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

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

▶ **To cite this version:**

Jerome Cartailler, Cyril Touchard, Pierre Parutto, Etienne Gayat, Claire Paquet, et al.. Brain fragility among middle-aged and elderly patients from electroencephalogram during induction of anaesthesia. European Journal of Anaesthesiology, 2021, 38 (12), pp.1304-1306. 10.1097/EJA.0000000000001524 . hal-03487108

HAL Id: hal-03487108
https://hal.inria.fr/hal-03487108

Submitted on 17 Dec 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Brain fragility among middle-aged and elderly patients from the anaesthesia induction EEG

J. Cartailler[*,a], C. Touchard[*,a], P. Parutto[b], E. Gayat[a], C. Paquet[†,c,d], F. Vallée[†, a, e]

Corresponding author: Jerome Cartailler, jerome.cartailler@inserm.fr, *, † : This authors contributed equally.

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

We propose to take advantage of general anaesthesia (GA) to address this issue; a controlled procedure where the cerebral activity can be monitored with a frontal ElectroEncephaloGram (EEG). Specifically, propofol-induced GA exhibits a characteristic EEG signature composed of simultaneous frontal slow (<1 Hz) and α (8-14Hz) waves with several studies outlining the association between α waves and CD or burst-suppressions[2–4]. However, both CD and alpha-wave changes are age-depended[5]. In this letter, we proceed with a prospective study, for patient age above 50yo. and for whom the propofol target brain concentration was systematically set to 5μg/ml during the GA induction.

We focus on predicting CD, characterized using the Montreal Cognitive Assessment method (MoCA), performed one day before GA. From anaesthesia's induction period, we analyse α-band power (αPow) and α waves transient amplitude decrease: TAD (Fig 1A-C), the low amplitude components of intra-operative alpha-oscillations that have been shown to predict burst-suppression onsets[6]. Given the non-stationarity of the EEG signal during the induction period, we tested a dynamic biomarker (TAD) and compared it to (αPow), a standard parameter of EEG spectral analysis.

We included 38 patients (69$\pm$10.6yr., 34.2% female), twenty-five underwent an orthopaedic surgery and 13 a neuroradiology intervention. Patients were divided into two groups: CD (n=18(47%), MoCA $<$ 25 points) and NoCD (n=20(53%), MoCA $\geq$25 points). The total dose of propofol administered during induction and the age were not significantly different between the two groups (see Table 1).

Every second, we estimated the fraction of the EEG signal represented by TADs over the last 4 minutes (Fig 1D) and used the slope of this time series as a variable (TAD-slope, Fig. 1E, dashed-black). We found that: 1. αPow and TAD-slope measured during the first 10 minutes of induction were significantly different between CD and NoCD groups (p=0.007 and p=0.004 respectively, Fig. 1E,F); 2. A larger TAD-slope was associated with CD (or was a biomarker of CD), independently of age (Adjusted OR = 4.01[1.44, 11.20], p=0.008, AUC = 0.80, logistic model); And 3. A weaker α Pow was significantly linked with CD (Adjusted/Corrected OR = 0.33[0.14, 0.78], p = 0.011, AUC = 0.76, Fig. G).

In summary, a rapid TAD increase as well as αPow decrease measured during the first 10 minutes of a Propofol-induced GA were associated to lower preoperative MOCA scores. These results confirm previous findings from Giattino, Koch, and recently Shao and their colleagues, retrospectively linking intra-operative α-band measured during the maintenance period to pre-existing cognitive impairments[2–4]. We also confirm that this effect persists independently of patients' age and the dose of propofol administered during anaesthesia induction. In addition, we show that the EEG brain response to GA, captured during induction, could be a proxy for CD.

Although our study focused on the relationships between alpha-band (maximal alpha power) variables and CD, a larger EEG database might improve CD detection using multivariate analysis of EEG variables and comorbidities. Furthermore, the systematic initial $5\mu g/ml$ 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 TCI.

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 patient's cognitive status. TAD measured at the beginning of GA 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 the post-operative care, optimizing intra-operative anaesthesia or even referring patients to a neurologist.

