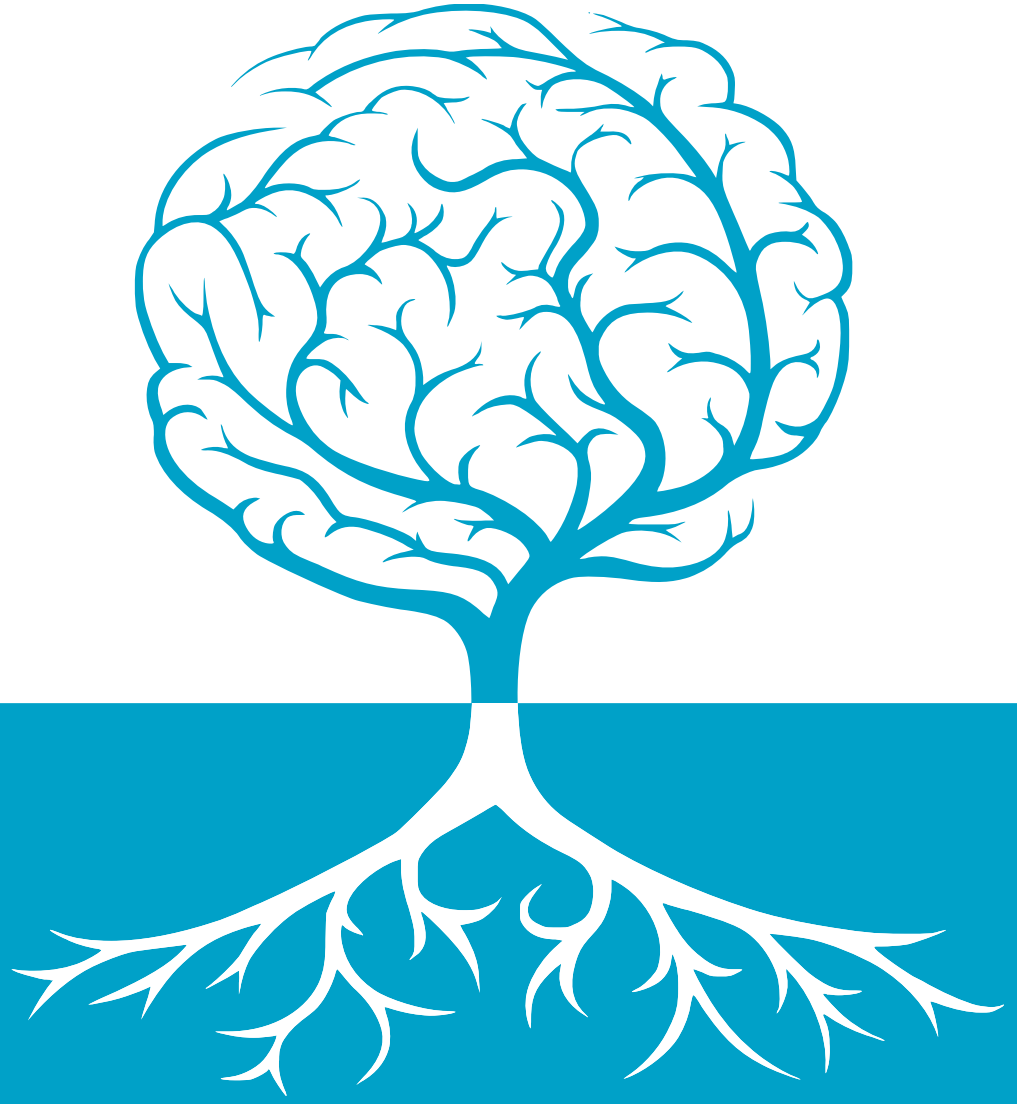


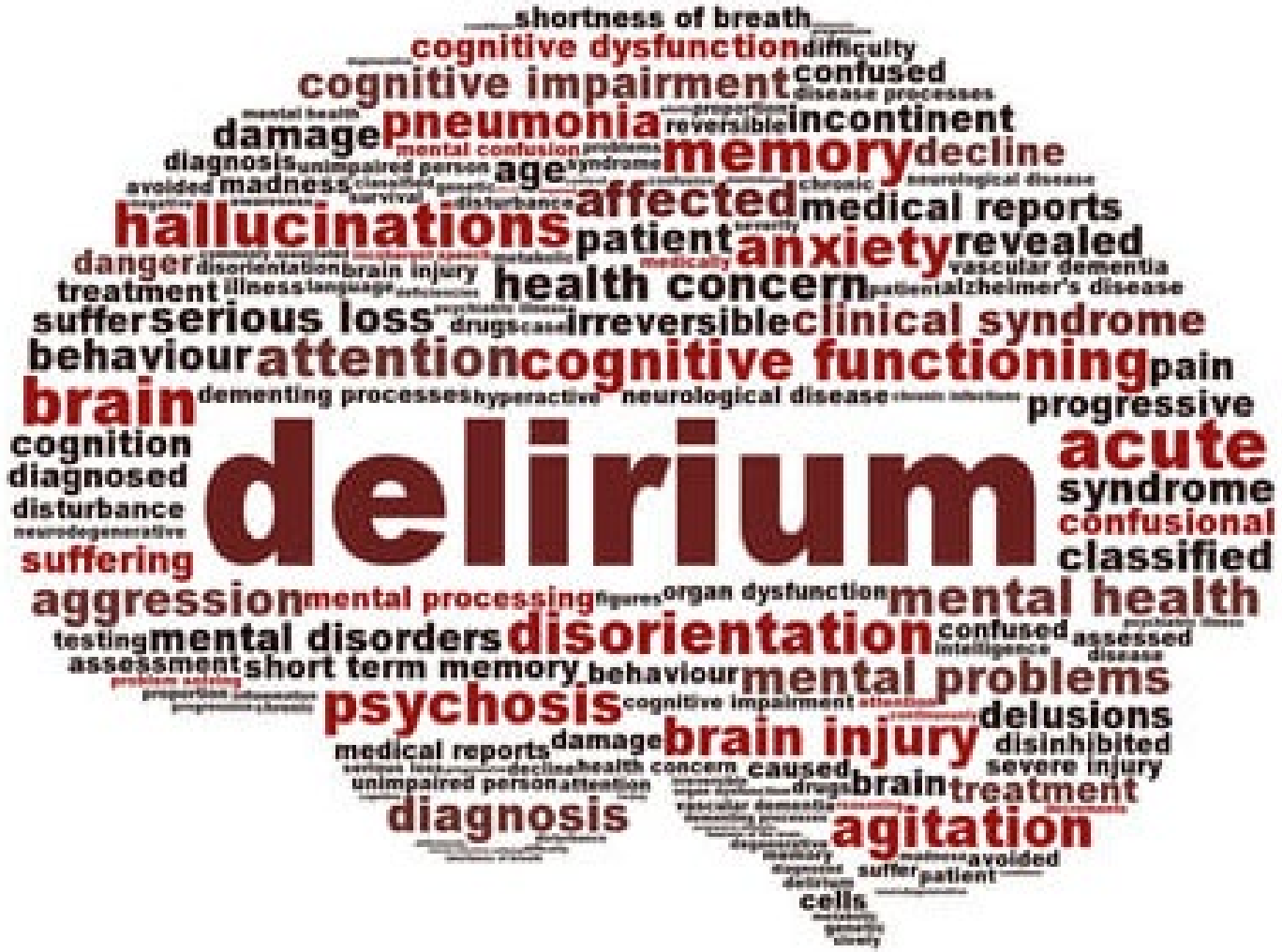
EEG as a Biomarker Window into Delirium

Eyal Y. Kimchi, MD, PhD

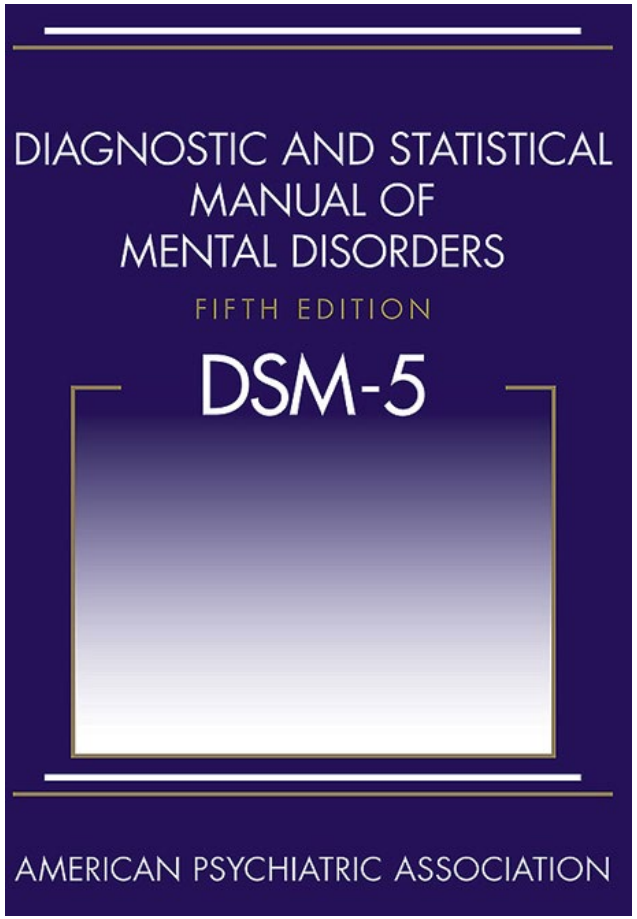
Northwestern University

Department of Neurology

Delirium is a Complex Mind/Brain Syndrome



How do we identify delirium?



Confusion Assessment Method (CAM)

