EEG during delirium

Arjen Slooter, MD, PhD
What is a Delirium?
A. Disturbance in attention (i.e. reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).

B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of the day.

C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception).

D. The disturbances in criteria A and C are not explained by another pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.

E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication or withdrawal (i.e. because of a drug of abuse medication), or exposure to a toxin, or is because of multiple etiologies.
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Essential Features

- (Slightly) decreased level of consciousness
- Decreased attention
- Acute onset with fluctuation in time
Consequences of Delirium
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- Is disturbing for the patient
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- Increases ICU and hospital admission
Consequences of Delirium

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- Increases the risk of cognitive impairment
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- Is disturbing for the patient
- Increases ICU and hospital admission
- Increases the risk of cognitive impairment
- Increases mortality
Consequences of Delirium

- Is disturbing for the patient
- Increases ICU and hospital admission
- Increases the risk of cognitive impairment
- Increases mortality
- Increases costs
Importance of early detection

- Delirium is, in part, a preventable condition

- The longer a patient is delirious,
the more difficult it becomes to treat delirium

Inouye 1999
Do We Recognize Delirium?
Which Test?

- Opinion of ICU physician

- Screening:
  - CAM-ICU
  - ICDSC
  - Nu-DESC
  - DDS
  - NEECHAM
Which Test?

- Opinion of ICU physician

- Screening:
  CAM-ICU
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- ICDSC
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Experts
<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
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<tbody>
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What About the CAM-ICU in Daily Practice?
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- There is a difference between a research setting and ‘real life’ clinical practice

- Cognitive testing does not fit well in the ‘ICU culture’
What About the CAM-ICU in Daily Practice?

Prof. dr. W.A. Eikelenboom, psychiatrist
Prof. dr. W.A. van Gool, neurologist
Dr. G. Izaks, geriatrician
Drs. A. Kalf, geriatrician
Drs. I.A.M. Klijn, psychiatrist
Dr. M.A. Kuiper, neurologist - intensivist
Dr. F.E. de Leeuw, neurologist
Drs. T. de Man, psychiatrist
Dr. R.J. van Marum, geriatrician
Prof. dr. R.C. van der Mast, psychiatrist
Drs. R.J. Osse, psychiatrist
Dr. S.E.J.A. de Rooij, geriatrician
Dr. A.J.C. Slooter, neurologist - intensivist

AND

Drs. M.M.J. van Eijk, research physician
Drs. M. van den Boogaard, nurse scientist
What About the CAM-ICU in Daily Practice?

<table>
<thead>
<tr>
<th>Overall:</th>
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<tbody>
<tr>
<td>Sensitivity</td>
</tr>
<tr>
<td>Specificity</td>
</tr>
<tr>
<td>Positive predictive value</td>
</tr>
<tr>
<td>Negative predictive value</td>
</tr>
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</table>

### Hypoactive delirium:

<table>
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<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>31% (95% CI 17-48%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>98% (95% CI 92-99%)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>85% (95% CI 54-97%)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>81% (95% CI 72-87%)</td>
</tr>
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**What About the CAM-ICU in Daily Practice?**
Other Limitations

- The CAM-ICU is either positive or negative

- There is no continuous scale for the likelihood or severity

- The effects of sedation are not considered
Can We Detect Delirium Based on an Objective Instrument?
Key Questions

Which physiological alterations occur in delirium, and can these be used for monitoring?
Key Questions

Which physiological alterations occur in delirium, and can these be used for monitoring?

1 - Movement pattern

2 - Temperature regulation

3 - EEG
Eye movements, in particular blinks, were affected in delirium, which holds promise for objective delirium monitoring.
Hypothesis:
delirium is associated with increased temperature variability
2. Temperature Regulation

Increased temperature variability in 21/24 patients during delirium-days

$\beta_{\text{adjusted}} = 0.005$, 95% CI = 0.002-0.008

$p < 0.001$
2. Temperature Regulation

Of 334 screened patients, only 24 were included as conditions affecting thermal regulation were excluded.

*Conclusion:* monitoring of temperature regulation seems not to be a promising component for delirium detection.
3. EEG
3. EEG

Hans Berger 1873 - 1941
EEG in Delirium

During delirium

Two months after delirium

Romano and Engel, 1944
Can We Use EEG for Delirium Detection?
Can We Use EEG for Delirium Detection?

