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Original Article

Electroencephalographic density spectral array monitoring during propofol/sevoflurane coadministration in children, an exploratory observational study

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ABSTRACT

Introduction: Propofol and sevoflurane have a long history in pediatric anesthesia. Combining both drugs at low dose levels offers new opportunities. However, monitoring the hypnotic effects of this drug combination in children is challenging, because the currently available processed EEG-based systems are insufficiently validated in young children and the co-administration of anesthetics. This study investigated electroencephalographic density spectral array monitoring during propofol/sevoflurane coadministration with fixed sevoflurane- and variable propofol dosages.

Patients and methods: We analyzed the density spectral array pattern recorded during propofol/sevoflurane anesthesia in pediatric patients from birth to 11 years of age. Data from 78 patients were suitable for analysis. The primary outcome parameter of this study was the correlation between variable propofol dosages and the expression of the four electroencephalogram frequency bands β, α, θ, and δ. The main secondary outcome parameters were the intra-operative total EEG power and the prevalence of burst suppression.

Results: In patients above the age of 1 year, a dose-dependent correlation between the propofol dosage and the relative percentage of β (−12.2%, $p < 0.001$) and δ (5.1%, $p < 0.001$) was found. There was an age-dependent trend toward increasing mean EEG power, with the most significant increase in the first year of life. In 14.1% of our patients, at least one episode of burst suppression occurred.

Conclusion: DSA-guided augmentation of propofol anesthesia with sevoflurane provides sufficient depth of anesthesia at doses usually considered sub-anesthetic in children, leading to less anesthetic drug exposure for the individual child.

Introduction

Both inhalation anesthesia with sevoflurane and intravenous infusion of propofol are commonly used techniques during general anesthesia. Both drugs have their own advantages: sevoflurane offers the opportunity to induce anesthesia through inhalation and has an additional dose-dependent analgesic effect [1,2], while propofol leads to less postoperative nausea and vomiting [3]. As recently demonstrated in adult patients [4–6], coadministration of propofol and sevoflurane combines the strengths of both drugs while fewer side effects occur [4,5]. However, a similar type of study in children is challenging because of the difficulties with anesthesia depth monitoring in children. Depth of hypnosis (DoH) monitoring using index-based processed electroencephalography has its limitations in pediatric patients due to the immature developing brain [7]. Unlike index-based DoH monitors, electroencephalographic density spectral array (DSA) monitoring, presents real-time EEG information with drug- and patient age-specific EEG signatures [7–10]. DSA is a unique two-dimensional approach to provide all the information of an originally three-dimensional plot, consisting of the EEG frequency (y-axis), the power of the EEG signal (originally the z-axis, but now color-coded to be integrated into a 2-d plot), and the development of the EEG power spectrum over time [8].

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To investigate propofol/sevoflurane coadministration with fixed sevoflurane- and variable propofol dosages in children we performed this exploratory observational study with DSA monitoring in pediatric patients aged 0−11 years. The primary outcome parameter of this study was the relationship between the propofol dosage and the relative power percentages of the EEG frequency bands of DSA presented as β (13−25 Hz), α (9−12 Hz), θ (5−8 Hz) and δ (1−4 Hz). The main secondary outcome parameters were the intra-operative total EEG power and the prevalence of burst suppression.

Patients and methods

This exploratory observational study was approved by the Institutional Review Board (IRB) of the Erasmus University Medical Center, Rotterdam, the Netherlands (MEC-2019-0673; October 14, 2019) and performed in accordance with the Declaration of Helsinki. All methods followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [11]. Written informed consent was obtained from all the children's parents or legal representatives.

We included patients from birth to 11 years of age, scheduled to undergo elective surgery at Erasmus MC-Sophia Children's Hospital, Rotterdam, the Netherlands, from June 2020 until June 2021. Anesthesia maintenance by coadministration of propofol and sevoflurane was the main inclusion criterion. Exclusion criteria were present neurological disease or chronic use of drugs that impact the EEG by affecting neurotransmitters such as antiepileptics or psychotropics. Other exclusion criteria were the need for premedication with midazolam or clonidine, and non-elective procedures.

