• **Thanks you to**
  – Dr. Lawrence J. Hirsch, M.D.
  – Susan T. Herman, M.D.
  – Jed A. Hartings, Ph.D.
  – Thomas P. Bleck MD
  – Denis Azzopardi

DID YOU INTEND THE PRESENTATION TO BE INCOMPREHENSIBLE, OR DO YOU HAVE SOME SORT OF RARE “POWER-POINT” DISABILITY?
Why do we need ICU-EEG?

Residual electrographic SE after control of visible SE in VACSP 265

• 130 overt GCSE patients in whom EEG monitoring was begun within 30 minutes of start of treatment
• 26/130 (20%) remained in electrographic SE after motor movements had stopped (twitchless electrical activity)

Faught *Epilepsia* 1998
Persistent nonconvulsive SE after the control of convulsive SE

- 52% had no after-SE ictal discharges
  - EEG showed generalized slowing, attenuation, PLEDS, focal slowing, and/or burst suppression
- The remaining 48% demonstrated persistent electrographic seizures
  - over 14% manifested NCSE, predominantly CPSE

DeLorenzo et al Epilepsia 1998;39:833-40

Unsuspected NCSE

- 8% of a consecutive series of patients referred for EEG because of coma had NCSE

Continuous EEG Monitoring in the Intensive Care Unit: An Overview

Lawrence J. Hirsch

Abstract: Due to technological advances, it is now feasible to record continuous digital EEG (CEEG), with or without video, in critically ill patients and review recordings remotely. Nonconvulsive seizures (NCSNs) are more common than previously recognized and are associated with worse outcome. The majority of seizures in ICU patients are nonconvulsive and will be missed without CEEG. Factors associated with an increased risk for NCSNs include coma, prior clinical seizures, CNS infection, brain tumor, recent neurosurgery, and periodic epileptiform discharges. In addition to detecting seizures, CEEG is also useful for characterizing paroxysmal spells such as posturing or autonomic changes, detecting ischemia, assessing level of sedation, following long-term EEG trends, and prognosticating. Most NCSNs will be detected in the first 24 hours of CEEG in comatose patients, but longer recording periods may be required in comatose patients or in those with periodic epileptiform discharges. EEG patterns in encephalopathic or comatose patients are often equivocal. How aggressively to treat NCSNs and equivocal EEG patterns in these patients is unclear and requires further research. Real-time detection of ischemia at a reversible stage is technologically feasible with CEEG and should be developed into a practical form for prevention of in-hospital infarction in the near future.

Key Words: Continuous EEG monitoring, Critically ill, Intensive care unit, Nonconvulsive seizures, Seizure detection, Ischemia detection.

The ACNS Subcommittee on Research Terminology for Continuous EEG Monitoring: Proposed Standardized Terminology for Rhythmic and Periodic EEG Patterns Encountered in Critically Ill Patients

Lawrence J. Hirsch,* Richard P. Brenner,† Frank W. Dridlake,‡ Elson So,§ Peter W. Kaplan,¶ Kenneth G. Jordan,‖ Susan T. Herman,§ Suzette M. LaRoche,** Bryan Young,†‖ Thomas P. Bleck,†‡ Mark L. Scheuer,‖ and Ronald G. Emerson*

Journal of Clinical Neurophysiology • Volume 22, Number 2, April 2005
FIGURE 1: SI-GRDA: Stimulus-induced generalized rhythmic delta activity. In this case, the pattern was elicited by suctioning the patient.

TABLE 1. Examples of Corresponding New Terms for Older Terms

<table>
<thead>
<tr>
<th>Old Term</th>
<th>New Term*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triphasic waves, most of record</td>
<td>Continuous 2/sec GPDs (with triphasic morphology can be added)</td>
</tr>
<tr>
<td>PLEDS</td>
<td>LPDs</td>
</tr>
<tr>
<td>BIPLEDs</td>
<td>BIPDs</td>
</tr>
<tr>
<td>GPEDs/PEDs</td>
<td>GPDs</td>
</tr>
<tr>
<td>FIRDA</td>
<td>Occasional brief 2/sec GRDA (if 1–10% of record); frontally predominant can be added</td>
</tr>
<tr>
<td>PLEDS+</td>
<td>LPDs+</td>
</tr>
<tr>
<td>SIRPDs w/focal evolving RDA</td>
<td>SI-Evolving LRDA</td>
</tr>
<tr>
<td>Lateralized seizure, delta frequency</td>
<td>Evolving LRDA</td>
</tr>
<tr>
<td>Semirhythmic delta</td>
<td>Quasi-RDA</td>
</tr>
</tbody>
</table>

*Some could have alternative new terms depending on the exact pattern.
SIRPDs, stimulus-induced rhythmic, periodic, or ictal discharges.
Continuous EEG in ICU

- EEG recorded continuously for hours to days
- Raw EEG
- Quantitative graphical displays

- Nonconvulsive seizure (NCS) and nonconvulsive status epilepticus (NCSE)
Continuous EEG in ICU

• EEG recorded continuously for hours to days
• Raw EEG
• Quantitative graphical displays
  – Which quantitative displays
  – How many trends
• Video
• Emerging VS Standard Techniques