1. Acute onset of mental status changes or a fluctuating course

and

2. Inattention

and

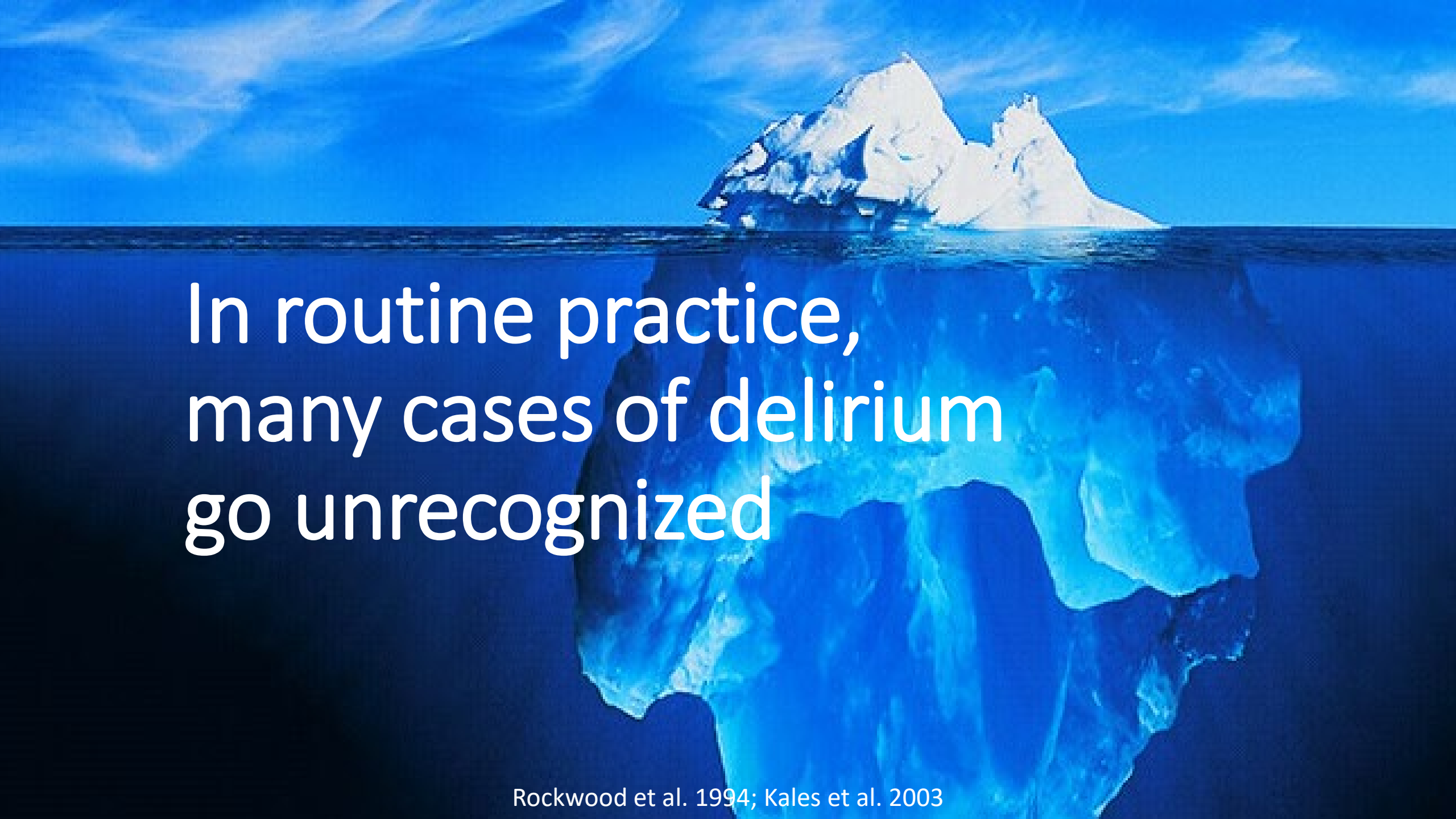
3. Disorganized thinking

or

4. Altered level of conciousness

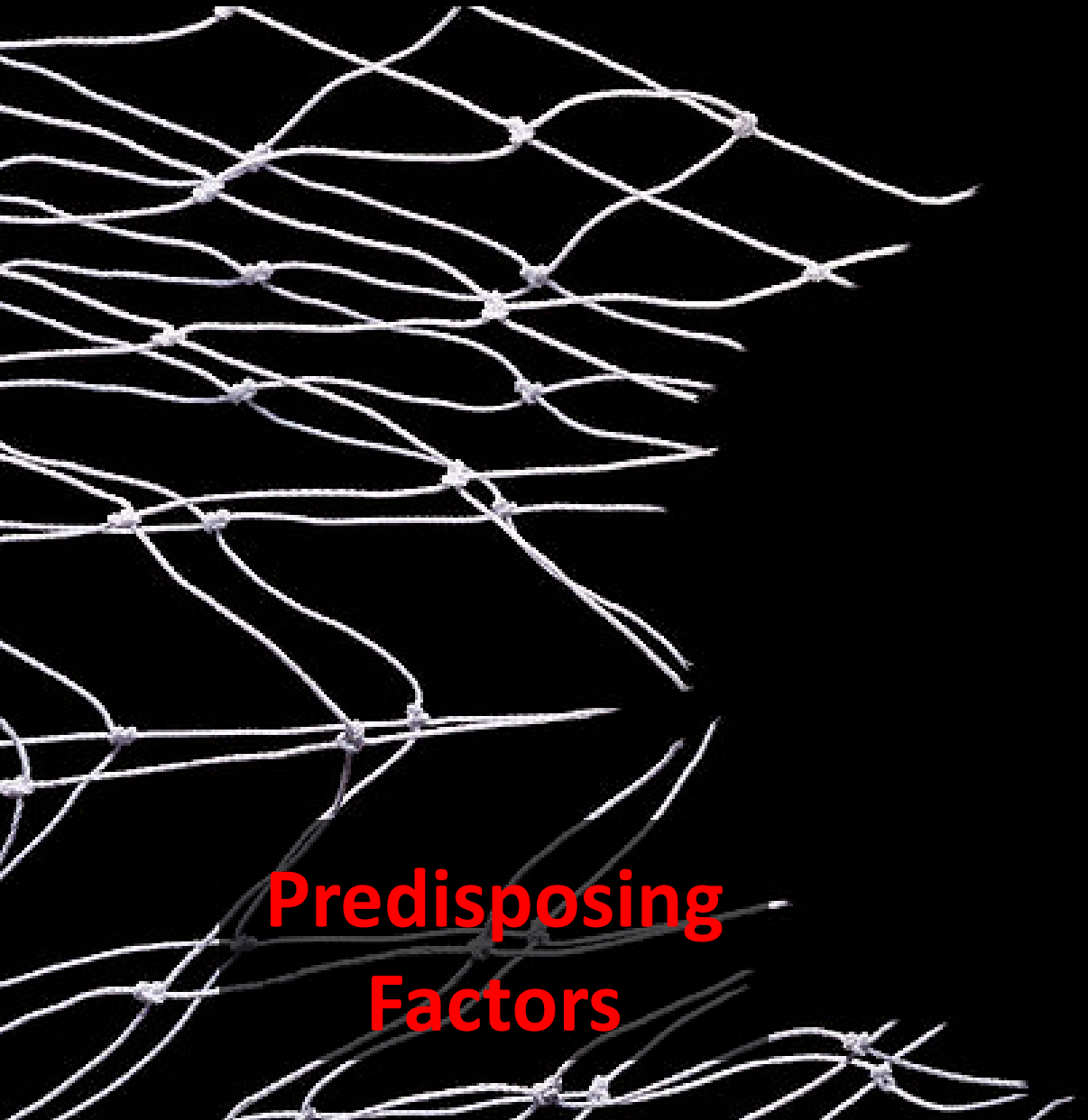
= Delirium

DSM-5; Inouye et al. Ann Intern Med. 1990



Rockwood et al. 1994; Kales et al. 2003

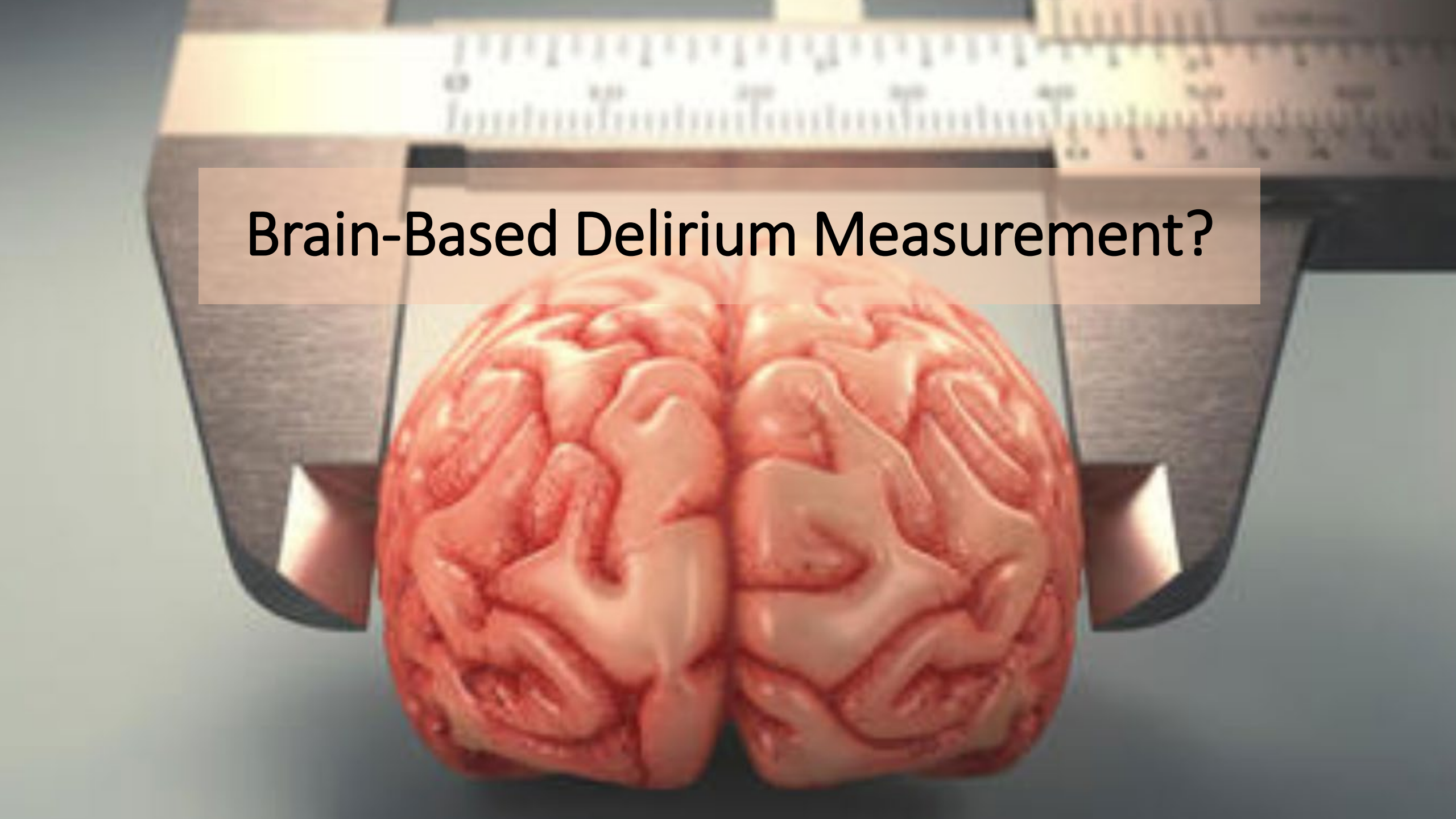
Delirium is Complex, but not Random



Predisposing Factors

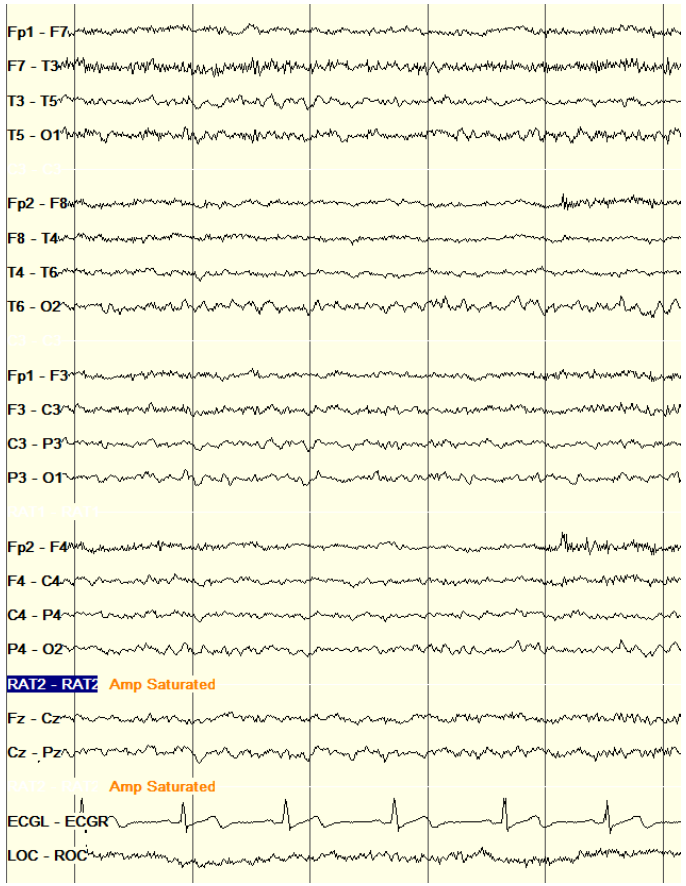
Precipitating Factors

Brain-Based Delirium Measurement?

