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Clinical Investigation

CLINICAL INVESTIGATION

Delirium detection using relative delta power based on 1 minute single-channel EEG: a multicentre study

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Abstract

Background: Delirium is frequently unrecognised. EEG shows slower frequencies (i.e. below 4 Hz) during delirium, which might be useful in improving delirium recognition. We studied the discriminative performance of a brief single-channel EEG recording for delirium detection in an independent cohort of patients.

Methods: In this prospective, multicentre study, postoperative patients aged ≥60 yr were included (n=159). Before operation and during the first 3 postoperative days, patients underwent a 5-min EEG recording, followed by a video-recorded standardised cognitive assessment. Two or, in case of disagreement, three delirium experts classified each postoperative day based on the video and chart review. Relative delta power (1–4 Hz) was based on 1-min artifact-free EEG. The diagnostic value of the relative delta power was evaluated by the area under the receiver operating characteristic curve (AUROC), using the expert classification as the gold standard.

Results: Experts classified 84 (23.3%) postoperative days as either delirium or possible delirium, and 276 (76.7%) non-delirium days. The AUROC of the relative EEG delta power was 0.75 [95% confidence interval (CI) 0.69–0.82]. Exploratory analysis showed that relative power from 1 to 6 Hz had significantly higher AUROC (0.78, 95% CI 0.72–0.84, P=0.014).

Conclusions: Delirium/possible delirium can be detected in older postoperative patients based on a single-channel EEG recording that can be automatically analysed. This objective detection method with a continuous scale instead of a dichotomised outcome is a promising approach for routine detection of delirium.

Clinical trial registration: NCT02404181.

Keywords: complications; postoperative; delirium; electroencephalography; monitoring; postoperative care; intensive care unit

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Editor's key points

- An objective monitor to detect postoperative delirium would be useful in optimising treatment and outcomes.
- An automated 1-min EEG analysis was compared with clinical assessment tools in older postoperative surgical patients.
- Analysis of relative delta EEG power recording in a single EEG channel correlated with clinical assessments of delirium.
- Further validation as a clinical monitoring approach is required, including in sedated ICU patients and patients with underlying cognitive dysfunction.

Delirium is common in hospitalised patients, particularly after surgery[1–4] and in the ICU.[5,6] Delirium is associated with prolonged hospitalisation,[7–9] long-term cognitive decline,[4,5,8,10,11] increased mortality,[8,12] institutionalisation[13] and cost,[12,14] and is therefore a serious healthcare problem. Early detection enables early treatment of delirium. However, delirium is often not recognised.[12,15,16] To improve detection of delirium, several screening tools have been developed. A systematic review showed a pooled sensitivity of 80% for the Confusion Assessment Method (CAM)-ICU,[17] the most frequently used delirium screening tool in the ICU. It should however be noted that all but one study in this systematic review was performed in a research setting where a small number of dedicated nurses or physicians administered CAM-ICU screening. In contrast, a multicentre study showed that in a routine, clinical setting where numerous bedside nurses administered the CAM-ICU, sensitivity was 47%,[18] and CAM-ICU assessed by clinical nurses in hospitalised older non-ICU patients showed a sensitivity of 25%.[19] These findings raise the question whether a more objective tool could be developed to detect delirium.

Delirium is associated with slowing of EEG background activity, specifically an increased relative delta power (1–4 Hz).[20,21] EEG-based monitoring and quantification could have great potential for predicting and detecting delirium in routine daily practice as it is objective and applicable in all patients despite language or sensory barriers.[22,23] EEG could further be used to quantify delirium severity on a continuous scale. In a previous proof of concept study, we showed that a 1-min EEG recording with three electrodes was enough to distinguish patients with delirium from non-delirious controls after cardiac surgery using relative delta power (i.e. the power of slow waves <4 Hz).[24] Based on these findings, we developed an EEG-based delirium monitor to be used irrespective of the presence or absence of delirium risk factors. The objective of the current study was to study the discriminative performance of this EEG-based monitor in an independent cohort of older postoperative patients. We hypothesised that delirium days can be distinguished from days without delirium based on relative delta power.[24]