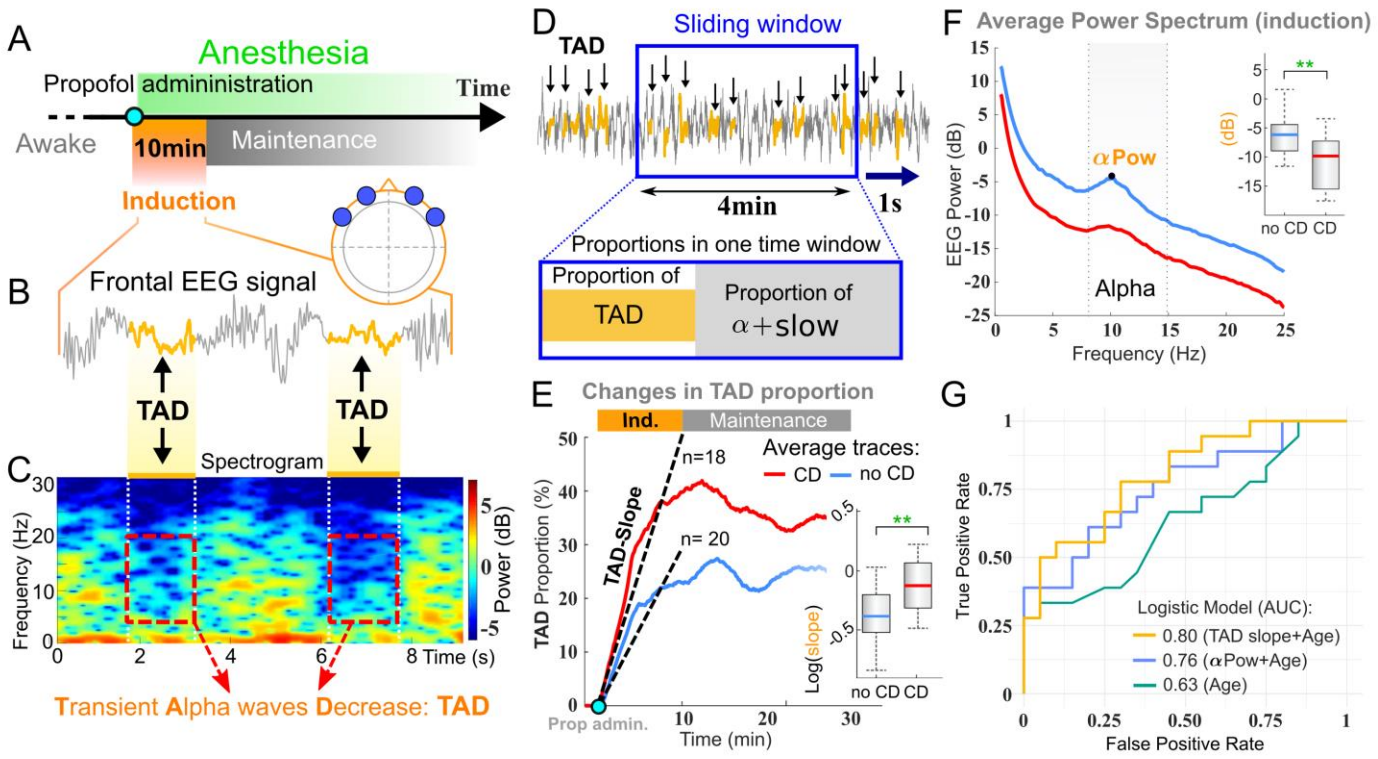

Figure 1: Increase of TAD during the 10 first minutes of GA is linked to pre-operative CD. A: Schematic representation of peri-anaesthesia periods. **B:** Example of EEG signal (grey) with two TADs (yellow). **C:** Spectrogram associated to B revealing two spots with low alpha power. **D:** TAD proportion estimation every second using a sliding window. **E:** Time series of TAD proportion. Averaged traces for patient with (red) and without (blue) CD. TAD-slope are shown as black dashed lines. **F:** Average power spectral density for CD (red) and no CD (blue) patients. **G:** ROC curves and theirs AUC obtained from adjusted logistic models.

METHODS: Study PROBRAIN ID NCT0387637, approved by the Société de réanimation de langue française ethics committee CE SRLF 11-356 05/01/2016 (Chairperson Dr Jean Reignier, 48, avenue Claude Vellefaux, Paris, France). Patients were provided an information letter and verbal consent was obtained before anaesthesia. Patient selection, anaesthetic protocol, EEG collection/analysis, MoCA for CD assessment, and αPow detection are described in[7]. The TAD-slope was computed then log-transformed using the alpha-Suppression pipeline in[6]. The induction period corresponds to the first ten minutes following alpha waves onset. Sample size (n=32) estimated for α=0.05 and β =85% (OR=3, P0=0.46, R2=0.05, age adjusted logistic models). Two-tailed Mann-Whitney test used for group comparison. For OR estimation, αP $\leq$ -13dB were mapped to -13dB. Authors declare no conflict of interest. JC-CT-CP-FV design the study and wrote the manuscript. JC-CT-PP-EG-CP-FV analysed and interpreted the data.

