Conflict of interest: unrelated to the topic, CSM is a founder of a start-up company, WARD24/7 ApS, with the aim of pursuing the regulatory and commercial activities of the WARD-project (Wireless Assessment of Respiratory and circulatory Distress, a project developing a clinical support system for continuous wireless monitoring of vital signs). WARD24/7 ApS has obtained license agreement for any WARD-project software and patents. One patent has been filed: ''Wireless Assessment of Respiratory and circulatory Distress (WARD), EP 21184712.4 and EP 21205557.8''.

Presentation: none.

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INFOGRAPHIC

Extracting electroencephalogram aperiodic activity from intraoperative frontal α-band power does not modify its association with delirium after cardiac surgery

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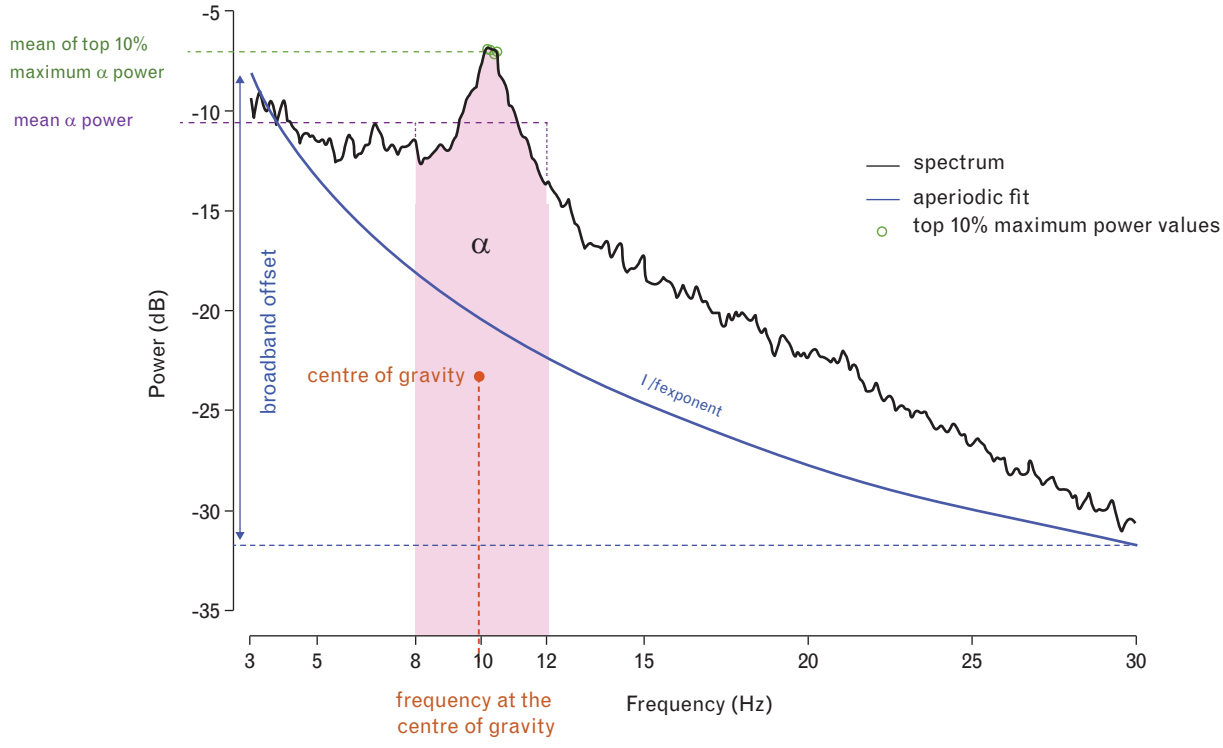
Editor,

Different electroencephalogram (EEG) features, as potential predictors of postoperative neurocognitive disorders, are currently the subject of extensive research. One promising marker is the magnitude of the α-band power under general anaesthesia. More specifically, it has been shown that a lower intraoperative frontal α-band power is associated with a higher incidence of postoperative delirium (POD).[1] It is now increasingly recognised that the EEG signal comprises both oscillatory and nonoscillatory components.[2] Separation of these components has not been considered in most clinical studies, but it has been suggested that the nonoscillatory or aperiodic activity of the EEG might influence previous estimates of the magnitude of oscillatory components such as α-band power.[3] Indeed, variations in the amount of aperiodic activity will influence estimates of oscillatory power such as maximum power, mean power or power at the centre of gravity, and prior extraction of the aperiodic activity may lead to better estimates of true oscillatory power and centre of gravity.[4] The aim of this study was to investigate whether the aperiodic activity significantly influenced α-band estimates observed in patients classified into two groups according to the presence or absence of POD by characterising their oscillatory activity once the modelled aperiodic activity was removed from individual spectra. We additionally assessed whether the aperiodic components were significantly different between both groups.