Methods

Study setting and population

This prospective, multicentre study [University Medical Center Utrecht (UMCU), Radboud University Medical Center Nijmegen, non-academic teaching hospital Isala] was approved by the UMCU ethical committee (protocol 13-634), registered at ClinicalTrials.gov (identifier: NCT02404181), and described in detail elsewhere.[25] Briefly, inclusion criteria were age ≥60 yr, planned major surgery with an expected stay of at least 2 days, and an estimated increased risk of delirium.[12] Exclusion criteria were planned neurosurgery and inability to perform cognitive testing due to deafness or a language barrier.

Data collection and classification

A well-trained researcher (both theoretically and practically totalling 60 min) visited the patients before surgery (T0), and on the first 3 consecutive days after surgery (T1, T2, and T3) to perform a 5-min eyes closed EEG recording (Fp2-Pz and T8-Pz) and cognitive assessment (10–15 min) which was recorded on video.

Relative delta power (1–4 Hz) was calculated as the primary EEG measure, and seven secondary EEG variables were studied as secondary measures: relative power from 1 to 5 Hz, relative power from 1 to 6 Hz, relative theta power (4–8 Hz), relative alpha power (8–13 Hz), relative beta power (13–30 Hz), slow-fast ratio (power 1–8 Hz/8–30 Hz), and peak frequency (between 4 and 13 Hz). Full description of data processing is described in the Online Data Supplement. The cognitive assessment included the Dutch version of the delirium rating scale—revised in 1998 (DRS-R-98) and the Dutch version of the CAM-ICU concerning the last 24 h.[26–28] Level of consciousness was assessed with the Richmond Agitation and Sedation Scale (RASS).[29] Assessment of patients was not performed at a specific time of day.

Each video-recorded assessment, together with the medical and nursing files, was assessed by two delirium experts, who independently classified the videos and patient records as 'no delirium', 'possible delirium', or 'delirium' according to Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria.[23,30] The severity of delirium (DRS-R-98), the likelihood of the patient being delirious [numeric rating scale (NRS)], and motor subtype were scored. In the case of classification disagreement, a third expert was consulted who was unaware of the classification of the first two experts. The experts had access to all available clinical information but were blinded to the EEG recordings.

Sample size calculation

The sample size was calculated based on a conservatively expected delirium incidence of 10% during the first 3 postoperative days.[31] The minimum acceptable specificity of a delirium monitor was set as 90% based on a meta-analysis of previous studies of the CAM-ICU.[32,33] With a precision of 5% and standard formula for diagnostic studies, the required minimum number of patients was 154.[34]

Statistical analysis

Clinical characteristics were described as mean (standard deviation) or median [inter-quartile range (IQR)] where appropriate. The main unit of analysis was a separate observation day. As possible delirium could progress to definite delirium, we combined 'possible delirium' with 'delirium' into (possible) delirium in the main analyses. Receiver operating characteristic (ROC) curves were

computed on EEG variables and '(possible) delirium' *vs* 'no delirium'. The areas under the ROC curves (AUROCs) were calculated with accompanying 95% confidence intervals (CI). In addition, the positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were calculated for three thresholds, 90% specificity, 90% sensitivity, and the sensitivity and specificity based on Youden's index. Using the Delong method, AUROCs of various EEG variables were compared with the AUROC of the relative delta power (1–4 Hz).[35] Spearman's rho correlation coefficient was calculated between relative delta power (1–4 Hz) and NRS, DRS-R-98, score of attentional deficits (i.e. item-10 of the DRS-R-98 score), and RASS score.