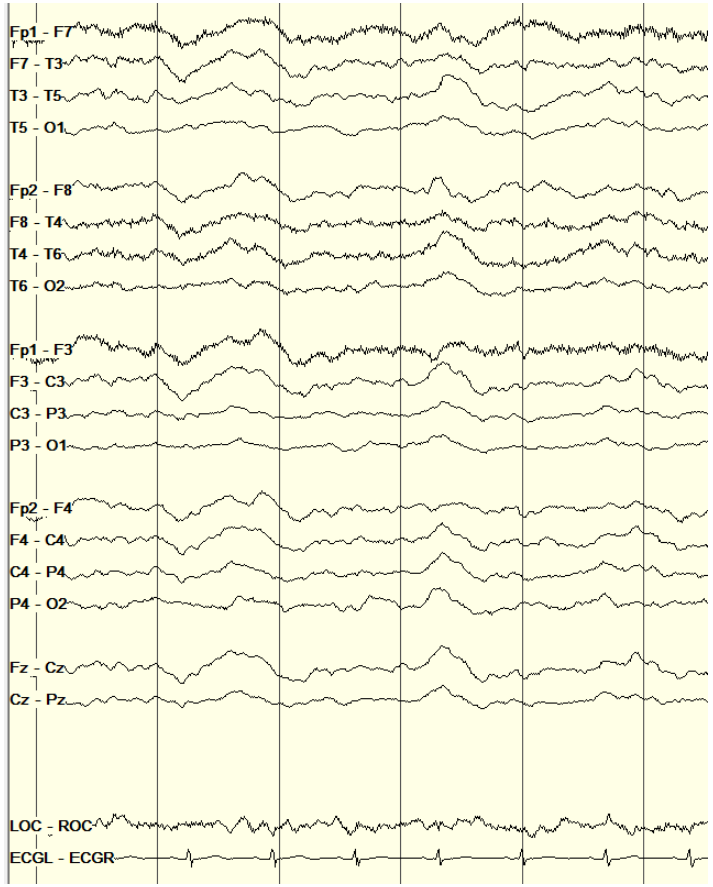


EEG as a Biomarker of Delirium

Patient without Delirium, Normal EEG

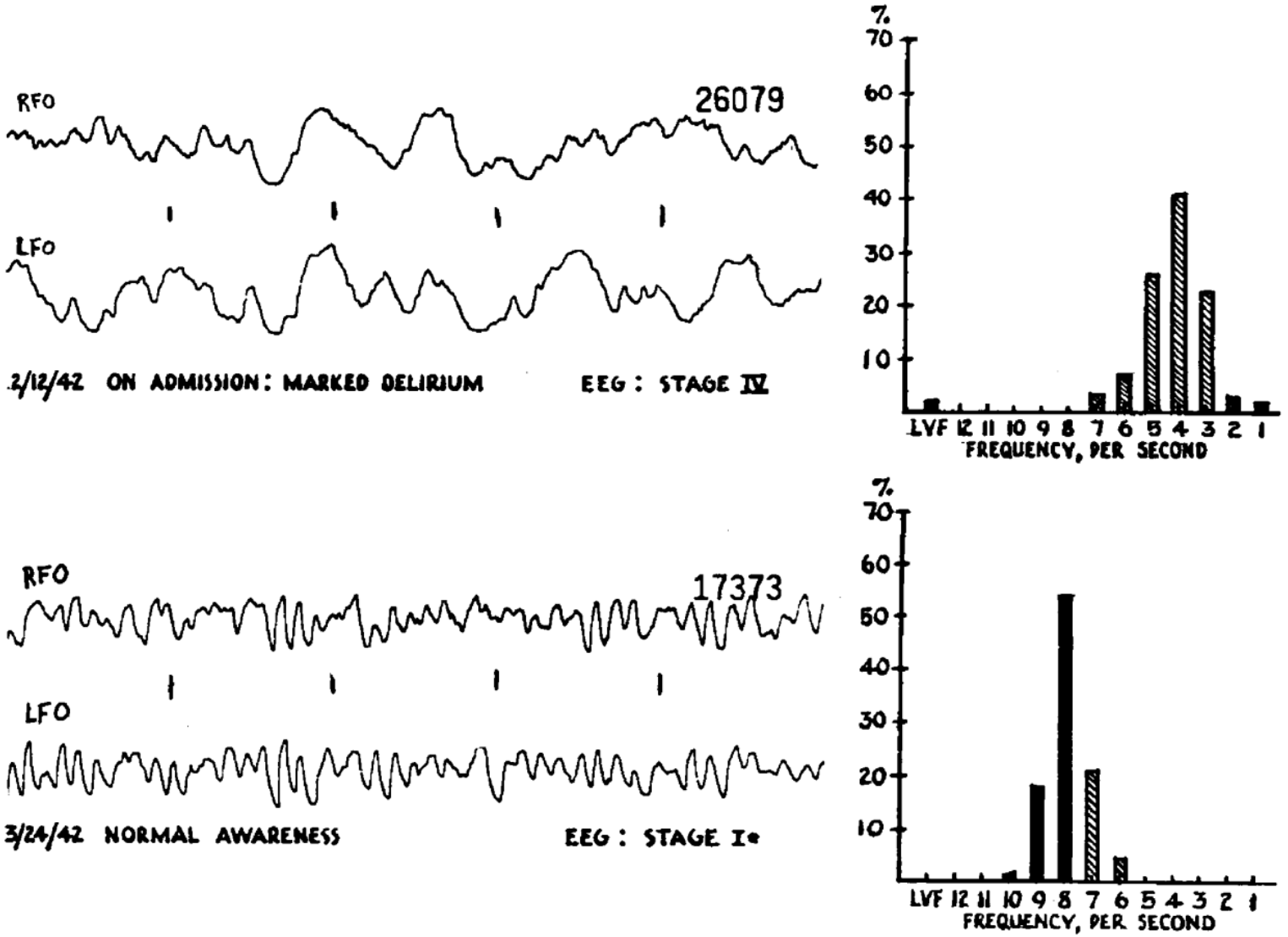


Patient with Delirium, EEG Slowing



Kimchi, [Clinical Samples], 2018

EEG as a Biomarker of Delirium Severity

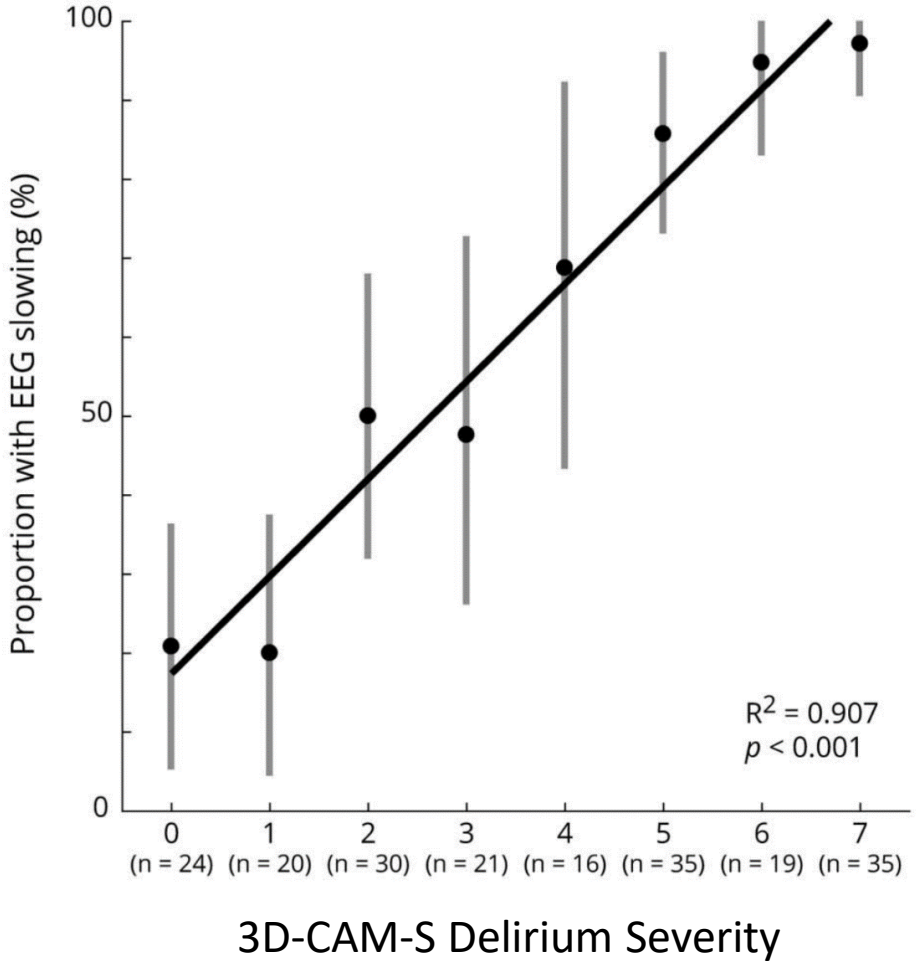


Romano & Engel, Arch Neuro Psych, 1944

Clinical EEG Slowing Correlates with Delirium Severity

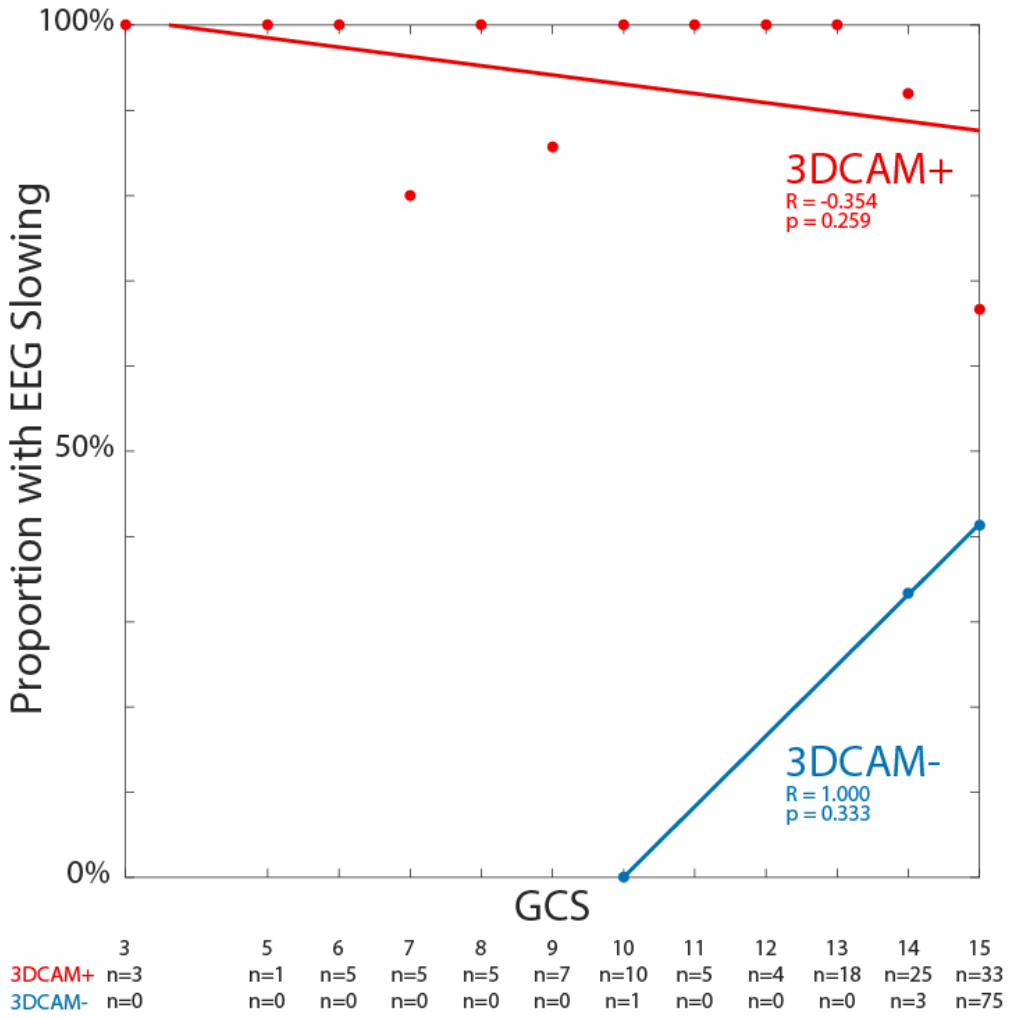
200 patients receiving EEG for Altered Mental Status