The current study is an exploratory analysis of a prospective observational trial in which we found that a lower frontal EEG α-band power under general anaesthesia was associated with the occurrence of POD in cardiac surgery patients.[1] The protocol was approved by the 'Comité d'Ethique Hospitalo-Facultaire' of Cliniques universitaires Saint-Luc, Brussels, Belgium (B403201837550 – chairman Professor J.M. Maloteaux) on September 2018, and registered in clinicaltrials.gov (NCT03706989) before the start of the study. From May 2019 to December 2021, we included 220 adult patients who underwent a first elective cardiac surgery with cardiopulmonary bypass in our institution. After written consent, an intraoperative 5-min EEG recording was collected using a 32-channel BioSemi ActiveTwo EEG recording system (BioSemi B. V., Amsterdam, The Netherlands) approximately 30 min after the induction of anaesthesia, but before the surgical incision. Sevoflurane was used for the maintenance of general anaesthesia, and intraoperative administration of ketamine was prohibited as per protocol. Enrolled patients were screened for POD by trained nurses using the Confusion Assessment Method for Intensive Care Unit (ICU) in the ICU, the Confusion Assessment Method in the ward, and a chart review by the research staff, two to three times a day from ICU admission to hospital discharge. EEG preprocessing steps are detailed in the main article.[1] To characterise the aperiodic activity, two parameters obtained from the aperiodic model fit computed using the FOOOF (Fitting Oscillatory and One Over F) toolbox[4] were extracted: the 'aperiodic exponent' and the 'broadband offset' (Fig. 1). EEG data were converted into dB before statistical analyses. Comparisons between patients with and without POD were performed using either Mann–Whitney U test or Student t test (depending on normality assumption), or using the χ^2 test.

Characteristics and perioperative clinical data of the cohort are detailed in Table 1. Sixty-five patients (29.5%) developed POD. Delirious patients were significantly older with

Fig. 1 Power spectrum including the investigated oscillatory and nonoscillatory EEG parameters.



Alpha (α)-band was canonically defined as 8 to 12 Hz. Oscillatory parameters included the mean α power, the maximum α power (calculated as the mean of the 10% frequency bins) and the frequency at α centre of gravity. Aperiodic exponent corresponds to the factor of the exponential decay of power ($1/f^{exponent}$), which corresponds to the negative slope of a linear fit of the spectrum in a log−−log space. The broadband offset refers to the shift in power throughout the frequency of interest.

a median [interquartile range, IQR] age of 74 [64 to 79] vs. 67 [59 to 74] years ($P < 0.001$) and had higher European System for Cardiac Operative Risk Evaluation (EuroSCORE) II scores, 2.4 [1.3 to 4] vs. 1.5 [0.9 to 2.5]% ($P < 0.001$). After extraction of aperiodic activity from the EEG power spectra, patients who experienced POD still had significantly lower frontal mean α-band power: -15.08 ± 5.69 vs. -12.17 ± 3.62 dB ($P < 0.001$) and maximum α-band power, -12.07 ± 5.93 vs. -9.25 ± 4.04 dB ($P < 0.001$) under general anaesthesia. Delirious patients also had significantly lower values of both broadband offset: -7.93 ± 4.18 vs. -6.04 ± 3.98 dB ($P = 0.002$) and aperiodic exponent, 3.22 ± 0.61 vs. 3.42 ± 0.60 dB Hz^{-1} ($P = 0.028$).

This exploratory secondary analysis first showed that extraction of the aperiodic components from the EEG spectrum does not eliminate the previously described association between lower frontal intraoperative oscillatory α-band power and the occurrence of POD in our cohort.[1] This observation has an important clinical significance. Indeed, it suggests that intraoperative mean α-band power, with or without considering aperiodic activity, remains a useful neurophysiological marker of a higher risk of delirium after surgery. Similar results have been recently published by Ostertag *et al.*[5] in a cohort of 169 surgical patients. In their *post hoc* secondary analysis, the authors showed that α-band power, even after removal of aperiodic activity using the FOOOF algorithm, was significantly higher in patients who did not develop POD in the postanaesthesia care unit (PACU), compared with patients who did experience it. They also observed that both conventional and FOOOF-derived power spectra can be used to effectively distinguish between patients with and without POD in the PACU during early to middle stages of emergence from anaesthesia.

