepime, Baclofen, Lithium

• Exam
  – Assess mental status and look for subtle clinical correlates

• Talk to Clinical Team
  – Understand treatment goals, co-morbid conditions
A Continuum along the Continuum?

Not Ictal

Generalized

Toxic Metabolic Disturbance

Anesthetic Withdrawal

Ictal

Focal

Acute Neurological Injury

History of Seizures
Treatment Trial Guidelines

• Initial bedside exam
  – Look for clinical correlate, establish baseline MS, evaluate airway

• Sedating ASD
  – Use small, incremental doses

• Non Sedating ASD
  – Use full loading dose

• Intermittent or Stimulation induced patterns
  – Must time the treatment trial

• Positive Treatment Trial
  – EEG and Clinical improvement required
Treatment Trial in Intubated Patients

• Assess baseline mental status and sedation level (if any)
• If not on sedation, consider a sedating ASD
  – Lorazepam, Midazolam, Propofol
• If on sedation, consider increasing dose vs. non-sedating ASD

• May have to rely on EEG changes alone and ancillary measures
Beyond Treatment Trials...

• **Imaging**
  • Perfusion: SPECT, **CT perfusion**
  • Functional: FDG-PET, fMRI

• **Multimodal Monitoring**
  • Assess metabolic impact
  • ICP, Tissue oxygenation, Microdialysis, serial NSE
Summary

• Patient history and clinical context is just as important as the EEG findings

• Talk with the clinical team, frequently
  – Pros vs Cons of more aggressive treatment
  – Be aware of end of life decision making

• Anti seizure medications may not work immediately

• Experience helps
  – IIC Symposium Saturday, 9:00-1030