Electrodes

• Disk: Plastic silver-chloride or metal
  – Imaging compatibility
  – Infection control
• Needle
  – Appropriate for some emergency situations
  – Not appropriate for long-term recordings
• Subdermal wire electrodes
• Apply with collodion, EC2 paste
• Maintenance every 24 hrs
• Intracranial electrodes
  – Mini-depths, ? Subdural strips
Electrode Location and Number

- International 10-20 system
- Minimum of 8 electrodes
- 16 or more electrodes optimal

- Inadequate spatial sampling
- Inability to distinguish artifact from cerebral activity

Limited Montages

<table>
<thead>
<tr>
<th></th>
<th>subhairline (1)</th>
<th>Hairline(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>70 patients</td>
<td>120</td>
</tr>
<tr>
<td>Methods</td>
<td>Commercial limited EEG</td>
<td>Reformatted from standard 10-20 digital</td>
</tr>
<tr>
<td>Channels</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Duration</td>
<td>24 hour</td>
<td>2-3 min samples</td>
</tr>
<tr>
<td>Seizures</td>
<td>Sensitivity 68%</td>
<td>72%</td>
</tr>
<tr>
<td></td>
<td>Specificity 98%</td>
<td>92%</td>
</tr>
<tr>
<td>PLEDs</td>
<td>Sensitivity 39%</td>
<td>54%</td>
</tr>
<tr>
<td></td>
<td>Specificity 92%</td>
<td>97%</td>
</tr>
</tbody>
</table>

1. Young GB et al. neurocrit Care 2009
2. Kolls BJ. Husain AM. Epilepsia 2007
**Video / Audio**

- **Strongly recommended**
  - Correlate clinical with EEG features
  - Avoid misinterpretation of artifacts

- **Optimal recoding requires both fixed wide-angle cameras and high resolution color cameras with remote zoom and pan-tilt functions**
  - Portability
  - Cost
  - Amount of data generated / network bandwidth

**Review**

- **Frequent enough to influence clinical management**
- **At least twice daily**
  - May occasionally require continuous or frequent review until patient stabilized
- **Written reports daily**
  - Interim verbal reports to clinical team as needed
- **Remote review should be available**

- **Optimal**
  - Continuous review of raw EEG, quantitative EEG and video
  - Trained personnel
Seizure Detection Algorithms

• Epilepsy monitoring
  – Sensitivity .33-.93
  – False positive rates: .11-3.1 per hour
  – Compared to human: sensitivity 92%. FP 0.1/h
• Utility in ICU has not been evaluated
  – Seizure patterns very different from those in epilepsy patients
  – Frequent incorrect notifications problematic when reviewed by inexpert staff
  – May need to record entire duration of event rather than just start of seizure


Trends

• Quantitative graphical displays of EEG
  – Fast Fourier transformation of EEG data
  – Color spectrograms
  – Hidden line compressed spectral arrays
  – Displays of total power in certain bands to broader EEG power
  – Envelope trend
  – Amplitude-integrated EEG
Trends

• No studies on sensitivity specificity for seizure detection in ICU
• Nearly limitless combinations of trend type, electrodes / brain regions, and time displays
  – Difficult to standardize
• Use of quantitative trends is encouraged
  – May detect gradual or subtle changes that are not visible with review of raw EEG
• Can not used alone for seizure or ischemia detection
  – Adjunct to review of raw EEG

Interrater Reliability

• Interrater reliability for seizures in ICU population (1)
  – 90 10s epochs from 23 comatose patients
  – 9 readers kappa
    • Experienced 0.5
• Research terminology (2)
  – 5 readers; 58 EEG samples from 11 SAH patients
  – Moderate agreement for main terms; others slight to fair
  – Agreement lower with longer EEG segments (20 min)
Diagnostic Accuracy

- How test compares to “gold standard” reference test
- No other diagnostic test comparison of CEEG results
  - Compare to shorter EEGs

<table>
<thead>
<tr>
<th>Recurrent or continuous (&gt;30 min) ictal discharges, frequencies &gt;=3Hz</th>
<th>Continuous ictal discharges, frequencies &lt; 3Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetitive or rhythmic spikes, sharp waves, rhythmic waveforms, frequency 3-20Hz</td>
<td>Repetitive or rhythmic spikes, sharp waves, rhythmic waveforms</td>
</tr>
<tr>
<td>Duration &gt; 10 sec</td>
<td>Gradual evolution in voltage, frequency, and/or field</td>
</tr>
<tr>
<td>Paroxysmal change from baseline</td>
<td>Significant improvement in clinical state or EEG after IV AED</td>
</tr>
<tr>
<td>Evolution in amplitude, frequency, and/or field</td>
<td>+ / - Postictal slowing or attenuation</td>
</tr>
<tr>
<td>+ / - Postictal slowing or attenuation</td>
<td>Yung GB et al. Neurology 1996;47:8389</td>
</tr>
</tbody>
</table>