Table 1: Main characteristics of patients with and without cognitive decline (CD). 'BS' Burst-Suppression; 'αPow' frontal alpha rhythm power; 'TAD' transient alpha decrease, 'TCI' target controlled infusion.

Variables	**All (n = 38)**	**CD (n=18)**	**No CD (n=20)**	**p**
Age (yr.), *Mean±SD*	69.3±10.7,	72.2±11.8,	66.7±9.2,	0.058
Gender (female), *n (%)*	13 (34.2%)	7 (38.9%)	6 (30.0%)	0.495
Education level (≤12yr), *n(%)*	19 (50%)	11 (61%)	8 (40%)	0.194
Hypertension, *n(%)*	25 (65.8%)	13 (72.2%)	12 (60%)	0.728
Smoker; Obese; Diabetes (%)	5.3; 21.1; 13.1%	11.1; 22.2; 11.1%	10%; 20%; 15%	-
INDUCTION EEG MARKERS (10 FIRST MINUTES)				
$\boldsymbol{TAD}$-Slope (percentage per min.)	8.9[5.1, 6.5]	11.47[7.5, 8.2]	5.9[4.1, 4.9]	0.004
$\boldsymbol{\alpha}$Pow ($\boldsymbol{dB}$), *Median[IQR]*	-8.3[-11.1, -4.9]	-9.9[-15.3, -7.3]	-6.2[-8.8, -4.5]	0.007
Propofol Dose (mg), *Median[IQR]*	195[187, 208]	194[177, 201]	201[191, 213]	0.058
Time in BS (s), *Median[IQR]*	5.3[0, 12.3]	10.6[2.2, 93.3]	1.46[0, 8.4]	0.031

REFERENCES

1. Fritz, B. A. *et al.* Preoperative Cognitive Abnormality, Intraoperative Electroencephalogram Suppression, and Postoperative Delirium: A Mediation Analysis. *Anesthesiology* **132**, 1458–1468 (2020).
2. Shao, Y. R. *et al.* Low Frontal Alpha Power Is Associated With the Propensity for Burst Suppression: An Electroencephalogram Phenotype for a 'Vulnerable Brain'. *Anesth. Analg.* **131**, 1529–1539 (2020).
3. Giattino, C. M. *et al.* Intraoperative Frontal Alpha-Band Power Correlates with Preoperative Neurocognitive Function in Older Adults. *Front. Syst. Neurosci.* **11**, (2017).
4. Koch, S. *et al.* Cognitive impairment is associated with absolute intraoperative frontal α-band power but not with baseline α-band power: a pilot study. *Dement. Geriatr. Cogn. Disord.* **48**, 83–92 (2019).
5. Purdon, P. L. *et al.* The ageing brain: age-dependent changes in the electroencephalogram during propofol and sevoflurane general anaesthesia. *Br. J. Anaesth.* **115**, i46–i57 (2015).
6. Cartailler, J., Parutto, P., Touchard, C., Vallée, F. & Holcman, D. Alpha rhythm collapse predicts iso-electric suppressions during anaesthesia. *Commun. Biol.* **2**, 1–10 (2019).
7. Touchard, C. *et al.* Propofol Requirement and EEG Alpha Band Power During General Anaesthesia Provide Complementary Views on Preoperative Cognitive Decline. *Front. Aging Neurosci.* **12**, (2020).

Affiliations:

a) Department of Anesthesiology and Intensive Care, Lariboisière – Saint Louis Hospitals, Paris, France. b) UK Dementia Research Institute at the University of Cambridge and Department of Clinical Neurosciences, University of Cambridge, Cambridge CB2 0AH, UK. c) Cognitive Neurology Center, Lariboisière Hospital Université de Paris, Paris France. d) INSERMU1144, Université de Paris, Paris France. e) MEDISIM, Inria Paris-Saclay, Palaiseau, France.

Acknowledgements

Pr. C. PAQUET is member of the International and National Advisory Boards of Lilly, ROCHE, 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. Other authors declare no conflict of interest.