To evaluate the effect of combining possible delirium cases with the delirium cases, a sensitivity analysis was performed. The AUROC curves were recalculated with the possible delirium cases added to the non-delirious cases. Finally, the effect of including repeated measures was assessed by recalculating the ROC curves based on T1, T2, and T3 assessments separately. The Benjamini-Hochberg correction for multiple testing was applied for all comparisons between groups for the calculated EEG variables.[36] Analyses were performed in Matlab (version 2015a, Mathworks, Natick, MA, USA) and SPSS (version 21, SPSS Inc., Chicago, IL, USA). Data were reported according to the Standards for Reporting Diagnostic accuracy studies.[37]

Results

Study population and delirium assessment

We included 196 patients, but excluded 7.7% (15/196) of patients and 7.1% (34/477) of the expected number of postoperative recordings because of technical difficulties. The study population comprised 159 patients who underwent surgery, with the majority having general anaesthesia using volatile anaesthetics and opioids, in whom 360 postoperative assessments were performed (Fig. 1). Table 1 shows patient characteristics. None of the patients were sedated or mechanically ventilated during cognitive assessments. EEGs were recorded in all patients immediately followed by the video-recorded interview with a standardised cognitive assessment. Diagnoses of delirium were made by delirium experts as previously described in detail,[25] based on all available information including the CAM-ICU as administered by a trained researcher (Supplementary Tables S9 and S10). In 77 (21.4%) assessment days, there was no agreement between the first two experts and a third delirium expert was consulted; the majority vote of the three delirium experts was used as the final classification. In the final classification, 43 postoperative assessment days (11.9%) were labelled as 'delirium', 41 (11.4%) as 'possible delirium', and 276 (76.7%) as 'no delirium'. This corresponded with 29 (18.2%) patients who were classified as delirious at least once during follow-up, 26 (16.4%) patients