Standard monitoring was applied, consisting of an electrocardiogram (ECG), a non-invasive blood pressure (NIBP), capnography, and pulse oximetry.

Electroencephalographic monitoring of the depth of anesthetic drug-induced hypnosis (DoH) was performed using the Narcotrend® EEG monitor (MT Monitortechnik, Bad Bramstedt, Germany). The Narcotrend calculates an index of hypnotic depth, the Narcotrend Index (NI), ranging from 100 (wakefulness) to 0 (very deep hypnosis). Besides this processed Narcotrend Index, the Narcotrend monitor also records the EEG power spectrum, relative power in Beta (β) (% β: 13−25 Hz), Alpha (α) (% α: 9−12 Hz), Theta (θ) (% θ: 5−8 Hz) and Delta (δ) (% δ: 1–4 Hz), and DSA. The Narcotrend monitor was attached to the patient's forehead, according to the manufacturer's recommendations, using three electrodes.

Induction was performed either intravenously (i.v.) with propofol or by inhalation of sevoflurane followed by a bolus of propofol of 1 mg/kg. After induction, anesthetic drug coadministration was started as a continuous infusion of propofol, and sevoflurane at a fixed end-tidal concentration (ET_{sevo}) of 0.5. The propofol dose was titrated by the attending anesthetist, aiming to maintain an adequate DoH defined by clinical parameters such as heart rate, blood pressure, and respiratory rate and a specific density spectral array pattern consisting of Delta and alpha activity and possibly beta activity [8,12].

Data collection

Intra-operative use of propofol, end-tidal sevoflurane, opioids, locoregional techniques, and the use of muscle relaxants were recorded. In addition, the start and end times of anesthesia and the start time of surgery were recorded. Any adverse events that occurred, such as laryngospasm, bronchospasm, arousal during the procedure, or a blood pressure drop of more than 2SD (adjusted for age and gender based on the reference values for noninvasive blood pressure in children during anesthesia) [13] were recorded. If a bolus of propofol was given either during induction or intraoperatively, the DSA data of the following 10 min were excluded from analysis, to avoid EEG contamination by the propofol bolus. At least 5 min after each change in propofol dose, the mean relative percentages of β, α, θ, and δ were calculated over a 10-s interval. To exclude the effect of fluctuations in ET_{sevo} concentration, only the measurements with an ET_{sevo} concentration of 0.5 were included in the analysis.

Mean total EEG power was calculated for each patient during the intraoperative phase, defined as 10 min after the start of surgery, for 5 min. Raw EEG data were continuously recorded in each patient and exported as Excel files for subsequent analyses using the EEG Viewer™ software package (Version 1.6, MT MonitorTechnik GmbH & Co. KG, Bad Bramstedt, Germany).

DSA patterns were visually assessed for the occurrence of burst suppression and the duration of any episode of burst suppression by IdH and FW.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics, version 27.0.1.0 SPSS Inc., Chicago, IL, USA) and GraphPad Prism (10) for Mac (version 10.0.3), GraphPad Software Inc., San Diego, CA, USA) for data visualization.

An alpha level of .05 was assumed for all tests. *p*-Values were interpreted after correcting for multiple comparisons through the Holm-Bonferroni method. Continuous variables were tested for normality with the Shapiro-Wilk normality test. Variables are presented as mean ± SD, median (IQR [range]), or number (proportion).

The relationship between the intraoperative total EEG power and age is visualized in a scatterplot with smoothing splines. The association between the propofol dose and the relative percentages of β, α, θ, and δ, were calculated through Generalized estimating equations (GEE).

The distribution and assumptions for each model were tested. The relative percentage of β, α, θ, and δ, were chosen as dependent variables. The propofol dose, weight, age, sex, opioid, muscle relaxant, and induction method as covariates.

Age subgroup analyses through GEE were done based on visual inspection of the scatterplot with smoothing splines.

Results

During the 1-year inclusion period, we collected data from 103 patients. Data from 25 patients had to be excluded from analysis for different reasons: data registration failure, such as surgical interference with the EEG signal or incomplete reporting by the investigator (n = 14), or a too short duration of surgery to calculate total EEG power or to establish an ET_{sevo} of 0.5% (n = 11). Data from 78 patients were suitable for analysis. The baseline characteristics of patients included in the study are shown in Table 1.