Diagnostic Impact

- Heterogeneous patient populations
  - Adults
  - Children
  - Neonates
  - Neuro ICU vs. general ICU
- Retrospective studies
  - Few centers with non-generaizable patient groups
  - No predetermined inclusion / exclusion criteria
  - Selection bias
    - Across and even within centers
Indications for CEEG

• Detection of subclinical seizures
  – Fluctuating mental status
  – Unexplained alteration of mental status
  – Acute supratentorial brain injury with altered mental status
  – After convulsive status epilepticus
• Characterization of spells
  – Episodic posturing, other paroxysmal movements
  – Subtle twitching, nystagmus, eye deviation, chewing
  – Paroxysmal autonomic spells including tachycardia
• Monitoring treatment efficacy in NCSE and refractory SE

Therapeutic Impact

• No prospective studies or pertinent
  – Seizure cortical
  – Impact on EEG features
  – Outcome
  – Adverse effects
• High mortality rates even with aggressive therapy
• Increased mortality in elderly with NCSE treated with benzodiazepines
conclusions

• Wide variability in practice of CEEG
• Optimal practices will change as technology evolves
• No evidence that treatment of detected seizures is effective or impacts outcome

• Cannot assess impact of seizures and treatment on outcome until can be rapidly and rapidly and reliably detected

CEEG:
The Cutting Edge and Beyond

December 8, 2009

Lawrence J. Hirsch, MD
Columbia University
New York, NY

American Epilepsy Society Annual Meeting
The era of NEUROTELEMETRY is here --almost

- Seizures
- Ischemia
- Hydrocophalus
- Hemorrhalus
- Hypotension/hypoxia/Co2 retention/sepsis
- Alarms feasible though not easy
  - Artifact detection and rejection in place
  - 24 hour EEG techs in place (but not ones continuously)
  - Networking in place
  - Imaging compatible electrodes available-invisible on CT and MR (?angio)-but expensive
CEEG IN THE Medical ICU
Oddo M, et al, Care Med 2009

• 201 patients 2004-2007
  – Mean of 3 days of ceeg
  – 60% sepsis, 48% comatose
• 22% had seizures or PEDs
• Seizures in 21
  – 67% patents with 52% had nonconv. only
• PEDs in 34

CEEG IN THE MICU, cont’d
Oddo M, et al, Care Med 2009

• Independent predictors of worse outcome
  – Electrographic Szs
  – PEDs
  – Each assoc’d with double the rate of poor outcome

• Sepsis subgroup: 31% had sis or PEDs
  – In multivariate analysis, presence of Sis or PEDs remained highly significant predictor of worse outcome (O.R. 10, p<0.001)
Intracortical EEG (mini-depth recordings) in acute brain injury

MCAo model of non-convulsive seizures

Animals subjected to permanent or temporary Middle Cerebral Artery Occlusion

Referential EEG recordings from 10 epidural skull screw electrodes

Continuous recordings obtained prior to and 24 h following MCAo in freely behaving animals

Seizures are Generalized, Episodic, and Non-Convulsive

Spreading depression in rabbit cortex (Leao, 1944)

Spreading Depression of Activity in the Cerebral Cortex

Adriano A. P. Leao
Department of Physiology, Harvard Medical School, Boston, Massachusetts

(Received for publication August 34, 1944)
What is Spreading Depression?

Sustained depolarization

Spike and wave seizure

200 μV

2 min

ECOG

DC potential

Treatments which inhibit PIDs are also neuroprotective

MK-801

Hypothermia

Mies et al., Neureport 4:709, 1993

Chen et al., JCBPM 13:389, 1993
Co-Operative Study on Brain Injury Depolarizations

Methods

- Subdural electrode strip placed on peri-lesion cortex during neurosurgery
- Continuous electrocorticography (ECoG) during neurointensive care
Identification of Spreading Depressions

‘Inverse’ coupling in the human brain: spreading ischemia
Cortical mini-depth electrode: 70 yo, SAH, R F depth

73. large R MCA infarct, hypothermia, R frontal + mini-depth
Starting 9:45 pm, discontinuity in depth

6:20 am: periodic delta waves in depth
Summary of Findings:

Intracortical EEG (ICE) in Acute brain Injury
Waziri A. Classen J. Connolly S. et al; Ann Neurol 2009

- 10/14 patients had seizure on the mini-depth
- 6/10 never had scalp EEG correlate, 2 showed non-ictal appearing rhythmic delta on scalp, and 2 showed scalp EEG correlate on occasion only.
- Some but not all seizure/PEDs showed corresponding microdialysis changes
If CEEG were readily available 24 hours/day for all patents, and was interpreted in real-time by an expert. Remote reader, I would order CEEG:

1. On every patient in the ICU
2. On every patient with impaired mental status in the ICU
3. On many more patients than I do now
4. On a few more patients than I do now
5. On some patients, but the same number of patients as I do now
6. Never, as I’m not convinced of the clinical utility

Conclusions, I of III

- Standard nomenclature & research consortium
- More practical electrodes, QEEG software, remote access and alarms
- Individualized, brain physiology-driven making
- Invasive EEG recordings are raising more fascinating questions
  - Theory: multimodal mini-seizures, non-synchronous
  - Metabolic effects
  - Peri-injury depolarizations