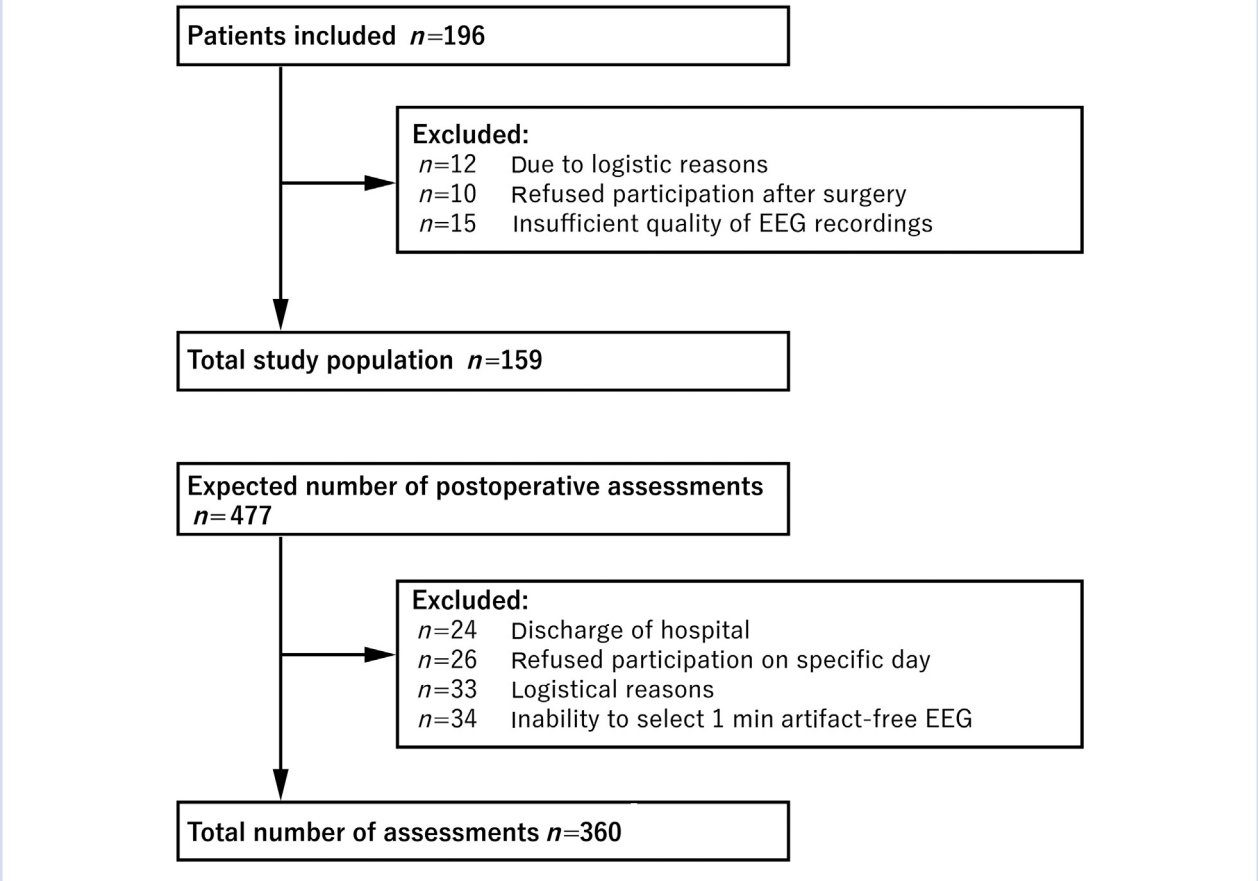

Fig 1. Flow chart of included patients and included postoperative assessments. Insufficient quality of the EEG recording (*n*=24), too short EEG recording (*n*=9), or no eyes closed EEG recording (*n*=1) were technical reasons that hampered 1-min selection of artifact-free EEG.

Table 1 Patient characteristics. Values are presented as mean (standard deviation), *n* (%), or median (range). Alcohol consumption, transient ischaemic attack or stroke, and psychiatric disease were self-reported by the patients.*We had five missing values for alcohol consumption, 41 missing values for MMSE, and four missing values for duration of surgery. Psychiatric diseases were depression (*n*=6), (early) dementia (*n*=3), and bipolar disorder (*n*=1). Other types of surgery were gastrointestinal (*n*=4), otorhinolaryngologic (*n*=3), urologic (*n*=1), and general surgery (*n*=1). MMSE, Mini-Mental State Examination

	All patients (*n*=159)
Mean age, yr (SD)	76.9 (6.2)
Male sex (%)	106 (66.7)
Alcohol consumption*	
N (%)	60 (37.7)
1–14 per week	70 (44.0)
>14 per week	24 (15.1)
Medical history	
Transient ischaemic attack or stroke	46 (28.9)
Psychiatric disease	10 (6.3)
Median MMSE (range)*	28 (18–30)
Surgery type	
Cardiothoracic or vascular	139 (87.4)
Orthopaedic	12 (7.5)
Other	8 (5.0)
Median duration of surgery (min, range)	171 (26–436)

with at most possible delirium, and 104 (65.4%) patients without any sign of delirium. None of the study participations were delirious before operation.

Relative delta power (1–4 Hz) in Fp2-Pz

The relative delta power (1–4 Hz) was significantly different ($P<0.001$) over the three groups: no delirium 0.44 (median, IQR 0.32–0.58), possible delirium 0.64 (median, IQR 0.48–0.73), and delirium 0.67 (median, IQR 0.55–0.74). In Figure 2, two examples of EEG recordings of 10 s are presented of a non-delirious patient and a delirious patient. The possible delirium and the delirium groups had a significantly higher relative delta power (1–4 Hz) compared with the no delirium group ($P<0.001$ and $P<0.001$, respectively). Possible delirium and delirium did not differ in relative delta power (1–4 Hz) ($P=0.187$), and were grouped into '(possible) delirium'. Figure 3 shows the ROC curve based on the distinction into no delirium *vs* (possible) delirium, and the relative delta power (1–4 Hz) on Fp2-Pz (AUROC 0.75, 95% CI 0.69–0.81). Table 2 shows diagnostic values of the relative delta power (1–4 Hz) for three cut-off points (Table 3).

