4 Gagnier JJ, Kienle G, Altman DG, *et al.* The CARE guidelines: consensus-based clinical case reporting guideline development. *BMJ Case Rep* 2013; **53**:1541–1547.

5 MacLennan AI, Smith AF. An analysis of critical incidents relevant to pediatric anesthesia reported to the UK National Reporting and Learning System, 2006–2008. *Paediatr Anaesth* 2011; **21**: 841–847.

6 Patient Safety Alert NHS/PSA/RE/2017/004: Resources to support safe transition from the luer connector to NRFitTM for intrathecal and epidural procedures, and delivery of regional blocks. NHS Improvement. 2017. https://improvement.nhs.uk/documents/1550/Patient_Safety_Alert_-_resources_to_support_transition_to_NRFit_Aug_2017v2.pdf [Accessed 10 December 2020]

DOI:10.1097/EJA.0000000000001460

OPEN

Brain fragility among middle-aged and elderly patients from electroencephalogram during induction of anaesthesia

Jerome Cartailler*, Cyril Touchard*, Pierre Parutto, Etienne Gayat, Claire Paquet* and Fabrice Vallée*

From the Department of Anesthesiology and Intensive Care, Lariboisière – Saint Louis Hospitals, Paris, France (JC, CT, EG, FV), UK Dementia Research Institute at the University of Cambridge and Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK (PP), Cognitive Neurology Center, Lariboisière Hospital Université de Paris (CP), INSERMU1144, Université de Paris, Paris (CP) and MEDISIM, Inria Paris-Saclay, Palaiseau, France (FV)

Correspondence to Jerome Cartailler, PhD, Department of Anesthesiology, Hopital Lariboisiere, APHP, Paris, France
E-mail: jerome.cartailler@inserm.fr

*Jerome Cartailler, Cyril Touchard, Claire Paquet and Fabrice Vallée have contributed equaly to this work.

Editor,

Cognitive decline is a common condition amongst the elderly, affecting memory, language or thinking. Patients experiencing cognitive decline have a higher incidence of postoperative neurocognitive disorders.[1] Moreover, for a fraction of these patients, occurrence of intra-operative burst suppressions result in postoperative delirium.[1] It is, therefore, important to know patients' cognitive status to adapt anaesthesia and postoperative care. Cognitive decline is routinely assessed through neurocognitive evaluation with first onset occurring around 50 years old, and affecting about 40% of patients.[1] However, with one-third of people over 50 years old scheduled for surgery, a systematic evaluation beforehand is difficult if not impossible in clinical practice.

We proposed to take advantage of general anaesthesia to address this issue. Anaesthesia is a controlled procedure during which cerebral activity can be monitored with a frontal electroencephalogram (EEG). Specifically, propofol-induced general anaesthesia exhibits a characteristic EEG signature constituting simultaneous frontal slow waves (<1 Hz) and α-waves (8 to 14 Hz), with several studies outlining the association between α-waves and cognitive decline or burst suppressions.[2–4] However, both cognitive decline and α-wave changes are age-dependent.[5] In this letter, we describe a prospective study of patients aged more than 50 years in whom the propofol target brain concentration was set to 5 $\mu g\,ml^{-1}$ during induction of general anaesthesia.

The Probrain Study (ID NCT0387637) was approved by the Société de Réanimation de Langue Française ethics committee CE SRLF 11-356 on 5 January 2016 (Chairperson Dr Jean Reignier). Patients were provided with an information letter and verbal consent was obtained before anaesthesia.