Secondly, we found that both the broadband offset and the aperiodic exponent were significantly lower in patients who developed POD. Similar results on broadband offset values were recently published in two distinct surgical cohorts.[5,6] The exact physiological significance of aperiodic brain activity has not been completely elucidated yet. However, once merely considered as 'noise', this non-oscillatory component of the EEG is now thought to contribute to transitions between different brain states, including during anaesthesia.[7] More specifically, it is hypothesised to be involved in excitatory-inhibitory

Table 1 Characteristics and perioperative clinical data of the cohort

	Nondelirious patients ($n = 155$)	Delirious patients ($n = 65$)	P value
Preoperative data			
Age (years)	67 [59 to 74]	74 [64 to 79]	<0.001*[a]
Sex (male)	128 [82.6]	52 [80.0]	0.651[c]
EuroSCORE II (%)	1.5 [0.9 to 2.5]	2.4 [1.3 to 4.0]	<0.001*[a]
Mini-Mental State Examination (/30)	29 [27 to 29]	28 [26 to 29]	0.047*
Intraoperative data			
α-band (8 to 12 Hz) components before extraction			
Mean α-band power (dB)	−11.59 ± 3.37	−14.03 ± 4.61	<0.001*[b]
Maximum α-band power (dB)	-8.85 ± 3.90	−11.36 ± 5.28	<0.001*[b]
α centre of gravity (Hz)	9.92 ± 0.38	9.85 ± 0.40	0.243[b]
α-band (8 to 12 Hz) components after extraction			
Flattened mean α-band power (dB)	−12.17 ± 3.62	−15.08 ± 5.69	<0.001*[b]
Flattened maximum α-band power (dB)	−9.25 ± 4.04	−12.07 ± 5.93	<0.001*[b]
Flattened α centre of gravity (Hz)	9.95 ± 0.43	9.91 ± 0.56	0.614[b]
Aperiodic components			
Broadband offset (dB)	−6.04 ± 3.98	−7.93 ± 4.18	0.002*[b]
Aperiodic exponent (dB Hz^{-1})	3.42 ± 0.60	3.22 ± 0.61	0.028*[b]
Type of surgery			0.180*[c]
Isolated CABG	74 (47.7)	26 (40.0)	
Single non-CABG	35 (22.6)	10 (15.4)	
2 interventions	30 (19.4)	20 (30.8)	
3 interventions or more	16 (10.3)	9 (13.8)	
Surgical time (min)	226 ± 57	238 ± 60	0.170[b]
Cardiopulmonary bypass time (min)	99 ± 33	112 ± 40	0.015*[b]
Postoperative data			
Mechanical ventilation time (hours)	7.3 ± 3.4 (n = 152)	9.8 ± 6.6	0.005*[b]
Intensive care unit length of stay (days)	2 ± 1	4 ± 3	0.004*[b]
Hospital length of stay (days)	8 [7 to 9]	8 [7 to 11]	0.006*[a]

Data are presented as mean ± SD, median [IQR], or n (%). The number of patients with available data are shown at the top of the columns. CABG, coronary artery bypass grafting; EuroSCORE, European System for Cardiac Operative Risk Evaluation. * $P < 0.05$. P values refer to group comparisons by [a]Mann–Whitney U test; [b]Student t test; [c]χ^2 test.

(E/I) neurotransmission balance in cortical circuits.[4] Delirium has been associated with impaired E/I balance and disrupted cortical connectivity.[8] It may thus manifest through alterations in the aperiodic components. Moreover, changes in broadband offset have been interpreted as markers of total neural spiking activity, which might underlie the lower offset values observed in delirious patients.[5,6] Interestingly, the aperiodic activity has also been associated with age-related changes in cognition and speed of information processing.[9]

Limitations have to be mentioned. First, this study was a secondary exploratory analysis of a previous prospective cohort, and as such, it was not originally designed to test hypotheses about the physiological mechanisms linking aperiodic activity and POD. Then, the study cohort was restricted to patients undergoing cardiac surgery under sevoflurane anaesthesia, which may limit the generalisability of the findings to other surgical populations or anaesthetic agents.