Relative power in β, α, θ, and δ frequency bands

Of all 78 patients, 185 different measurements were made of relative power in each frequency band at various propofol dosages. The number of measurements taken varied from 1 to 6 per patient.

GEE analyses revealed that the relative expression of β and δ frequency bands were significantly correlated with every increase of 1 mg kg^{-1} h^{-1} propofol, with a negative correlation in β, and a positive correlation in δ; details are presented in Table 2.

Table 1
Baseline characteristics.

Characteristic	*Patients (n = 78)*
Age (years)	1.0 (6 [0–11])
Weight (kg)	11.0 (13.8 [3.0–54.3])
Sex	
Male	64 (82%)
Female	14 (18%)
Induction method	
Intravenous	18 (23%)
Mask	60 (77%)
Muscle relaxant	
Rocuronium	4 (5%)
None	74 (95%)
Opioid	
Fentanyl	14 (18%)
Sufentanil	46 (59%)
Remifentanil	14 (18%)
None	4 (5%)
Additional analgesia	
Neuraxial/caudal	50 (64%)
Ilioinguinal	1 (1%)
Plexus block	6 (8%)
Local infiltration	5 (6%)
None	16 (21%)

Values are median (IQR [range]), number (proportion).

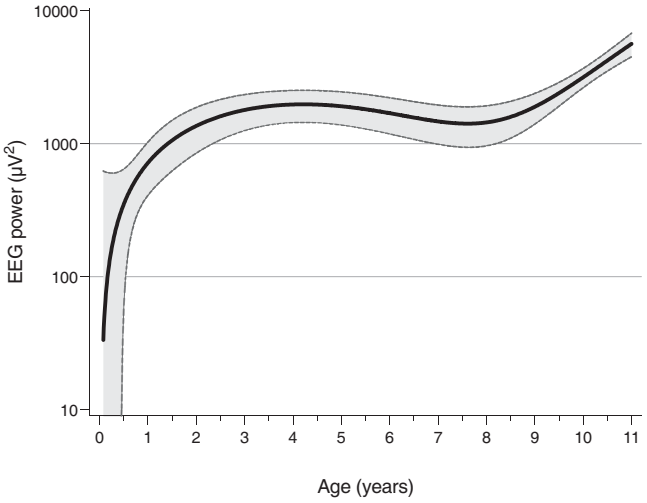

Fig. 1. The average total EEG power during the intra-operative phase.

Average total intraoperative EEG power

Fig. 1 shows the trend of mean total EEG power during the intraoperative phase in relation to patient age. Based on this trend, we used the following age classifications: 0–5 months, 6–11 months, and ≥1 year. The average total EEG power in each of the subgroups was 165.2 ± 110.2 μV^2 (0–5 months), 348.0 ± 113.8 μV^2 (6–11 months), and 1713.17 ± 1509.0 μV^2 (≥1 year).

Subgroup GEE analyses, based on the age categories above revealed no significant correlation in the age groups 0–5 months and 6–11 months. In the age group ≥1 year, results were comparable with the overall GEE analyses (see Table 2).

Burst suppression

The overall prevalence of burst suppression was 14.1%. Table 3 shows the prevalence of burst suppression, the duration of the burst suppression periods, and the operative phase in which burst suppression occurred for the different age groups.

The median propofol dosage across the entire cohort was 4.60 (2.49 [2.05–13.06]) mg kg^{-1} h^{-1}. Neither airway-related events nor substantial blood pressure drops were seen in any patient. Arousal occurred in two patients. In one patient a subcutaneous infusion of propofol occurred immediately after induction and in one patient suboptimal communication with the surgeon regarding the end of the procedure led to a short period of arousal.

Fig. 2 shows three examples of a typical DSA pattern during propofol/sevoflurane coadministration.

Fig. 2a shows an example of a premature-born baby, having surgery for cleft lip repair at 55 weeks postconceptional age. At

Table 2
Generalized Estimating Equations results.