Additional EEG algorithms and derivations

Of various EEG algorithms, the relative power from 1 to 6 Hz on Fp2-Pz showed a statistically significantly higher AUROC value (0.78, 95% CI 0.72–0.84) than the relative delta power (1–4 Hz) at the same derivation ($P=0.014$, Fig 3). See Supplementary Table S1 for the results of all secondary EEG algorithms. Moreover, normalised relative delta power (1–4 Hz) and normalised relative power from 1 to 6 Hz were calculated as the differences compared with baseline (T0). This yielded similar AUROC values as in analyses on uncorrected EEG variables (Supplementary Table S2). Patients who developed postoperative delirium or possible delirium had, before operation, a relative delta power that was similar to recordings in patients without delirium [delirium: median 0.35 (IQR 0.23–0.52), possible delirium: median 0.37 (IQR 0.22–0.57), and no delirium: median 0.43 (IQR 0.28–0.56), $P=0.59$].

For sensitivity analysis, the possible delirious patients were included in the non-delirious group. We found an AUROC of 0.76 (95% CI 0.69–0.83) for the relative delta power (1–4 Hz) and 0.79 (95% CI 0.72–0.85) for the relative power from 1 to 6 Hz. In Table 2, the diagnostic values are presented for three thresholds.

Correlation of EEG variables with clinical scores

The likelihood of delirium (NRS), severity of delirium (DRS-R-98), attentional level (DRS-R-98 item 10), and level of consciousness (RASS) were all significantly, but weakly, correlated with both the relative delta power (1–4 Hz) and the relative power from 1 to 6 Hz, (Table 3 and Supplementary Figs S1 and S2).

Subgroup analysis

When we stratified according to the presence or absence of a previous transient ischemic attack or stroke, there were no major differences in relative delta power (1–4 Hz) and relative power from 1 to 6 Hz. Moreover, the AUROC values for the relative delta power (1–4 Hz) or the relative power from 1 to 6 Hz were very similar (Supplementary Table S3). When we stratified according to the presence or absence of benzodiazepines or opioid use in the preceding 24 h, we observed similar AUROC values for both relative delta power (1–4 Hz) and relative power from 1 to 6 Hz (Supplementary Tables S4 and S5).

As an additional analysis, patients were stratified according to age based on quartiles. There was no consistent trend of the AUROC for relative delta power with age, although the AUROC of the first quartile (age <72 yr) might be lower compared with older patients (see Supplementary Table S6).

The delirium experts included motor subtype in each patient who was considered possible delirious or delirious (Table S7). In 24 (28.6%) assessments, delirium was classified as hypoactive, in 48 (57.1%) as mixed type, and in 12 (14.3%) as hyperactive. No significant difference in relative delta power ($P=0.18$) or relative power 1–6 Hz ($P=0.11$) was found between these groups.

Effect of repeated measurements

To assess the effect of repeated measurements in our main analyses, AUROC values were recalculated for relative delta power (1–4 Hz) and relative power from 1 to 6 Hz for assessments at time point T1, T2, and T3 separately (Supplementary Table S8 and Figure S3). There was a minor reduction in AUROC values when only T1 assessments were included [relative delta power (1–4 Hz) AUROC 0.72 (95% CI 0.62–0.81), relative power from 1 to 6 Hz AUROC 0.75 (95% CI 0.66–0.84)] compared with the main analysis. Similar AUROC values were found based on T2 assessments only [relative delta power (1–4