- A standard 21-channel EEG is not practical

- EEG reading needs expertise in neurophysiology
Characteristics of EEG in Delirium

- Increase in relative delta (0.5 - 4 Hz) power
- Increase in relative theta (4 - 8 Hz) power
- Decrease in relative alpha (8 - 13 Hz) power
- Decrease in peak frequency
- Postoperative cardiac surgery patients

28 with delirium, 28 without delirium

- Standard 21-channel EEG

- For each derivation, 6 EEG parameters were tested

- All combinations were compared and p-values ranked
For eyes closed, the optimal combination was:

F8-Pz and relative delta power

\[ p = 1.8 \times 10^{-12} \]
## Results

### Eyes Closed

<table>
<thead>
<tr>
<th>Rank</th>
<th>p-value*</th>
<th>Derivation</th>
<th>Characteristic</th>
<th>Delirium, median (IQR)</th>
<th>Non-delirium, median (IQR)</th>
<th>AUC</th>
<th>Sens (%)</th>
<th>Spec (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.8e-12</td>
<td>F8-Pz</td>
<td>Relative delta</td>
<td>0.59 (0.47-0.71)</td>
<td>0.20 (0.17-0.26)</td>
<td>0.99</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>3.7e-12</td>
<td>F8-P3</td>
<td>Relative delta</td>
<td>0.59 (0.46-0.69)</td>
<td>0.19 (0.15-0.26)</td>
<td>0.99</td>
<td>96</td>
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<tr>
<td>3</td>
<td>1.1e-11</td>
<td>F8-O2</td>
<td>Relative delta</td>
<td>0.60 (0.49-0.73)</td>
<td>0.23 (0.18-0.30)</td>
<td>0.99</td>
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<td>4</td>
<td>1.5e-11</td>
<td>Fp2-O1</td>
<td>Relative delta</td>
<td>0.66 (0.60-0.75)</td>
<td>0.27 (0.23-0.36)</td>
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<td>5</td>
<td>1.7e-11</td>
<td>F8-F4</td>
<td>Relative delta</td>
<td>0.60 (0.43-0.70)</td>
<td>0.20 (0.17-0.26)</td>
<td>0.98</td>
<td>96</td>
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<tr>
<td>6</td>
<td>2.2e-11</td>
<td>F8-O1</td>
<td>Relative delta</td>
<td>0.62 (0.48-0.72)</td>
<td>0.22 (0.17-0.26)</td>
<td>0.99</td>
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<tr>
<td>7</td>
<td>2.4e-11</td>
<td>F8-Cz</td>
<td>Relative delta</td>
<td>0.57 (0.46-0.67)</td>
<td>0.26 (0.20-0.33)</td>
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<td>3.0e-11</td>
<td>Cz-O1</td>
<td>Relative delta</td>
<td>0.50 (0.37-0.57)</td>
<td>0.17 (0.10-0.25)</td>
<td>0.96</td>
<td>92</td>
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Results
1. Delirium is associated with physiological alterations

2. EEG is the most promising approach for monitoring
Future Studies
Prototype
Next steps

1. Confirmation in an independent population

- n=154 elderly, postoperative patients
- 5 minutes monitoring before-, and 3 days after surgery
- Reference standard: geriatrician, psychiatrist or neurologist
- AUROC, sensitivity, specificity and predictive values
2. Integrated artifact detection

- Eye-movements
- Muscle activity
- Head movements

Philip Zeman, PhD
Next steps

3. Optimizing usability

- Collaborate with industrial designers
- As short as possible recording time
- Integration with other measurements such as blood pressure and temperature
Next steps

4. Distinction with light levels of sedation

- Patients immediately after cardiac surgery
- Non-neurological patients who receive propofol (n=30) or midazolam (n=30) to RASS -1 to -3
- Which EEG parameters distinguish hypo-active delirium from light levels of sedation?
Conclusion
Delirium is frequent in ICU patients and impairs outcome
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Current recognition is poor, objective tools are needed
Delirium is frequent in ICU patients and impairs outcome

Current recognition is poor, objective tools are needed

Promising approach: EEG-based monitoring
Thank you for your attention