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EEG and clinical assessment in delirium and acute encephalopathy

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Studies on delirium detection tools usually have a delirium expert as a reference rater. However, experts appear to frequently disagree on the diagnosis of delirium, even if considering exactly the same clinical and cognitive information.[1] Acute encephalopathy is a rapidly developing (over less than 4 weeks, but usually within hours to days) pathobiological process in the brain which can lead to a clinical presentation of (sub)syndromal delirium,[2] and can be detected with electroencephalography (EEG) as slow wave activity in theta and delta ranges.[3–7] Because of its objective character, EEG seems to be a promising method to detect delirium.[7,8] To the best of our knowledge, there are no previous reports on the extent to which clinical signs of delirium concur with signs of encephalopathy in EEG. The aim of this study was to investigate the overlap between the clinical and EEG classifications of delirium and acute encephalopathy, and to explore whether EEG may provide additional information to the classification of delirium by clinical experts.

In this study (details: Appendix S1), 2 minutes of 321 postoperative one-channel (Fp2 – Pz) EEG recordings of 145 awake elderly surgical patients were assessed by three EEG experts with at least 15 years of clinical EEG experience, independently of each other and unaware of clinical information. Four criteria were assessed to determine the presence of acute encephalopathy: (i) slow wave activity should lie between 0.5 and 5 Hz; (ii) polymorphic delta waves should have higher amplitudes than alpha waves; (iii) runs of at least two consecutive polymorphic delta waves should be present; and (iv) runs of polymorphic delta activity should be present at least three times per minute. The clinical diagnosis of delirium was based on video-recorded standardized cognitive assessments, administered directly after the EEG recording. This included the Delirium Rating Scale-Revised-98 (DRS-R-98) to assess delirium severity,[9] and notes from the electronic patient file on the 24 h before the EEG recording. Different pairs of two clinical experts with at least 5 years of expertise in delirium diagnosis classified each patient independently of each other and unaware of the EEG classification. In case of discordance, a third expert was consulted. Final classifications were based on a majority vote of each expert panel.

Study population characteristics and extended results are found in Appendix S1, Table S1–S5. We found that EEG experts classified 119 of 321 recordings (37.1%) as 'acute encephalopathy' (AE+), whereas clinical experts classified 'delirium' (D+) in 73/321 assessments (22.7%). A total of 233 assessments (72.6%) showed overlap between the clinical and EEG classifications of the presence/absence of delirium and acute encephalopathy. A positive diagnosis by both expert panels (AE + D+) was associated with the highest DRS-R-98 score (mean 12.4, Standard Deviation (SD) 5.6). Mean DRS-R-98 scores gradually decreased along with the level of consensus between expert panels (see Table 1; AE-D + 7.9, SD 3.0; AE + D- 3.8, SD 1.9; AE − D- 2.8, SD 1.7; test for trend $P < 0.001$).

This study shows that identification of acute encephalopathy by EEG experts and a diagnosis of delirium by clinical experts largely overlap, using one-channel EEG in which eye artifacts should be distinguished from slow wave activity. Interestingly, if 'acute encephalopathy' was present without clinical delirium, a significantly higher severity of delirium score (DRS-R-98) was observed, compared to a negative classification by both expert panels. Similarly, a significantly lower delirium severity score was found for cases classified as 'no acute encephalopathy' but 'delirium', compared to a positive classification by both expert panels.

As delirium severity appears to differ in these subgroups in an intuitive way, we may speculate that EEG could be more sensitive to changes in cognitive dysfunction. In some cases these changes may have been too subtle for experts to diagnose these as 'delirium', or potentially, the cognitive reserve of a patient may have obscured dysfunction. These findings are consistent with a prior study that showed a correlation between slow wave EEG activity and delirium severity, where patients with subsyndromal delirium – not fulfilling all clinical criteria for delirium - had intermediate rates of EEG slowing compared to patients who met all criteria for delirium.[10]

In conclusion, acute encephalopathy in EEG largely overlaps with a clinical diagnosis of delirium. EEG may be sensitive to brain state changes that may not be classified as clinically apparent delirium. The use of an EEG classification of acute encephalopathy in combination with a clinical classification of delirium may be an interesting approach as a reference standard in future studies on delirium detection tools, especially when EEG-based classification can be automated to eliminate challenges in the interpretation of one-channel EEG.

Table 1. Delirium severity as estimated with DRS-R-98 scores and classification of delirium by clinical experts and acute encephalopathy by EEG experts[†]

Classification by clinical experts	Classification by EEG experts	N	Mean DRS-R-98 score	SD	Range
Delirium	Acute encephalopathy	52	12.4	5.6	5.0–29.0
Delirium	No acute encephalopathy	21	7.9	3.0	4.3–16.3
No delirium	Acute encephalopathy	67	3.8	1.9	0.5–10.0
No delirium	No acute encephalopathy	181	2.8	1.7	0.0–8.7
Total		*321*	*4.9*	*4.5*	*0.0–29.0*

[†]Delirium Rating Scale Revision 1998 (DRS-R-98) scores (mean, standard deviation (SD) and observed range of minimum and maximum values) for each classification category where clinical experts agree or did not agree. A significant linear relationship was found between the classification categories and the DRS-R-98 scores ($R^2 = 0.581$, test for trend $P < 0.001$).

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Disclosure statement
The authors declare no conflicts of interest.

Ethical approval statement
The study protocol was reviewed by the Medical Ethical Committee of the University Medical Center Utrecht and registered at ClinicalTrials.gov under identifier NCT02404181. Study protocols conformed to the provisions of the Declaration of Helsinki.

Informed consent statement
Witten informed consent was obtained from each patient before elective surgery, and anonymity was preserved. All data were pseudonymized.

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Supporting information
Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1 Supporting information.

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