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PAEDIATRIC ANAESTHESIA

Frontal electroencephalogram activity during emergence from general anaesthesia in children with and without emergence delirium

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Abstract

Background: Emergence delirium (ED) in children after general anaesthesia causes significant distress in patients, their family members, and clinicians; however, electroencephalogram (EEG) markers predicting ED have not been fully investigated.

Methods: This prospective, single-centre observational study enrolled children aged 2–10 yr old under sevoflurane anaesthesia. ED was assessed according to Diagnostic and Statistical Manual of Mental Disorders (DSM) IV or 5 criteria. The relative power of low-frequency (delta and theta) and high-frequency (alpha and beta) EEG waves during the emergence period was compared between the children with and without ED. The linear relationships between the relative power and peak Paediatric Assessment of Emergence Delirium (PAED) score were investigated.

Results: Among the 60 patients, 22 developed ED (ED group), whereas the other 38 did not (non-ED group). The relative power of the delta wave was higher (mean [standard deviation], 0.579 [0.083] *vs* 0.453 [0.090], respectively, $P<0.001$) in the ED group, whereas that of the alpha and beta waves was lower in the ED group, than in the non-ED group (0.155 [0.063] *vs* 0.218 [0.088], $P=0.005$ and 0.114 [0.069] *vs* 0.186 [0.070], $P<0.001$, respectively). The areas under the receiver operating characteristic curves of the relative power of the delta wave, low-to-high frequency power ratio, and delta-to-alpha ratio were 0.837 (95% confidence interval, 0.737–0.938), 0.835 (0.735–0.934), and 0.768 (0.649–0.887), respectively. The relative power of the delta wave and the two ratios had a positive linear relationship with the peak PAED scores.

Conclusions: Paediatric patients developing ED have increased low-frequency (delta) frontal EEG activity with reduced high-frequency (alpha and beta) activity during emergence from general anaesthesia.

Clinical trial registration: NCT03797274.

Keywords: brain waves; children; electroencephalogram (EEG); emergence delirium; neurocognitive disorders; post operative delirium; sevoflurane anaesthesia

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Editor's key points

- Electrical oscillations between the cortex and thalamus, and between cortical regions and hemispheres, appear to provide important information on different states of consciousness, including general anaesthesia and delirium.
- Emergence delirium is a challenge in paediatric anaesthesia, and it occurs commonly in children during emergence from general anaesthesia.
- This research shows that certain EEG patterns before emergence from anaesthesia are strongly associated with emergence delirium in children, including high relative delta power and an increased ratio of low-frequency (i.e. delta and theta) to high-frequency (i.e. alpha and beta) oscillations.
- Transitioning rapidly from deep anaesthesia to wakefulness, reflected by the absence of an EEG pattern resembling non-rapid eye movement stage 2 sleep, might predispose children to emergence delirium.

Emergence delirium (ED) is a disturbance in a child's awareness of and attention to his/her environment with disorientation and perceptual alterations, including hypersensitivity to stimuli and hyperactive motor behaviour, in the immediate postoperative period.[1–3] Although ED typically resolves within 1 h without complications, delirious children have been found to be at greater risk of having postoperative maladaptive behavioural changes that extend several weeks after surgery.[4]

In adults, the analysis of electroencephalograms (EEGs) in an alert state showed high delta relative power (RP) in patients with postoperative delirium.[5,6] In children with ED, epileptiform EEG discharges were observed during anaesthesia induction.[7,8] However, the use of EEG data from anaesthesia induction is limited because confounding factors after the end of anaesthesia induction (e.g. anaesthetics for maintenance of anaesthesia, surgical stimuli, etc.) can also affect the development of ED.[9] Although emergence from anaesthesia before the onset of sleep-like EEG patterns was found to be associated with ED,[10] the sample size (n=12) was too small to generalise the results.

Given the lack of evidence for the use of EEG to predict paediatric ED, we assessed delta and alpha activity during emergence from sevoflurane anaesthesia to test the hypothesis that children with ED have delta and alpha activity different from those of children without ED.

Methods

This prospective, single-centre, observational study was approved by the Institutional Review Board of Daegu Catholic University Medical Centre (CR-19-004) and registered at ClinicalTrials.gov (NCT03797274) before enrolment. Informed consent was obtained from the parents or legal guardians of the patients at outpatient clinics or during preoperative visits. The study was conducted in a tertiary university hospital between February 2019 and June 2019 and followed Good Clinical Practice guidelines and the principles of the Declaration of Helsinki.

Participants

Children aged 2–10 yr with an American Society of Anesthesiologists (ASA) physical status of 1 or 2 who were undergoing elective ophthalmological or otorhinolaryngological surgery requiring general anaesthesia were recruited. The exclusion criteria were the presence of: (i) developmental delays or neurological or psychiatric diseases associated with symptoms of agitation, anxiety, attention deficit, sleep disturbances, and others; (ii) autism; (iii) a recent history (within a month) of receiving general anaesthesia or surgery; or (iv) congenital or other genetic conditions thought to influence brain development.