	Percentages (%)[a]	Estimate[b]	95%CI[c]	p-Value
Overall				
Beta	−9.0	0.910	[0.863, 0.960]	<0.001*
Alpha	−1.1	0.989	[0.959, 1.019]	0.466
Theta	−0.7	0.993	[0.970, 1.017]	0.564
Delta	3.5	1.035	[1.012, 1.058]	0.002*
Age 0–5 months (n = 24)				
Beta	−5.8	0.942	[0.862, 1.031]	0.193
Alpha	−8.9	0.911	[0.833, 0.996]	0.039
Theta	−3.4	0.966	[0.887, 1.052]	0.421
Delta	1.7	1.017	[0.987, 1.048]	0.268
Age 6–11 months (n = 45)				
Beta	−1.3	0.987	[0.908, 1.073]	0.757
Alpha	4.3	1.043	[0.986, 1.103]	0.139
Theta	0.5	1.005	[0.963, 1.049]	0.818
Delta	−1.6	0.984	[0.913, 1.061]	0.679
Age ≥ 1 year (n = 115)				
Beta	−12.2	0.878	[0.840, 0.918]	<0.001*
Alpha	2.5	0.975	[0.941, 1.012]	0.181
Theta	0.5	0.995	[0.974, 1.016]	0.622
Delta	5.1	1.051	[1.029, 1.074]	<0.001*

[a] Change in percentage with every increase of 1 mg kg^{-1} h^{-1} propofol.
[b] Exponential of equation estimates.
[c] 95% confidence intervals of exponential of estimates.
* Statistical significance determined through the Holm-Bonferroni method.

Table 3
Occurrence of burst suppression during coadministration of propofol and sevoflurane.

	Age 0–5 months	Age 6–11 months	Age > 1 year
Occurrence of burst suppression	36.4% (n = 4)	27.8% (n = 5)	4.1% (n = 2)
Duration burst suppression period[a]	3.0 (10.5 [1–20])	3.0 (1.5 [2–4])	1 and 4
Anesthetic phase			
Induction phase	25%	40%	50%
Pre-incision phase	25%	60%	50%
Surgical phase	50%	0%	0%

[a] In minutes, median (IQR [range]).