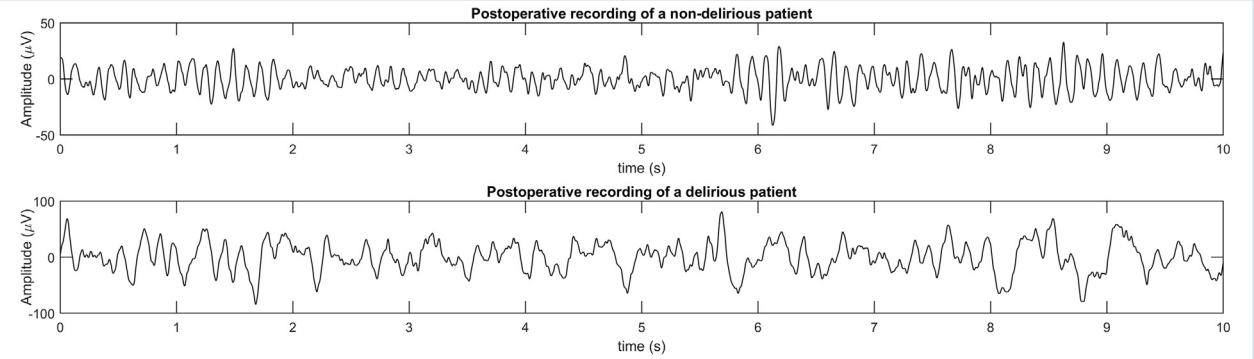

Fig 2. Example EEG segments of a non-delirious patient (upper panel) and a delirious patient (lower panel) after surgery. The segments were filtered as described in the supplementary text to reduce possible muscle artifacts and 50 Hz components. In the non-delirious patient, the alpha rhythm (8–13 Hz) is prominent, whereas the delirious patient shows a slower pattern in the range of 1–6 Hz with a high amplitude.

Hz) AUROC 0.76 (95% CI 0.64–0.87), relative power from 1 to 6 Hz AUROC 0.78 (95% CI 0.67–0.89), and slightly higher based on T3 assessments only, relative delta power (1–4 Hz) AUROC 0.80 (95% CI 0.70–0.91), relative power from 1 to 6 Hz AUROC 0.83 (95% CI 0.73–0.94)]. We could not conduct a formal statistical comparison because of the different number of assessments per day.

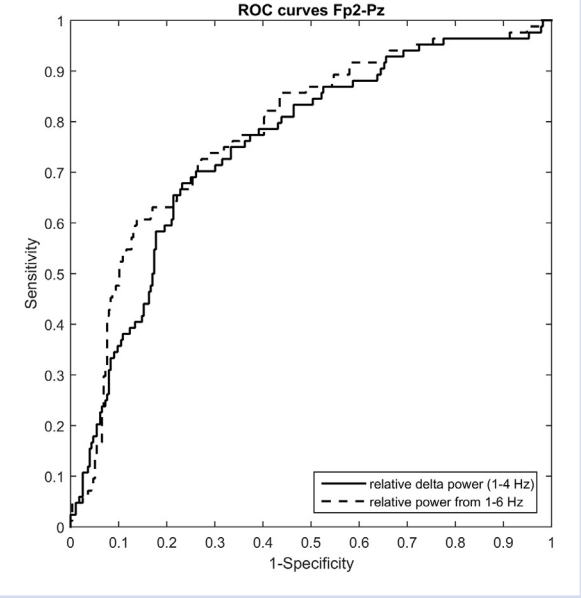

Fig 3. Receiver operating characteristic (ROC) curves of relative delta power (1–4 Hz) and relative power from 1 to 6 Hz on deviation Fp2-Pz. Postoperative assessments were defined as positive when classified as either possible delirium (n=41) or delirium (n=43), and negative in case of no delirium (n=276). Relative delta power (1–4 Hz) AUROC: 0.75 (95% CI 0.69–0.81), relative power from 1 to 6 Hz AUROC: 0.78 (95% CI 0.72–0.84). AUROC, area under the receiver operating characteristic curve; CI, confidence interval.

Discussion

We used an independent cohort of older postoperative patients to investigate our previous finding from a proof-of-concept study[24] that delirium can be detected based on 1 min of single-channel EEG. We found an AUROC value of 0.75 with the relative delta power (1–4 Hz), and a significantly higher AUROC value (0.78) when relative power from 1 to 6 Hz was used as a *post hoc* exploratory analysis. With these algorithms, we found correlations with scores on the likelihood and severity of delirium, inattention, and level of consciousness.Our approach differed from bispectral index (BIS) monitoring with regard to both the location and to the detection algorithm. BIS monitoring was developed to provide information about depth of anaesthesia.[38] The BIS value correlates with arousal but could not monitor delirium.[39]

In the main analysis, 'possible delirium' and 'delirium' were combined for two reasons. Possible delirium may have similar relevance in clinical practice, as doubtful cases of delirium may represent a prodromal phase in which treating the underlying cause may prevent progression to delirium. Secondly, 'possible delirium' and 'delirium' were associated with similar values on a variety of EEG variables (Supplementary Table S1), supporting grouping of both entities into one category.