Generalized theta or delta slowing was associated with delirium (OR 10.3, 95% CI 5.3–20.1)

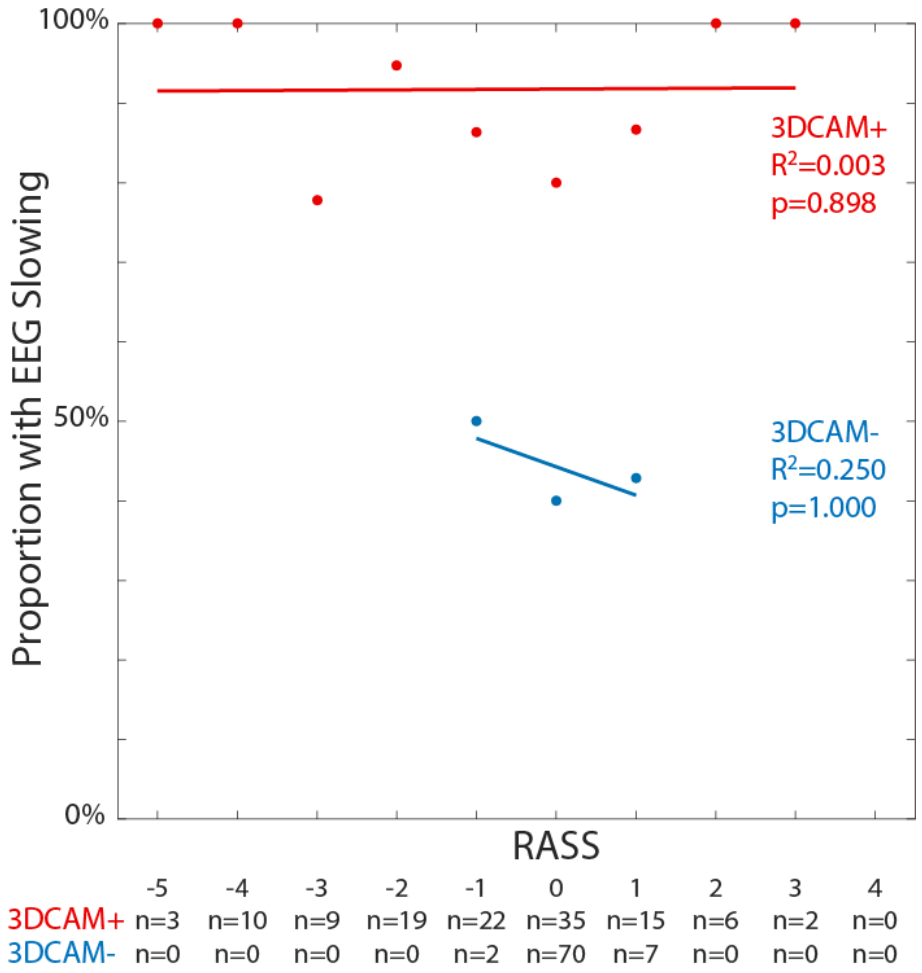


Kimchi et al. Neurology. 2019

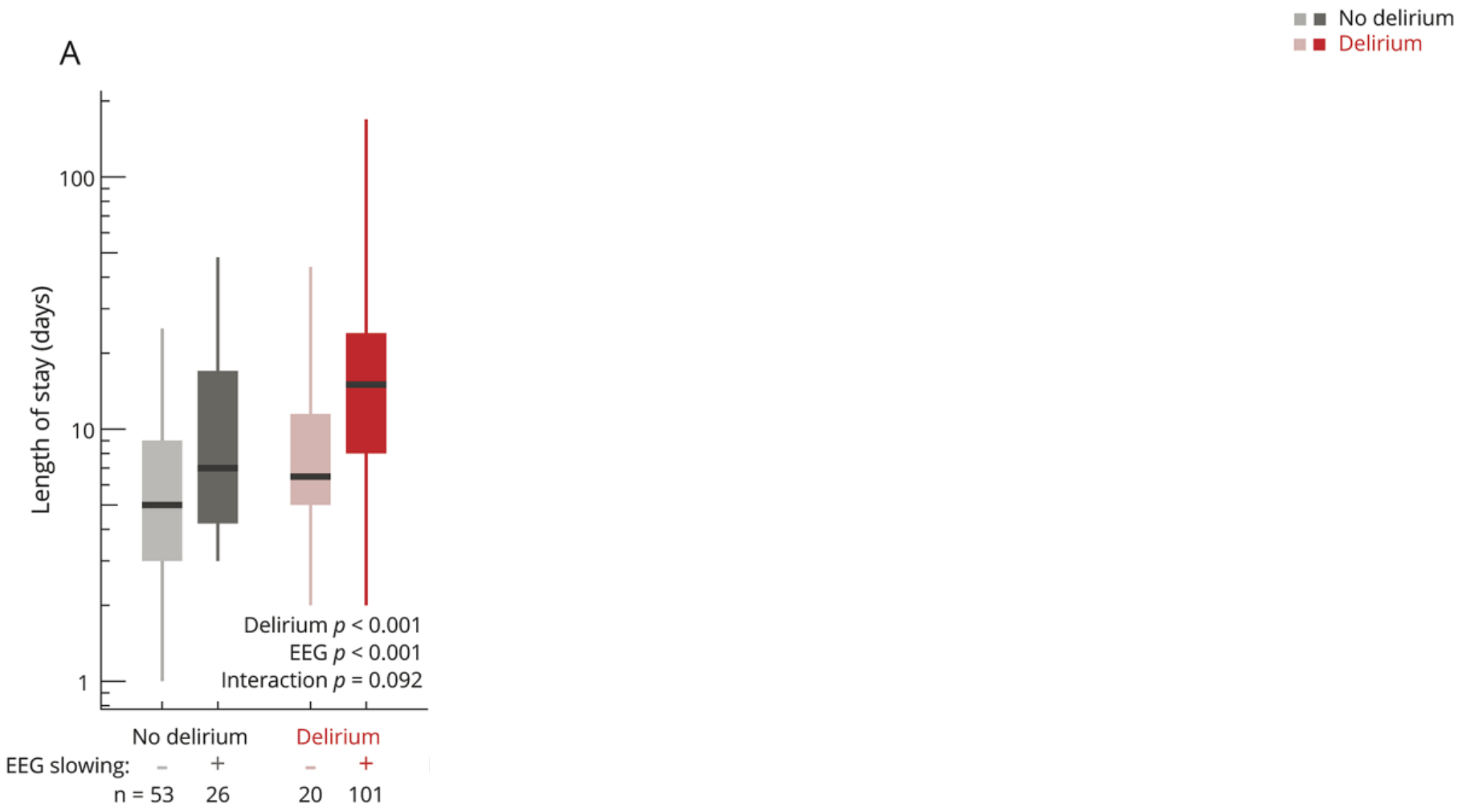
EEG Slowing reflects Delirium more than Arousal



EEG Slowing is present in patients with Hypoactive and Hyperactive Delirium



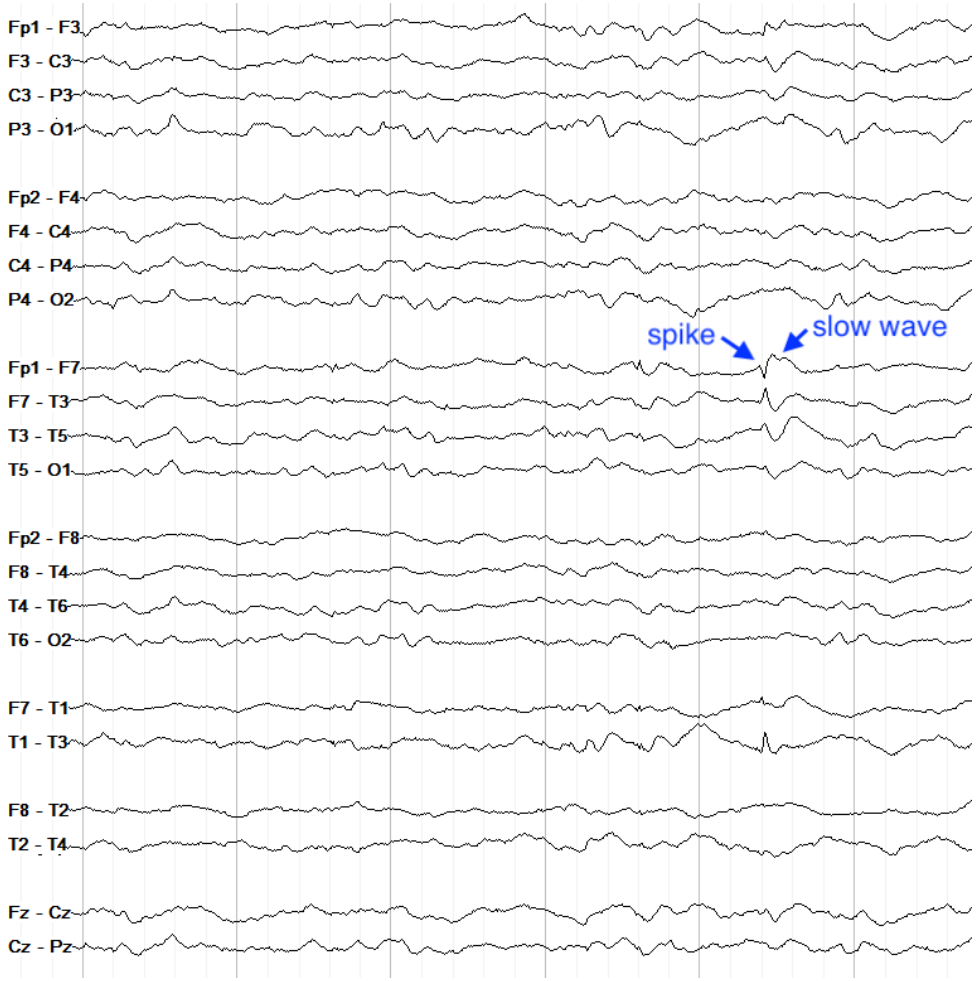
EEG Slowing Correlates with Clinical Outcomes



Kimchi et al. Neurology. 2019


What about EEG features other than slowing?