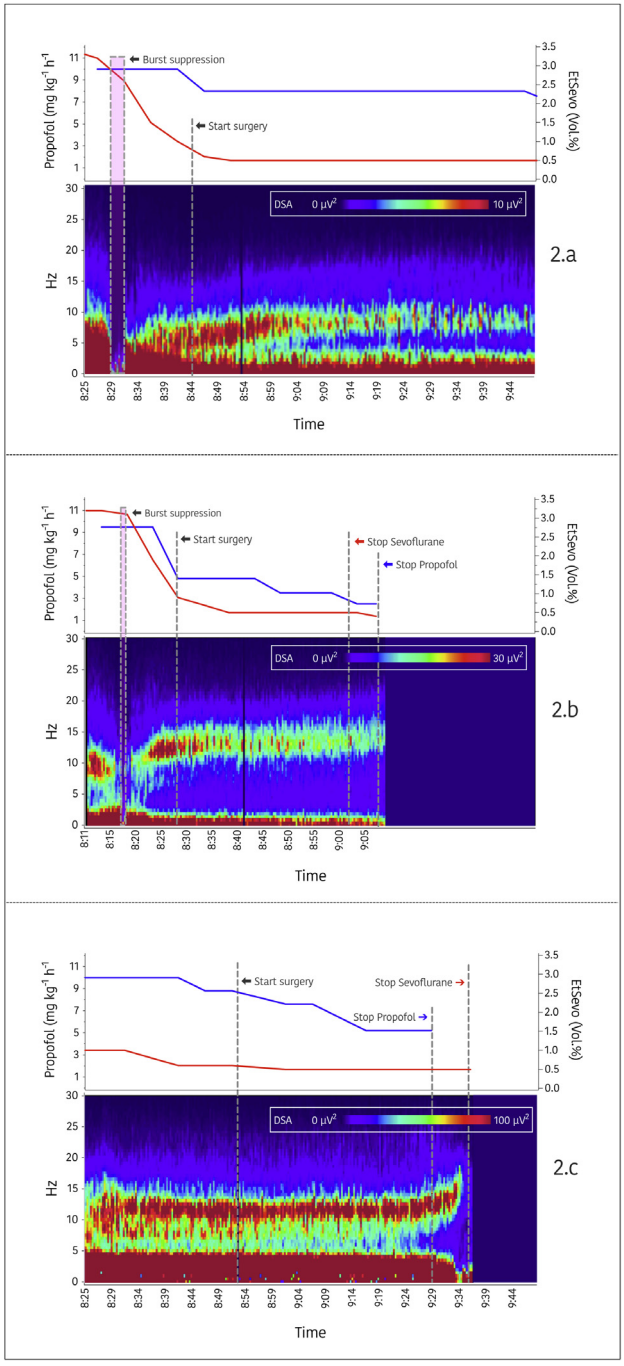

Fig. 2. Three examples of a typical DSA pattern during propofol/sevoflurane coadministration in each age group; (a) represents a premature-born baby at 55 weeks postconceptional age, a 1-year-old infant (b), and an 11-year-old child (c). The red line indicates the ET_{sevo} concentration and the blue line propofol dosage in mg $kg^{-1}h^{-1}$.

08:19 h a mask induction was performed followed by a bolus of propofol (1 mg/kg) and the start of continuous propofol infusion at 08:27 h. At 08:29 h burst suppression was noticed followed by a decrease in propofol infusion resulting in a slow returning α and δ pattern.

Fig. 2b shows an example of a 1-year-old during an orchidopexy undergoing general anesthesia supplemented with caudal anesthesia. This boy received a mask induction at 08:05 h followed by a propofol bolus of 1 mg/kg and the start of continuous propofol infusion at 08:14 h. At 08:17 a short period of burst suppression occurred followed by a decrease in propofol infusion and the occurrence of β, α, and δ oscillations.

Fig. 2c shows an example of an 11-year-old during a desyndactylisation of the first web spaces of the hand undergoing general anesthesia supplemented with a plexus blockade. In this patient, a gradual decrease in propofol and sevoflurane (following inhalation induction) resulted in a decrease in the power of α oscillations.

Discussion

This exploratory observational study provides initial evidence for the applicability of DSA as a valuable tool during the co-administration of propofol and sevoflurane in children. This approach could achieve and maintain the desired DoH level with almost subanesthetic doses of propofol and sevoflurane.

Consistent with our recent study using propofol as the sole anesthetic during procedural sedation in teenagers [14], we found a dose-dependent correlation between the propofol dosage and the relative percentage of β and δ in the overall study population and the age group of patients above the age of 1 year. An increase in propofol dosage thereby causes a significant decrease in the amplitude of frontal β oscillations and a significant increase in the amplitude of frontal δ oscillations.

Unconsciousness at a surgical level during propofol- or sevoflurane anesthesia is characterized by high power δ-, α-, and possibly β oscillations, in children aged > 6 months old [8,12,14–19]. However, we could not depict a significant correlation between the propofol dose and the expression of alpha oscillations in this study. This could possibly be explained by the biphasic pattern that α oscillations show with the increasing propofol dosage [14].

An age-dependent trend was observed by analyzing mean total power during the operative phase, with mean total power increasing most during the first year of life. This increase in total EEG power with increasing age was previously described by Akeju et al. during general anesthesia with solely sevoflurane [9]. However, the study by Akeju et al. described a peak in total EEG power at the age of 5–8 years. This peak at the age of 5–8 years was not seen in our study.

Sub-analyses to examine the dose-dependent effect of propofol by the different age groups showed no significant correlation between the relative EEG frequencies and propofol dosage in the age category of 0–6 months and 6 months—1 year. This could be

due to the strong development in the power of different EEG frequencies until the age of 1 year. In 2015, Cornelissen et al. described this developmental effect in children up to 6 months using full-scale EEG. The increase in power in the different EEG frequencies with increasing age is described as likely due to developmental factors such as regional differences in synaptogenesis, glucose metabolism, and myelination across the cortex [10].