The presented ROC curves were calculated without additional clinical information as the EEG-based delirium monitor was developed with the aim to replace current screenings tools to be applicable without the need to incorporate clinical characteristics. As delirium can be regarded as a condition with a spectrum of severities instead of a dichotomous phenomenon, no threshold values for EEG variables were determined. For monitoring delirium over the course of days, a continuous representation seems to be more appropriate as well.

Based on previous studies,[24,40] we investigated several EEG variables. Other known EEG characteristics of delirium or encephalopathy, which were not included in the current study, are spectral variability and complexity,[41] triphasic waves, and (inter)ictal epileptiform discharges.[42–45] The current algorithm could be improved by using some of these features. Strengths of this investigation include the prospective nature of this

Table 2 Diagnostic values of relative delta power (1–4 Hz) and relative power from 1 to 6 Hz for three thresholds, CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value

Cut–off method	Cut–off value	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Specificity 90%							
Relative delta power (1–4 Hz)	0.70	0.36 (0.26–0.47)	0.90 (0.86–0.93)	0.51 (0.38–0.65)	0.82 (0.77–0.86)	3.51 (2.25–5.47)	0.71 (0.60–0.83)
Relative power from 1 to 6 Hz	0.80	0.52 (0.41–0.63)	0.90 (0.86–0.93)	0.61 (0.49–0.72)	0.86 (0.82–0.90)	4.87 (3.19–7.43)	0.59 (0.47–0.71)
Sensitivity 90%							
Relative delta power (1–4 Hz)	0.37	0.90 (0.82–0.96)	0.36 (0.30–0.42)	0.30 (0.24–0.36)	0.92 (0.85–0.96)	1.38 (1.23–1.55)	0.30 (0.16–0.57)
Relative power from 1 to 6 Hz	0.51	0.90 (0.82–0.96)	0.42 (0.36–0.48)	0.32 (0.26–0.39)	0.94 (0.87–0.97)	1.58 (1.39–1.79)	0.25 (0.13–0.46)
Youden's index							
Relative delta power (1–4 Hz)	0.59	0.68 (0.57–0.77)	0.77 (0.71–0.82)	0.47 (0.38–0.56)	0.89 (0.84–0.92)	2.88 (2.88–3.73)	0.42 (0.31–0.58)
Relative power from 1 to 6 Hz	0.76	0.61 (0.49–0.71)	0.86 (0.81–0.90)	0.57 (0.46–0.68)	0.88 (0.83–0.91)	4.30 (3.06–6.02)	0.46 (0.35–0.60)

multicentre study with a large sample size. We used a thorough diagnostic work-up that included the DRS-R-98 and the CAM-ICU administered by well-trained researchers. The final diagnosis was based on the judgment of two or three delirium experts who evaluated all available information truly independently. Moreover, the availability of preoperative assessments facilitated the diagnosis of postoperative delirium. All experts had extensive experience in diagnosing delirium.

Several limitations of this study need to be addressed. Firstly, 7.1% of EEG recordings had to be excluded for analysis because of technical difficulties. Secondly, EEG recordings were performed once a day, which might have resulted in overlooking periods of slowing of the EEG. Thirdly, we analysed repeated measures of each patient as independent observations which could have influenced the results. However, this is unlikely as restriction to T1, T2, or T3 assessments separately resulted in similar results to the analysis of all postoperative recordings. Fourthly, as this study only included older surgical patients during the first 3 postoperative days, the results may not be generalisable to other patients. Finally, it could be argued that observed differences in EEG characteristics between patients classified with or without (possible) delirium were the result of differences in drowsiness, sleep, or administration of benzodiazepines or opioids. However, stratified analyses based on the administration of benzodiazepines and opioids in the preceding 24 h yielded similar results.