Routine Clinical EEG Interpretation



Background Rhythms (Sleep)

- Posterior dominant rhythm
- Theta slowing
- Delta slowing

Discharges (Epilepsy)

- Epileptiform discharges
- Periodic discharges
- Triphasic waves

Visual EEG-Based Grading of Delirium Severity

404 patients receiving EEG for Altered Mental Status

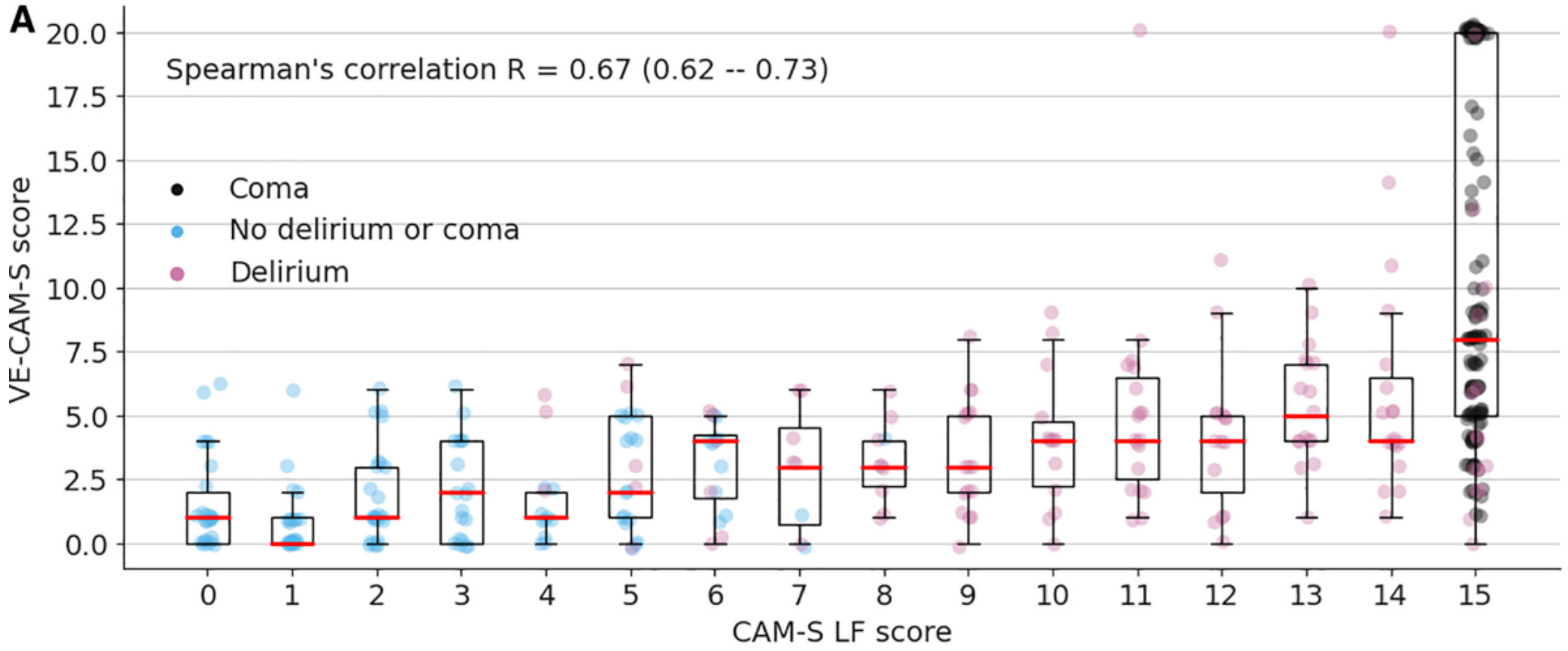
- 33% without delirium or coma
- 35% with delirium (CAM-LF)
- 32% with coma (RASS -4 or -5)

Constrained ElasticNet regression to predict determined CAM-S-LF (cross validated approach)

Visual EEG-Based Grading of Delirium Severity (VE-CAM-S)

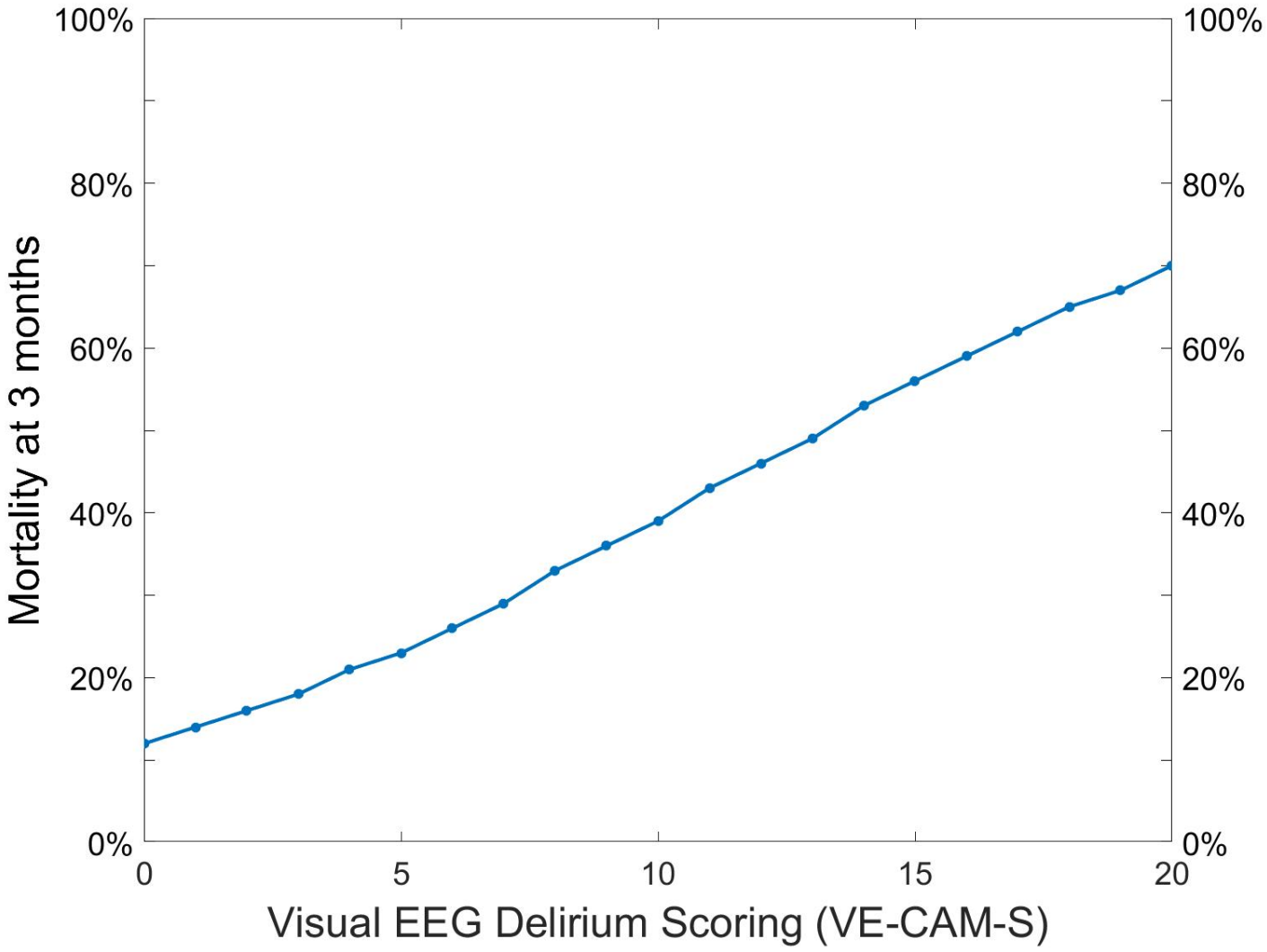
Score	Visual EEG Features
1	•Absent sleep transients (spindles, K-complexes, vertex waves) •Generalized/diffuse theta slowing •Generalized rhythmic delta activity •Lateralized rhythmic delta activity
2	•Generalized/diffuse delta slowing •Lateralized periodic discharges •Low voltage: moderate (<20 µV)
4	•Generalized periodic discharges or bilateral independent periodic discharges
8	•Intermittent brief attenuation
20 (worst severity)	•Extreme delta brush •Nonconvulsive status epilepticus: generalized •Low voltage: extreme/electrocerebral silence •Burst suppression •Unreactive EEG

Visual EEG-Based Grading of Delirium Severity (VE-CAM-S)