In this exploratory observational study with propofol/sevoflurane coadministration, the median propofol requirement was 4.6 mg kg^{-1} h^{-1} (2.49 [2.05–13.06]), which is significantly less than the recently reported doses of 13.5 mg kg^{-1} h^{-1} [20] and 10 mg kg^{-1} h^{-1} [21] during propofol mono anesthesia. DSA monitoring resulted in low-dose application of propofol/sevoflurane preventing the child from unnecessary exposure to anesthetic drugs.

Speaking from our own experience, especially in neonates and young infants, vasopressors are frequently needed during sevoflurane or propofol anesthesia. In this study, we saw no relevant drops in blood pressure and, thus, no need to administer vasopressors, even in infants younger than 5 months.

EEG burst suppression is often associated with moderate or severe hypotension and lower Pediatric Quality of Life scores at baseline and 30-day follow-up [22]. In two recent pediatric studies published by Yuan et al., the overall prevalence of EEG burst suppression was as high as 32% [22] and 63% [20]. This is about 2–4 times higher than our study's 14.1% overall burst suppression prevalence. Therefore, also with a view to the hemodynamic stability of our patients, we allow ourselves to tentatively conclude that DSA-guided co-administration of sevoflurane and propofol also benefits patient safety.

When propofol and sevoflurane are combined, the term co-administration is usually used [4–6]. In this study, sevoflurane was used as an additive to propofol anesthesia. Minimizing the use of sevoflurane is a core component of the environmentally oriented Green Anesthesia concept [23]. DSA-guided sevoflurane-augmented propofol anesthesia has the potential to contribute to the emerging efforts [24–27] to make pediatric anesthesia more environmentally friendly.

This exploratory observational study has some limitations. A proper power analysis could not be performed beforehand due to the lack of previously published data. There is thus a chance that the absence of a significant correlation between the propofol dosage and the relative EEG percentages in the <1 year age group is due to insufficient power. Moreover, additional post-operative data, such as delirium scores and formal assessment of intraoperative awareness, would be desirable.

Conclusion

This exploratory observational study provides initial evidence of the applicability and safety of DSA-guided co-administration of propofol and sevoflurane in children. Achieving sufficient hypnotic depth with doses of propofol and sevoflurane, which are usually considered to be sub-anesthetic, means less exposure to anesthetic drugs for the individual child.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article. The authors also confirm that the personal details of the patients and/or volunteers have been removed.

Disclosure of interest

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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References