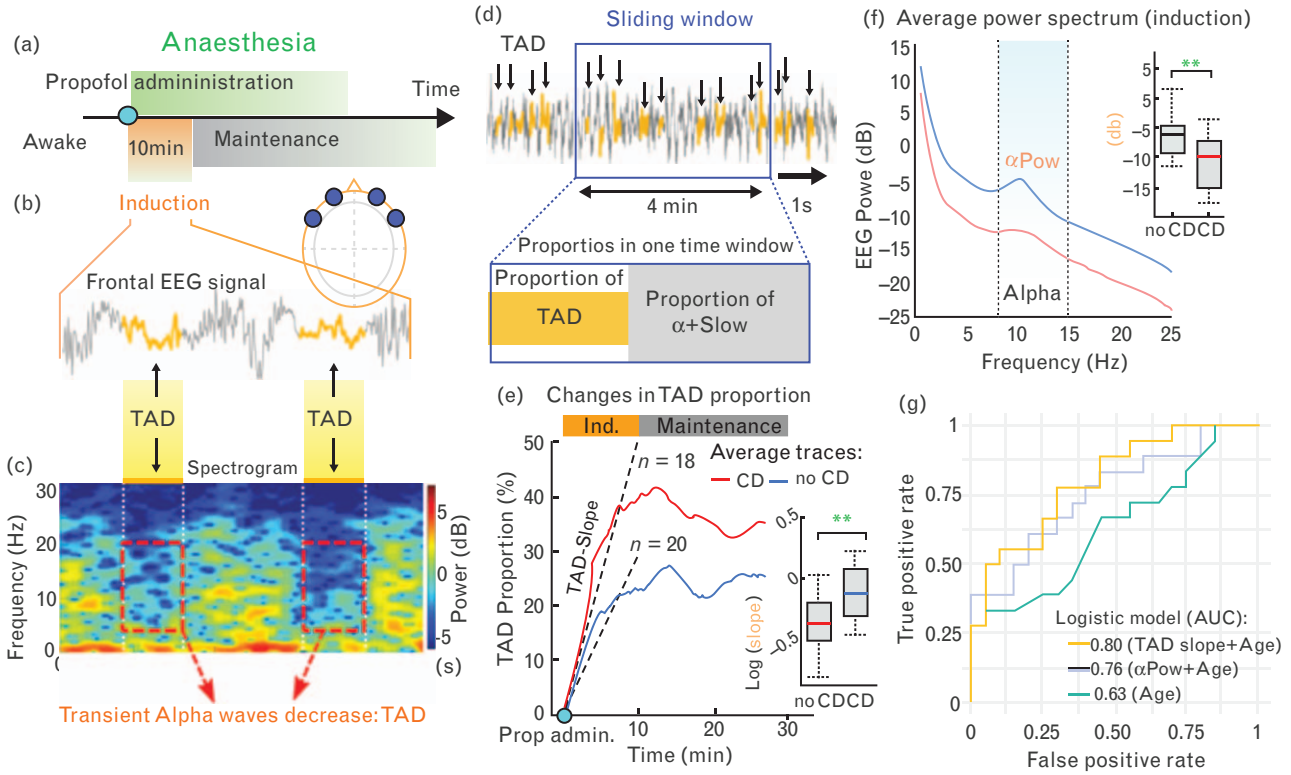
Patient selection, anaesthetic protocol, EEG collection/analysis, the Montreal Cognitive Assessment method (MoCA) for cognitive decline assessment and α-band power (αPow) detection are described elsewhere by Touchard *et al.*[6] The α-wave transient amplitude decreases (TAD) slope was computed; then log-transformed using the α-suppression pipeline described by Cartailler *et al.*[7] The induction period corresponds to the first 10 min following α-wave onset. Sample size (n=32) was estimated for $\alpha = 0.05$ and $\beta = 85\%$ [odds ratio (OR) = 3, P0 = 0.46, $R^2 = 0.05$, age-adjusted logistic models). The two-tailed Mann–Whitney test was used for group comparisons. For OR estimation, αPow at least −13 dB were mapped to −13dB.

We focused on predicting cognitive decline, characterised using MoCA, performed 1 day before anaesthesia. During the period of induction of anaesthesia, we analysed αPow and TAD (Figs. 1a–c), the low amplitude components of intra-operative α-oscillations that have been shown to predict onset of burst suppression.[7] Given the variability of the EEG signal during the induction period, we tested a dynamic biomarker (TAD) and compared it with αPow, a standard parameter of EEG spectral analysis.

We included 38 patients (aged 69 ± 10.6 years, 34.2% women), 25 of whom underwent orthopaedic surgery and 13 a neuroradiology intervention. Patients were divided into two groups: cognitive decline [n=18 (47%), MoCA <25 points] and no cognitive decline (NoCD) [n=20 (53%), MoCA ≥25 points]. The total dose of propofol administered during induction and the age were not significantly different between the two groups (Table 1).

Every second, we estimated the fraction of the EEG signal represented by TADs over the last 4 min (Fig. 1d) and used the slope of this time series as a variable (TAD slope, Fig. 1e, dashed-black). We found that αPow and TAD slope measured during the first 10 min of induction

Fig. 1 Increase of α-wave transient amplitude decreases during the 10 first minutes of general anaesthesia is linked to preoperative cognitive decline



(a) Schematic representation of peri-anaesthesia periods. (b) Example of electroencephalogram signal (grey) with two TADs (yellow). (c) Spectrogram associated with B revealing two spots with low α power. (d) TAD proportion estimation every second using a sliding window. (e) Time series of TAD proportion. Averaged traces for patient with (red) and without (blue) cognitive decline. TAD slopes are shown as black dashed lines. (f) Average power spectral density for cognitive decline (red) and no cognitive decline (NoCD) (blue) patients. (g) ROC curves and their AUC obtained from adjusted logistic models. AUC, area under the curve; CD, cognitive decline; EEG, electroencephalogram; ROC, receiver operating curve; TAD, α-wave transient amplitude decreases.

were significantly different between cognitive decline and NoCD groups ($P = 0.007$ and $P = 0.004$ respectively, Fig. 1e and d); a larger TAD slope was associated with cognitive decline (or was a biomarker of cognitive decline), independently of age [adjusted OR = 4.01 (1.44 to 11.20), $P = 0.008$, AUC = 0.80, logistic model]; and a weaker αPow was significantly linked with cognitive decline [adjusted/corrected OR = 0.33 (0.14 to 0.78), $P = 0.011$, AUC = 0.76, Fig. 1g).