Tesh*, Sun*, Jing*, …, Kimchi**, Westover**. Crit Care Explor. 2022

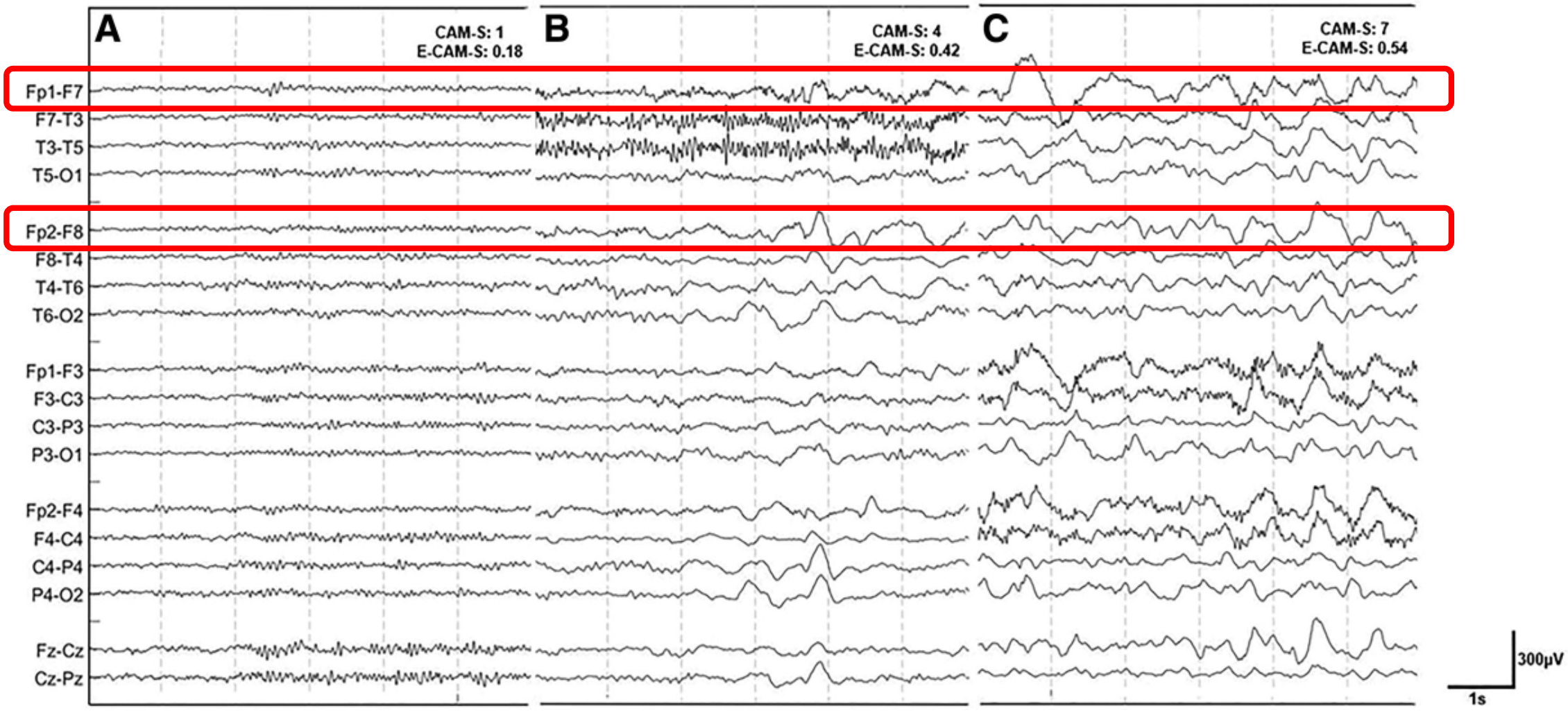
Visual EEG-CAM-S is Correlated with Mortality



Tesh*, Sun*, Jing*, …, Kimchi**, Westover**. Crit Care Explor. 2022

What about EEG features that are hard to see?

Machine Learning EEG Delirium Severity Prediction



Van Sleuwen*, Sun*, Eckhardt*, …, Kimchi**, Westover**. Crit Care Med. 2022

Machine Learning EEG Delirium Severity Prediction

Quantitative EEG Features

- Mean
- Percentiles (25, 50, 75)
- Standard deviation
- Variance
- Mean absolute gradient
- Line-length
- Zero Crossing Rate
- Skewness
- Kurtosis
- Hjorth mobility
- Hjorth complexity
- Shannon entropy
- Higuchi fractal dimension
- Mean spectral frequency
- Power at center frequency
- Spectral bandwidth
- Spectral entropy
- Spectral edge frequencies
- Absolute and Relative Power in different frequency bands
  - Delta (0.5-4 Hz)
  - Theta (4-8 Hz)
  - Alpha (8-12 Hz)
  - Beta (13-20 Hz)
- FOOOF parameterization of power spectra (Donoghue et al, 2020)

Van Sleuwen*, Sun*, Eckhardt*, …, Kimchi**, Westover**. Crit Care Med. 2022

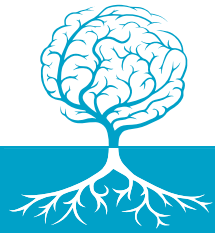
E-CAM-S: EEG Confusion Assessment Method Severity Score

373 patients receiving EEG for Altered Mental Status

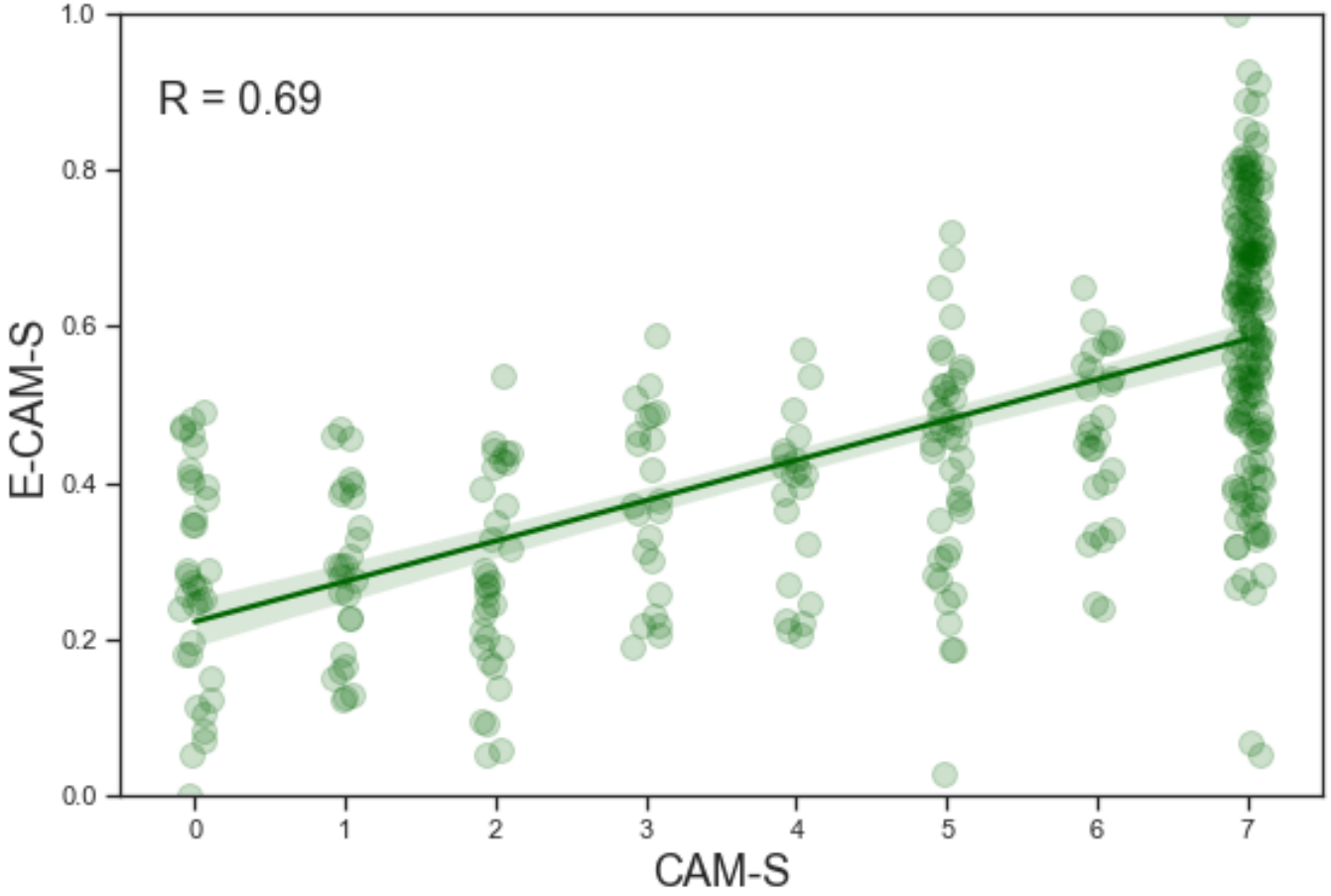
- 32% without delirium or coma
- 35% with delirium (CAM-SF)
- 33% with coma (RASS -4 or -5)

20-60 min 4 channel frontal EEG (split into 6 sec epochs)

Learning-to-Rank Ordinal Regression to predict determined CAM-S (cross validated approach)



E-CAM-S: EEG Confusion Assessment Method Severity Score



Meike van Sleuwen

Haoqi Sun, PhD

Christine Eckhardt, MD, PhD

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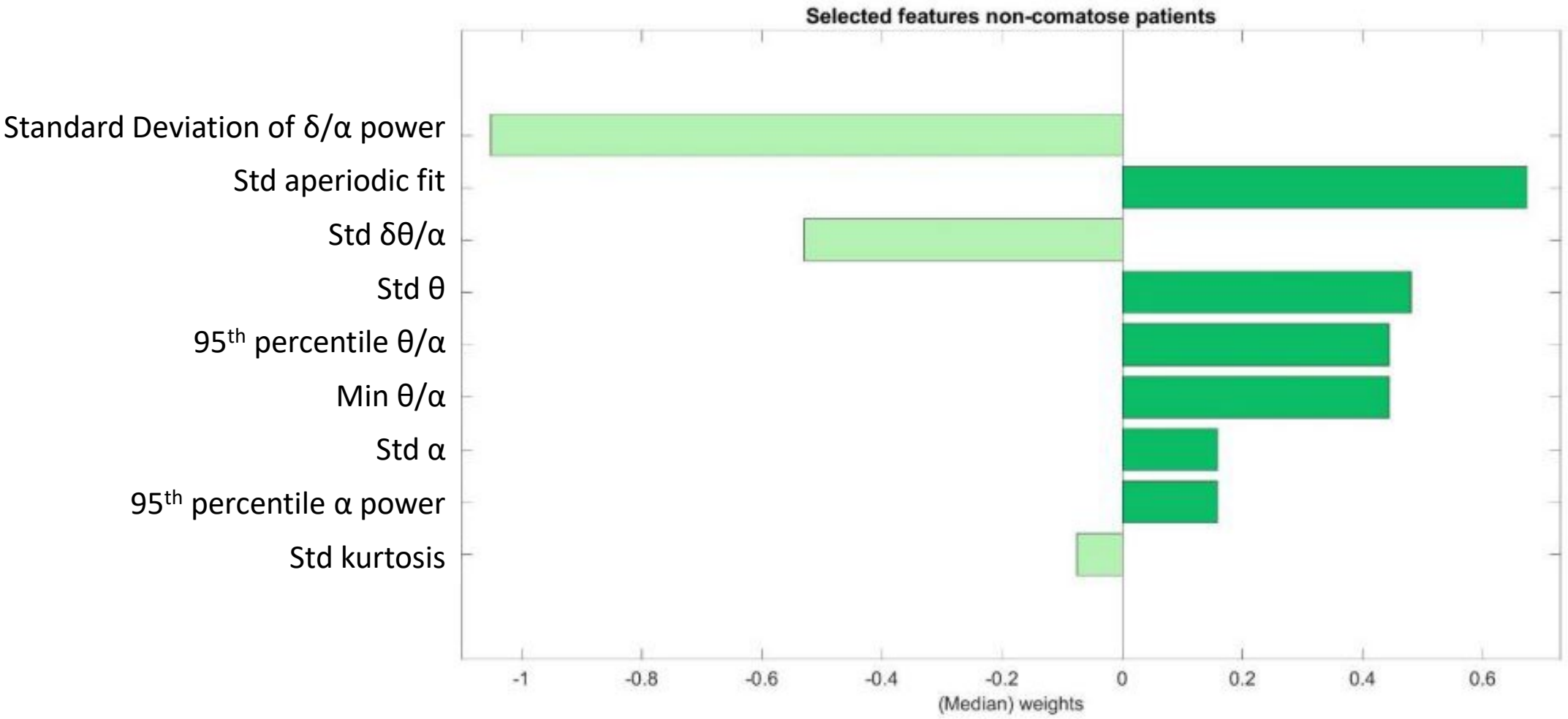
Importance of variability of EEG features over time