1. Grover S, Wilkinson DJ. Sevoflurane and analgesia. Br J Anaesth 2007;98(5):691. author reply-2.
2. Campagna JA, Miller KW, Forman SA. Mechanisms of actions of inhaled anesthetics. N Engl J Med 2003;348(21):2110–24.
3. Zhao Y, Qin F, Liu Y, Dai Y, Cen X. The safety of propofol versus sevoflurane for general anesthesia in children: a meta-analysis of randomized controlled trials. Front Surg 2022;9924647.
4. Wang XH, Zhang SY, Huang Y, Wang Q, Zou L, Zhao G, et al. Multimodal analgesia with sevoflurane provides enhanced intraoperative analgesic effects in percutaneous nephrolithotomy: a randomized, blinded clinical trial. Pain Physician 2022;25(3):283–91.
5. Liang C, Ding M, Du F, Cang J, Xue Z. Sevoflurane/propofol coadministration provides better recovery than sevoflurane in combined general/epidural anesthesia: a randomized clinical trial. J Anesth 2014;28(5):721–6.
6. Wolf A, Selpien H, Haberl H, Unterberg M. Does a combined intravenous-volatile anesthesia offer advantages compared to an intravenous or volatile anesthesia alone: a systematic review and meta-analysis. BMC Anesthesiol 2021;21(1):52.
7. Purdon PL, Pavone KJ, Akeju O, Smith AC, Sampson AL, Lee J, et al. The ageing brain: age-dependent changes in the electroencephalogram during propofol and sevoflurane general anaesthesia. Br J Anaesth 2015;115(Suppl 1):i46–57.
8. Purdon PL, Sampson A, Pavone KJ, Brown EN. Clinical electroencephalography for anesthesiologists: part I: background and basic signatures. Anesthesiology 2015;123(4):937–60.
9. Akeju O, Pavone KJ, Thum JA, Firth PG, Westover MB, Puglia M, et al. Age-dependency of sevoflurane-induced electroencephalogram dynamics in children. Br J Anaesth 2015;115(Suppl 1):i66–76.
10. Cornelissen L, Kim SE, Purdon PL, Brown EN, Berde CB. Age-dependent electroencephalogram (EEG) patterns during sevoflurane general anesthesia in infants. Elife 2015;4e06513.
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 2014;12(12):1495–9.
12. de Heer IJ, Weber F. Electroencephalographic density spectral array monitoring in pediatric anesthesia: clinical background and practical applications. Minerva Anestesiol 2023;89(4):351–8.
13. de Graaff JC, Pasma W, van Buuren S, Duijghuisen JJ, Nafiu OO, Kheterpal S, et al. Reference values for noninvasive blood pressure in children during anesthesia: a multicentered retrospective observational cohort study. Anesthesiology 2016;125(5):904–13.
14. de Heer IJ, Warmenhoven AT, Weber F. Electroencephalographic density spectral array monitoring during propofol sedation in teenagers, using the narcotrend electroencephalographic monitor. Minerva Anestesiol 2020;86(6):601–7.
15. Bong CL, Balanza GA, Khoo CE, Tan JS, Desel T, Purdon PL. A narrative review illustrating the clinical utility of electroencephalogram-guided anesthesia care in children. Anesth Analg 2023;137(1):108–23.
16. de Heer IJ, Bouman SJM, Weber F. Electroencephalographic (EEG) density spectral array monitoring in children during sevoflurane anaesthesia: a prospective observational study. Anaesthesia 2019;74(1):45–50.
17. Akeju O, Westover MB, Pavone KJ, Sampson AL, Hartnack KE, Brown EN, et al. Effects of sevoflurane and propofol on frontal electroencephalogram power and coherence. Anesthesiology 2014;121(5):990–8.
18. Yuan I, Missett RM, Jones-Oguh S, Massa CB, Babus LW, Garcia-Marcinkiewicz AG, et al. Implementation of an electroencephalogram-guided propofol anesthesia education program in an academic pediatric anesthesia practice. Paediatr Anaesth 2022.

19. Lee JM, Akeju O, Terzakis K, Pavone KJ, Deng H, Houle TT, et al. A prospective study of age-dependent changes in propofol-induced electroencephalogram oscillations in children. Anesthesiology 2017;127(2):293–306.
20. Yuan I, Landis WP, Topjian AA, Abend NS, Lang SS, Huh JW, et al. Prevalence of isoelectric electroencephalography events in infants and young children undergoing general anesthesia. Anesth Analg 2020;130(2):462–71.
21. Louvet N, Rigouzzo A, Sabourdin N, Constant I. Bispectral index under propofol anesthesia in children: a comparative randomized study between TIVA and TCI. Paediatr Anaesth 2016;26(9):899–908.
22. Yuan I, Xu T, Skowno J, Zhang B, Davidson A, von Ungern-Sternberg BS, et al. Isoelectric electroencephalography in infants and toddlers during anesthesia for surgery: an international observational study. Anesthesiology 2022;137(2):187–200.
23. Wyssusek K, Chan KL, Eames G, Whately Y. Greenhouse gas reduction in anaesthesia practice: a departmental environmental strategy. BMJ Open Qual 2022;11(3).
24. Narayanan H, Raistrick C, Tom Pierce JM, Shelton C. Carbon footprint of inhalational and total intravenous anaesthesia for paediatric anaesthesia: a modelling study. Br J Anaesth 2022;129(2):231–43.
25. Isserman RS, Yuan I, Elliott EM, Muhly WT, Iyer RS, Farrell HA, et al. Reducing the environmental impact of mask inductions in children: a quality improvement report. Paediatr Anaesth 2023;33(9):728–35.
26. Goh AN, Bagshaw O, Courtman S. A follow-up survey of total intravenous anesthesia usage in children in the U.K. and Ireland. Paediatr Anaesth 2019;29(2):180–5.
27. Lewis H, Groome J, Arnold P, Brooks P, Patrn. How green is pediatric anesthesia? The pediatric anesthesia trainee research network 2021 UK national survey. Paediatr Anaesth 2022;32(6):772–5.