In summary, a rapid TAD increase as well as a αPow decrease measured during the first 10 min of a propofol-induced general anaesthesia were associated with lower preoperative MoCA scores. These results confirm previous findings from Giattino *et al.*,[3] Koch *et al.*[4] and recently Shao *et al.*,[2] linking intra-operative α-band measured during the maintenance period to preexisting cognitive impairments. We also confirmed that this effect persists independently of patients' age and the dose of propofol

Table 1 Main characteristics of patients with and without cognitive decline

Variables	All (*n*=38)	CD (*n*=18)	No CD (*n*=20)	*P*
Age (years)	69.3 ± 10.7	72.2 ± 11.8	66.7 ± 9.2	0.058
Female	13 (34.2)	7 (38.9)	6 (30.0)	0.495
Education level (≤12 years)	19 (50)	11 (61)	8 (40)	0.194
Hypertension	25 (65.8)	13 (72.2)	12 (60)	0.728
Smoker/obese/diabetic patient (%)	5.3/21.1/13.1	11.1/22.2/11.1	10/20/15	–
Induction EEG markers (first 10 min)				
TAD slope (% min^{-1})	8.90	11.47	5.9	0.004
αPow (dB)	−8.3 [−11.1 to −4.9]	−9.9 [−15.3 to −7.3]	−6.2 [−8.8 to −4.5]	0.007
Propofol dose (mg)	195 [187 to 208]	194 [177 to 201]	201 [191 to 213]	0.058
Time in BS (s)	5.3 [0 to 12.3]	10.6 [2.2 to 93.3]	1.46 [0 to 8.4]	0.031

Values are mean ± SD, median [IQR] or number (%). BS, burst suppression; CD, cognitive decline; αPow, frontal alpha rhythm power; TAD, transient alpha decrease; TCI, target-controlled infusion.

administered during anaesthesia induction. In addition, we showed that the EEG brain response to general anaesthesia, captured during induction, could be a proxy for cognitive decline.

Although our study focused on the relationships between α-band (maximal α power) variables and cognitive decline, a larger EEG database might improve cognitive decline detection using multivariate analysis of EEG variables and comorbidities. Furthermore, the systematic initial 5 $\mu g\,ml^{-1}$ target concentration used here would not suit very fragile patients (despite infusion models adapting for age, sex, height and weight). Thus, further studies should explore the present findings for various propofol target-control systems.

We previously showed that the TAD slope measured during induction captured patient propensity to burst suppression.[6] We now suggest that it also correlates with the patient's cognitive status. TAD measured at the beginning of general anaesthesia might reflect brain sensitivity to anaesthetics and probably reveal cognitive impairment, while also screening for patients for whom maintaining an appropriate depth of anaesthesia will be challenging.

The present method is not a substitute for a neurocognitive evaluation, but a possible complementary examination for guiding postoperative care, optimising intra-operative anaesthesia or referring patients to a neurologist.

Acknowledgements relating to this article

Assistance with the letter: none.

Financial support and sponsorship none.

Conflicts of interest: CP is member of the International and National Advisory Boards of Lilly, Roche and Biogen. She is consultant of Fujiribio, Alzohis, Neuroimmune and Gilead, and is involved as investigator in several clinical trials for Roche, Esai, Lilly, Biogen, Astra-Zeneca, Lundbeck, Neuroimmune. No other conflicts of interest.

References

1 Fritz BA, King CR, Ben Abdallah A, *et al.*, ENGAGES Research Group. Preoperative cognitive abnormality, intraoperative electroencephalogram suppression, and postoperative delirium: a mediation analysis. *Anesthesiology* 2020; **132**:1458–1468.
2 Shao YR, Kahali P, Houle TT, *et al.* Low frontal alpha power is associated with the propensity for burst suppression: an electroencephalogram phenotype for a 'vulnerable brain'. *Anesth Analg* 2020; **131**:1529–1539.
3 Giattino CM, Gardner JE, Sbahi FM, *et al.*, MADCO-PC Investigators. Intraoperative frontal alpha-band power correlates with preoperative neurocognitive function in older adults. *Front Syst Neurosci* 2017; **11**:24.
4 Koch S, Feinkohl I, Chakravarty S, *et al.* Cognitive impairment is associated with absolute intraoperative frontal (-band power but not with baseline (-band power: a pilot study. *Dement Geriatr Cogn Disord* 2019; **48**:83–92.
5 Purdon PL, Pavone KJ, Akeju O, *et al.* The ageing brain: age-dependent changes in the electroencephalogram during propofol and sevoflurane general anaesthesia. *Br J Anaesth* 2015; **115 (Suppl 1)**:i46–i57.
6 Touchard C, Cartailler J, Levé C, *et al.* Propofol requirement and EEG alpha band power during general anaesthesia provide complementary views on preoperative cognitive decline. *Front Aging Neurosci* 2020; **12**:593320.
7 Cartailler J, Parutto P, Touchard C, *et al.* Alpha rhythm collapse predicts iso-electric suppressions during anaesthesia. *Commun Biol* 2019; **2**:1–10.

DOI:10.1097/EJA.0000000000001524