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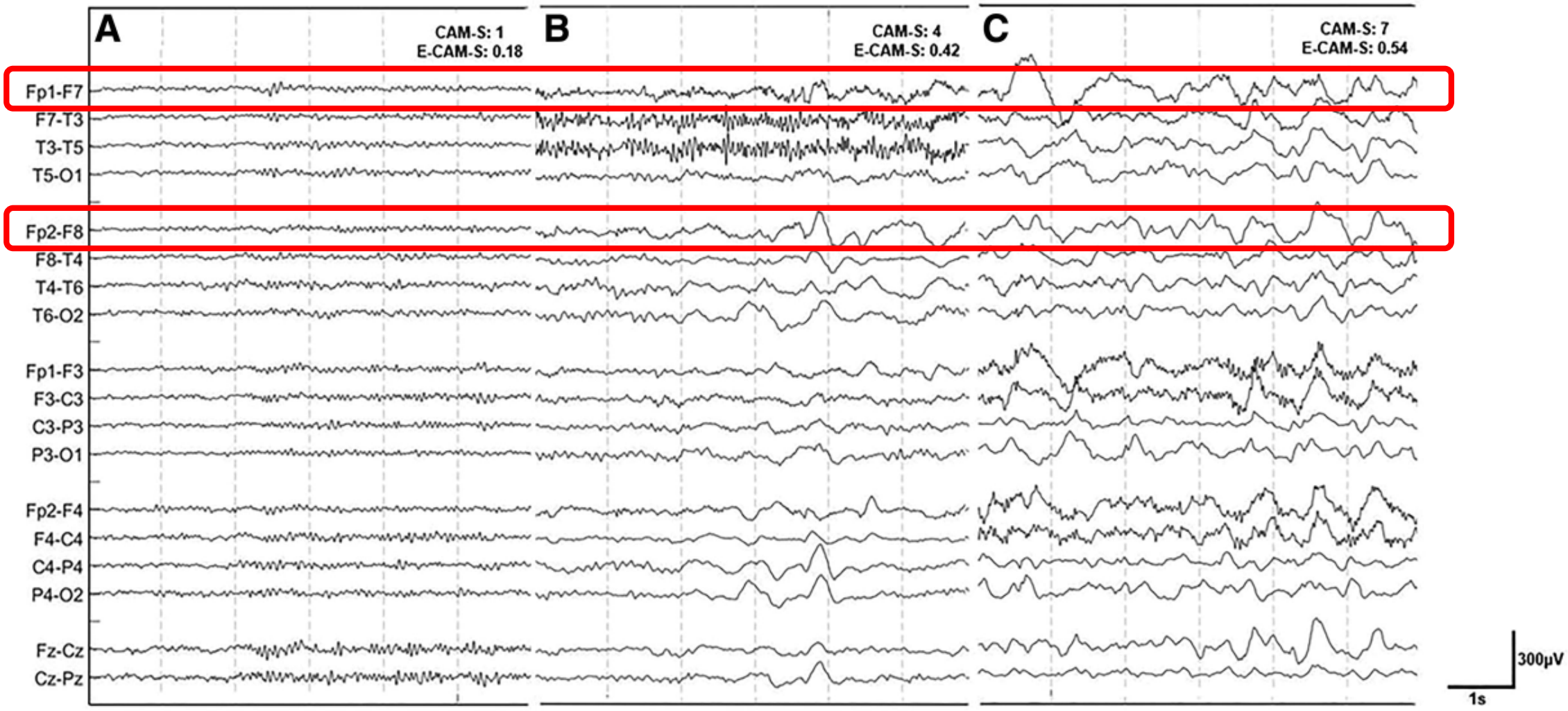
Spatial Topography of Delirium Pathophysiology?



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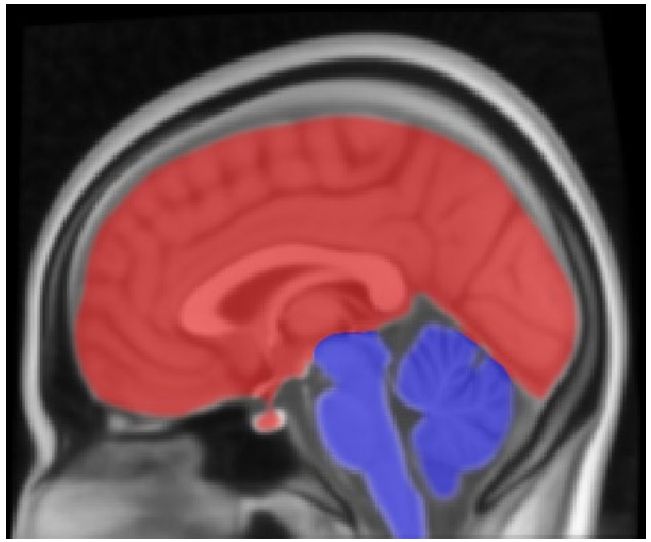
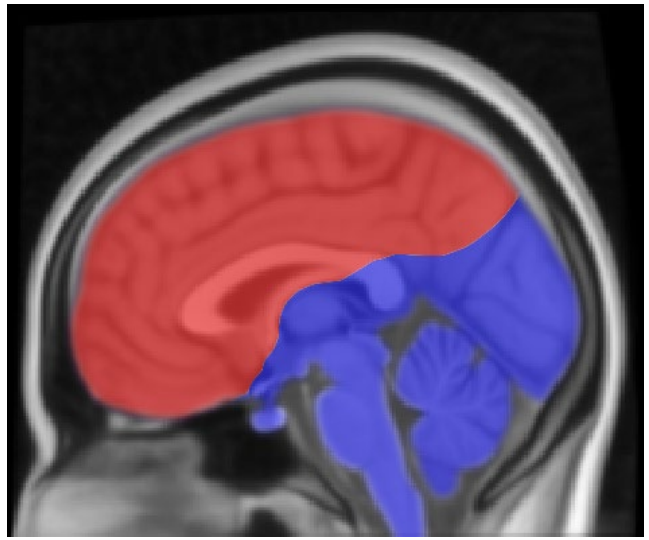
Spatial Organization of Delirium in Stroke

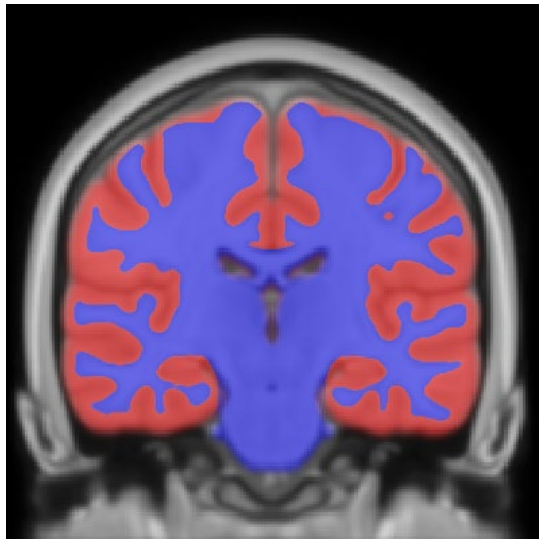
Meta-analysis of 31 cohorts with a total of 8,329 patients