Altogether, our results confirm that intraoperative frontal α-band power is a promising predictor of POD even without considering the aperiodic component of the EEG spectrum. Our observations also suggest perspectives in clinical research on nonoscillatory EEG features that might potentially be associated with postoperative neurocognitive disorders, especially in older and/or more vulnerable patients.

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Conflict of interest: none.

Presentation: preliminary results of this explanatory study have been presented at the annual congress of the European Society of Anaesthesiology and Intensive Care (Euroanaesthesia) on May 2024 in Munich, Germany.

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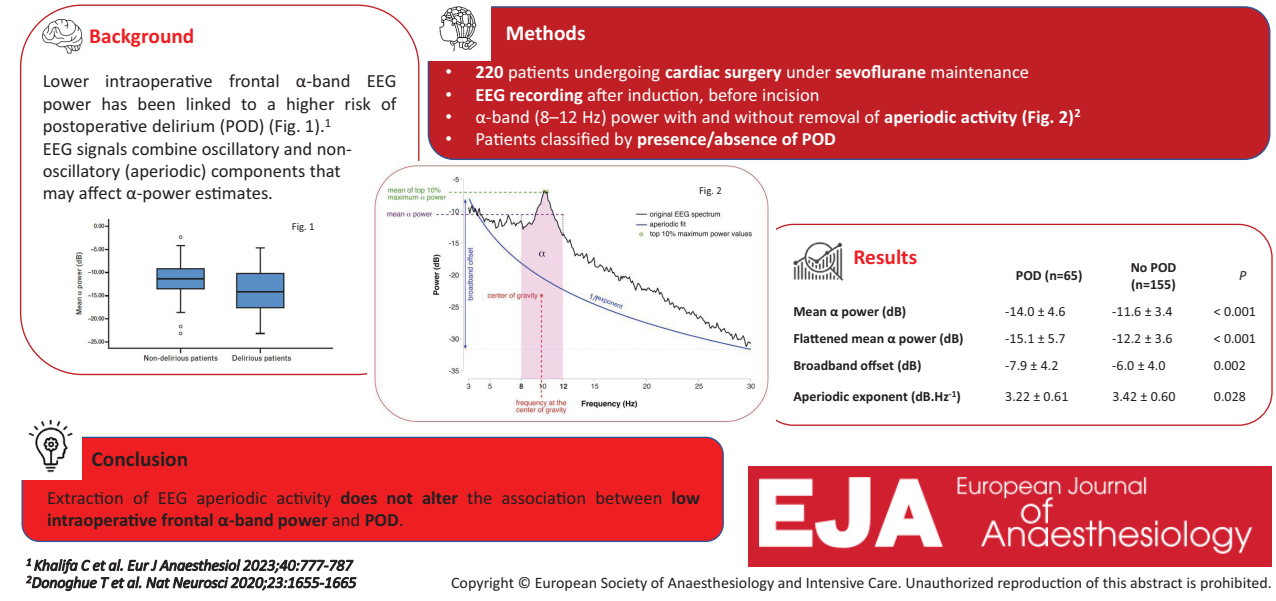
VISUAL ABSTRACT

Extracting electroencephalogram (EEG) aperiodic activity from intraoperative frontal alpha-band power does not modify its association with delirium after cardiac surgery



Double dural puncture epidural; once is more than enough

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Editor,

We read with interest the recently published trial titled 'Double dural puncture epidural improves quality of labour analgesia without increasing adverse effects in primipara'.[1]

The authors conducted a randomised controlled trial assessing a double dural puncture epidural (DDPE) technique. With DDPE, a Tuohy needle is inserted into the epidural space with the bevel directed caudally, a spinal needle is introduced, then the Tuohy needle is rotated 180 degrees, and the spinal needle is reintroduced. They concluded that DDPE improved labour analgesia quality without increasing adverse effects. Although small analgesic benefits were shown, we are very concerned that the safety claim of 'without increasing adverse effects' is not warranted for a trial of this size. There is clinical evidence that this technique may significantly increase the risk of post dural puncture headache (PDPH), both through accidental dural trauma sustained by rotating the Tuohy 180 degrees,[2] and by intentional double dural puncture with the 25-gauge spinal needle.

In a standard trial, a result of $P > 0.05$ means 'there is insufficient evidence to say there is a difference'. It does not mean 'there is no difference'. Unfortunately, with only 120 participants (60 per group), the trial was markedly underpowered to detect clinically relevant differences in PDPH. Whether DDPE increases the risk of PDPH could only be answered in a very large trial. For example, in a noninferiority trial design, assuming a 1 to 2%