Our findings suggest that a simple one-channel EEG recording with a simple algorithm calculating the relative delta power (1–4 Hz) or relative power from 1 to 6 Hz is an approach that could be used to monitor delirium by bedside nurses as part of the clinical routine, especially in the ICU setting where nurses monitor a broad range of information. An objective delirium monitor with a continuous scale, instead of a dichotomised outcome, would be a major step forward for both clinical practice and research on delirium. Currently used tools to estimate delirium have subjective elements and disappointing sensitivity in routine daily practice,[18,19] where numerous nurses assess delirium at different time points. Before a delirium monitor can be used in clinical or research settings, several steps are required. Firstly, the current study is a technical validation of a prototype monitor. Optimising feasibility with input from nurses and patients is necessary for successful implementation. Secondly, diagnostic performance of the algorithm could be further optimised. This includes the use of different algorithms simultaneously and real-time automatic artifact detection and rejection. Moreover, we included two less frequently used measures for relative powers (relative power from 1 to 5 Hz and relative power from 1 to 6 Hz) based on previous literature[40] as exploratory

Table 3 Correlation of relative delta power (1–4 Hz) and relative power from 1 to 6 Hz with the likelihood and severity of delirium, attention, and consciousness level. CI, confidence interval; DRS-R-98, delirium rating scale revised '98; NRS, numeric rating scale; RASS, Richmond agitation and sedation scale

	Relative delta power (1–4 Hz) Fp2-Pz		Relative power (1–6 Hz) Fp2-Pz	
	Correlation coefficient (95% CI)	P-value	Correlation coefficient (95% CI)	P-value
Likelihood of delirium, (NRS)	0.33 (0.23–0.42)	<0.001	0.38 (0.28–0.47)	<0.001
Severity of delirium, (DRS-R-98)	0.39 (0.29–0.47)	<0.001	0.44 (0.34–0.53)	<0.001
Attention level, (item 10 of DRS-R-98)	0.27 (0.17–0.37)	<0.001	0.31 (0.21–0.40)	<0.001
Level of consciousness, (RASS)	−0.29 (−0.38 to −0.19)	<0.001	−0.30 (−0.40 to −0.19)	<0.001

analyses, thereby correcting for multiple testing. Further research should confirm the reliability of these EEG parameters in relation to delirium. Thirdly, the optimal number of recordings per day should be established. Fourthly, the results should be evaluated in other patient populations, such as ICU patients being sedated and dementia patients. Both use of sedatives and dementia result in slowing of the EEG,[4,46,47] and may therefore interfere with the current algorithm. Finally, the relation of EEG parameters with factors associated with (postoperative) delirium (e.g. age, use of benzodiazepines, history of delirium or previous stroke) should be studied, and could be combined in a multivariate model to optimize delirium diagnosis.

Delirium involves a continuum of mental status changes that can be mild or severe. A continuous scale to monitor delirium thus seems to be more appropriate than a dichotomised score. To improve the current gold standard, analysis of a delirium expert using DSM-5 criteria, we acknowledge that external validation is required. This could be achieved by comparing the continuous scale with the gold standard diagnosis in predicting long-term cognitive dysfunction.

Our findings suggest that delirium and possible delirium can be detected in older postoperative patients using a 1 min single-channel EEG recording analysed automatically. This method could enable objective detection of delirium, providing a continuous scale instead of a dichotomised outcome.

Authors' contributions

Study concept and design: T.N., L.M.P., A.J.C.S.
Data collection: T.N., M.vd.B., A.M.K., P.J.T.R., A.J.C.S.
Analysis: T.N., L.M.P.
Preparation and revision of the manuscript: T.N., M vd.B., A.M.K., P.J.T.R., L.M.P., A.J.C.S.
Classification of delirium: M.vd.B., A.M.K., A.J.C.S.

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Declarations of interest

A.J.C.S. has the following patent pending: Method and system for determining a parameter which is indicative for whether a patient is delirious. A.J.C.S. develops EEG-based monitors for delirium detection in routine, clinical practice.

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Appendix A. Supplementary data

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