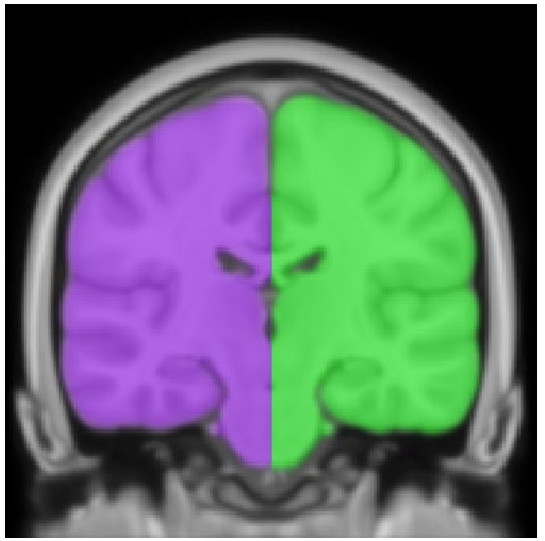
Supratentorial
RR 2.01



Anterior
RR 1.41

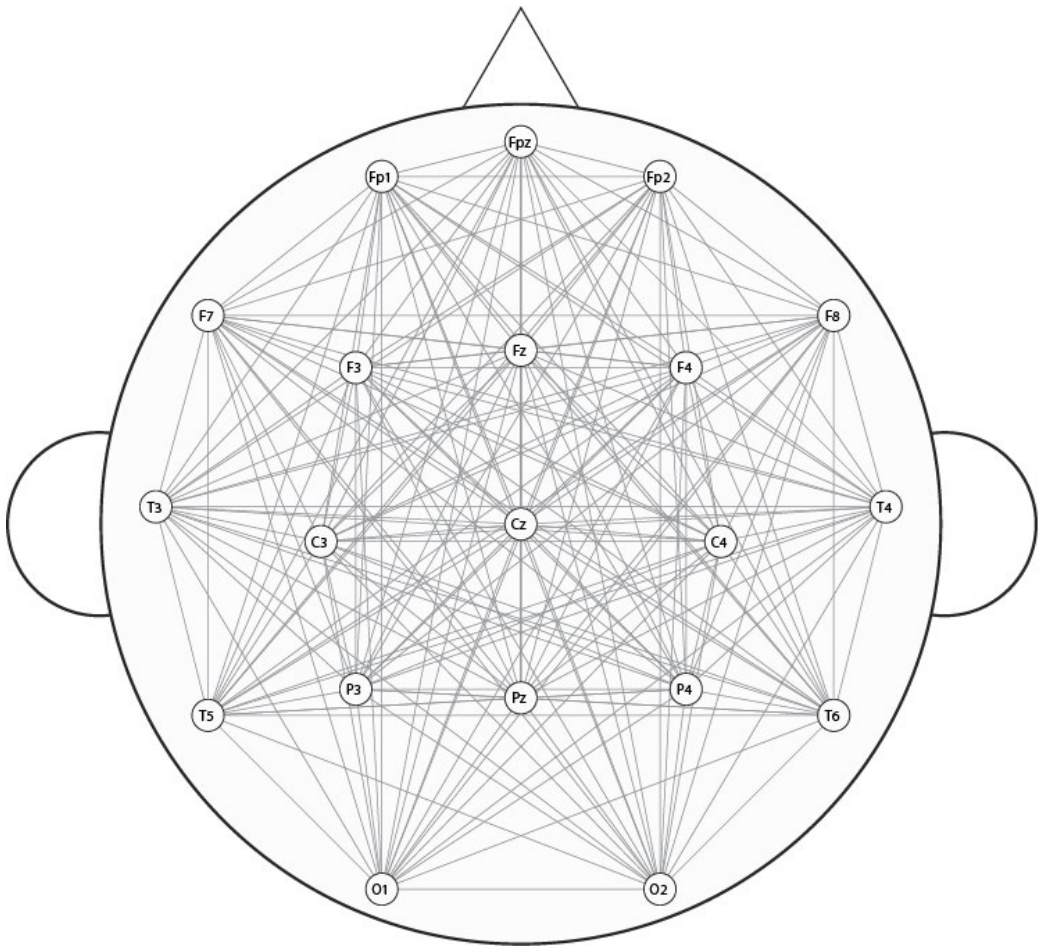


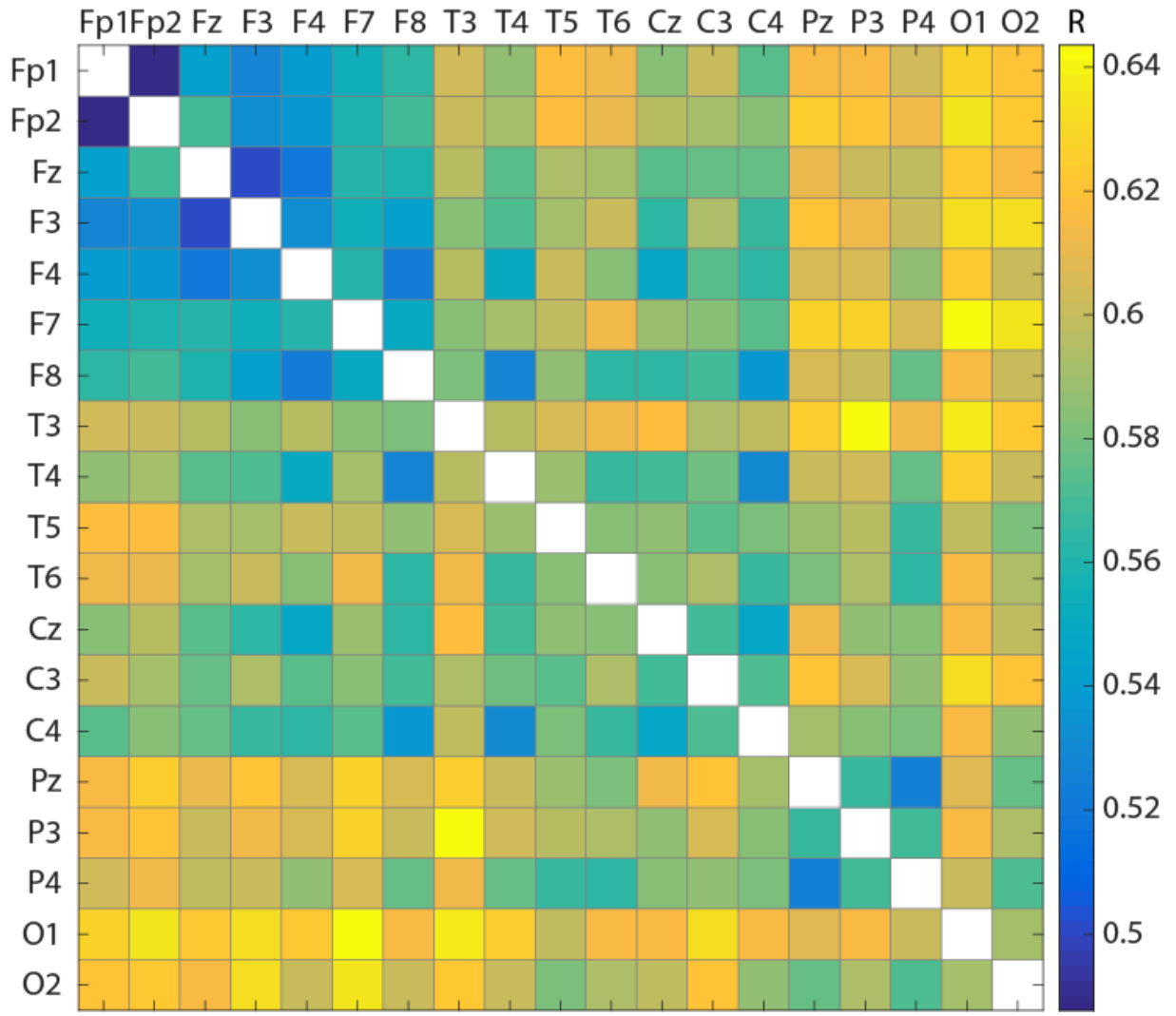
Cortical
RR 1.54



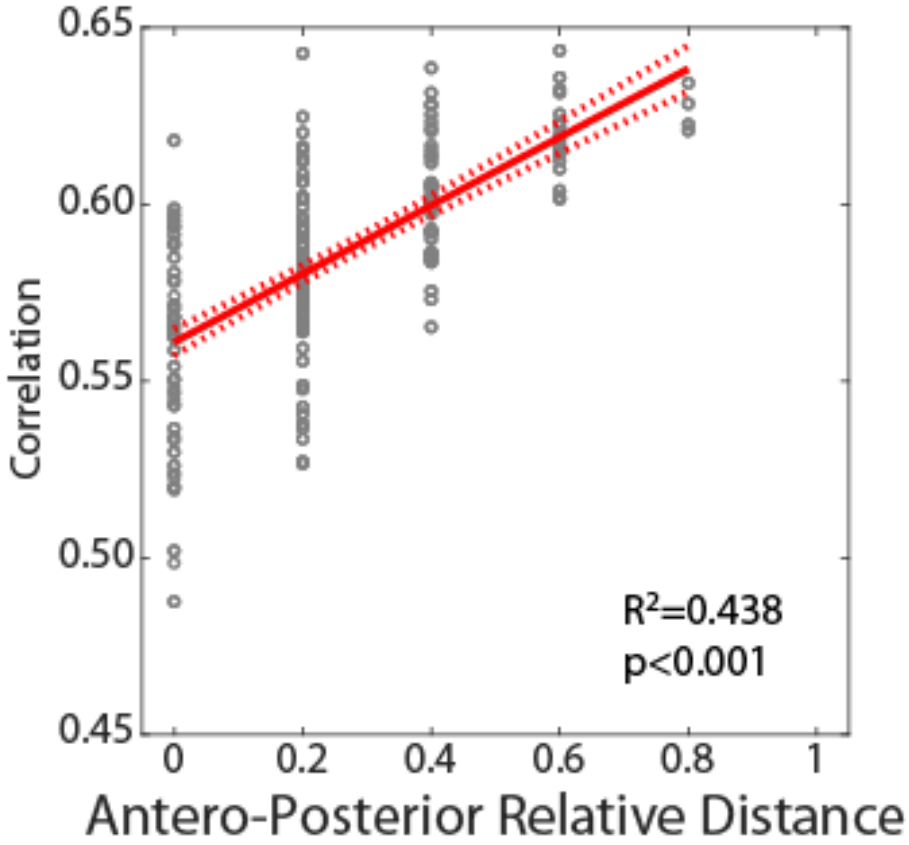
Right vs. Left
RR 0.99

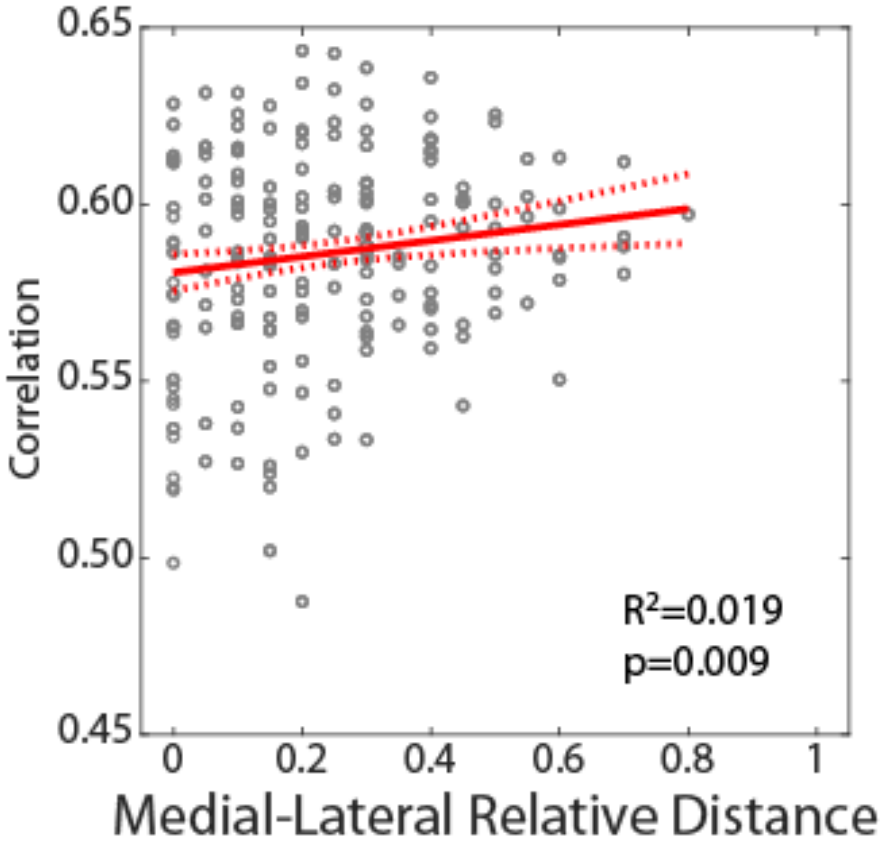
Spatial Topography of Delirium Pathophysiology



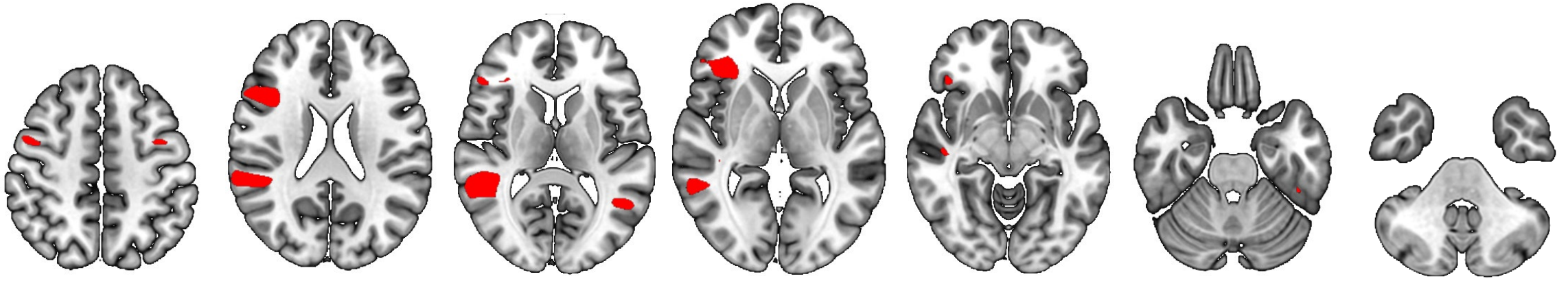


Antero-Posterior Topography of Delirium Electrophysiology





Significant Positive Peaks



Two-sample t-test

|t| < 4.7, peak (4.69-4.7)

- MRIcroCL

Organization of Delirium Pathophysiology

1. Slowing is the single most informative EEG feature for delirium
2. Visual or quantitative EEG features beyond slowing may help predict delirium severity
3. The variability of EEG features over time may help predict delirium severity
4. Delirium pathophysiology may particularly involve anterior-posterior cortical brain networks

Some EEG Advantages & Limitations

Advantages

- Applicable at the bedside
- Reflects core delirium features
- Validity across phenotypes (hypoactive & hyperactive)
- Quantitative data
- *High temporal resolution*

Limitations

- Something is placed on the patient
- Spatial limitations
  - Samples large brain regions
  - Samples primarily superficial cortex
- Limited etiologic information
- Traditionally requires expertise
  - Placement of EEG
  - Interpretation of EEG