Anaesthesia

Anaesthetic management was at the discretion of the attending anaesthesiologists. In the preoperative waiting room, each patient was premedicated with midazolam 0.1–0.2 mg kg^{-1} or ketamine 0.5–1.0 mg kg^{-1} i.v. under parental surveillance. After patients entered the operating theatre, electrocardiography, noninvasive arterial blood pressure (BP), pulse oximetry, neuromuscular block (TOF-Watch, Organon Teknika, Boxtel, Netherlands), and bispectral index (BIS; VISTA monitoring system; Aspect Medical Systems Inc., Norwood, MA, USA) were monitored. They were given sevoflurane 5.0–6.0 vol% with oxygen 100%. If neuromuscular block was needed, rocuronium 0.3–0.6 mg kg^{-1} was administered according to the type of surgery. A tracheal tube or laryngeal mask airway was inserted for airway management. Anaesthesia was maintained with fentanyl 1 μg kg^{-1}, sevoflurane 2.0–4.0 vol%, and oxygen 50%, with a BIS target range of 40–60. At the end of the surgery, neuromuscular block was antagonised with pyridostigmine and glycopyrrolate when neuromuscular blocking agents had been used, sevoflurane was discontinued from an age-adjusted minimum alveolar concentration[11,12] of 0.8–1.0, and total gas flows were increased to 8 L min^{-1}. External stimuli were minimised after orotracheal suction. After spontaneous ventilation returned with a train-of-four ratio >0.9, the anaesthesiologists removed the airway devices and carefully observed the patients until they achieved haemodynamic stability and consciousness, which was determined to return if patients cried or grimaced on minor stimulation because patients receiving ophthalmologic surgery could not open the eyes on command because of the dressings around the eyes.

When the patients arrived in the post-anaesthetic care unit (PACU), their ED and pain scores were measured by two well-trained researchers every 10 min until discharge. Paediatric Assessment of Emergence Delirium (PAED)[1] and Watcha scales[13] were measured to assess the severity of ED. The PAED scale is an observational measure of five aspects of child behaviour (caregiver eye contact, purposeful movement, evidence of awareness of surroundings, restlessness, and inconsolability). Ratings are summed to produce a total score ranging from 0 to 20; greater scores indicate greater severity. The Watcha scale has four levels (1: calm; 2: crying, but can be consoled; 3: crying, cannot be consoled; and 4: agitated and thrashing around). If the PAED scores disagreed between the two researchers, the lower score was chosen. Pain was measured using Face, Legs, Activity, Cry, and Consolability (FLACC) scores.[14] If any change in patients' condition was detected within the 10-min interval or if ED developed before arrival to the

PACU, ED or pain scores were measured. If the subject was asleep, the investigators suspended rating the scores until he/she awoke to discriminate the residual anaesthetic effect from a calm sleeping state. If the PAED score was >12 with a Watcha score >2 or if the FLACC score was >4, fentanyl 0.5 μg kg^{-1} was administered and repeated unless the agitation subsided.[15] Patients were discharged when they became alert and calm with a modified Aldrete score ≥9. At the end of each case, the two researchers shared their case report forms and made agreement on the determination of ED based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV or 5 criteria (impaired consciousness/attention/awareness and cognition).[16]

EEG recording and analysis

After the skin was prepared with alcohol, self-sticking surface electrodes connected to the BIS monitor were placed on the patient's forehead and outer malar bone (corresponding to the 10–20 international system). Because the BIS monitoring system utilises a referential montage, two EEG recordings can be achieved (Channel 1 for Fpz–F7 and Channel 2 for Fpz–F3). The frontal raw EEG data, vital signs (such as arterial pressure, pulse oximetry oxygen saturation, and heart rate [HR]), and end-tidal sevoflurane concentration were recorded throughout the anaesthesia using Vital Recorder software (ver. 1.8.7.12, VitalDB.net, Seoul, Republic of Korea).[17] EEG data were obtained at a rate of 128 Hz. The EEG data for three periods were analysed, which were during the whole emergence period (between the cessation of sevoflurane and the discharge from operating theatre), for 1–2 min at approximately 10 min after anaesthesia induction, and for 2–3 min before the end of surgery.

DADiSP 6.7 software (Data Analysis and Display; DSP Development Corp., Newton, MA, USA) with an advanced digital signal processing and filter design modules was used to analyse the EEG data. The raw EEG waveform was bandpass-filtered at 1–50 Hz using a finite impulse response filter with a Kaiser window[18] and was manually inspected to identify and discard artifacts induced by movement or electrode impedance check. The EEG epoch was divided into 4-s-long segments overlapping adjacent segments by 50%. Each segment was windowed by the Hamming window and then submitted to fast Fourier transform to obtain their periodogram. The power spectra from the periodograms were averaged.[19] By integrating the spectral powers corresponding to frequency ranges of four EEG waves (1–4 Hz for the delta, 4–8 Hz for the theta, 8–13 Hz for the alpha, and 13–30 Hz for the beta wave), the absolute powers of each wave were obtained. The RP of each band was computed as the ratio of the absolute power of each band to the total summed power across the 1–30 Hz range.

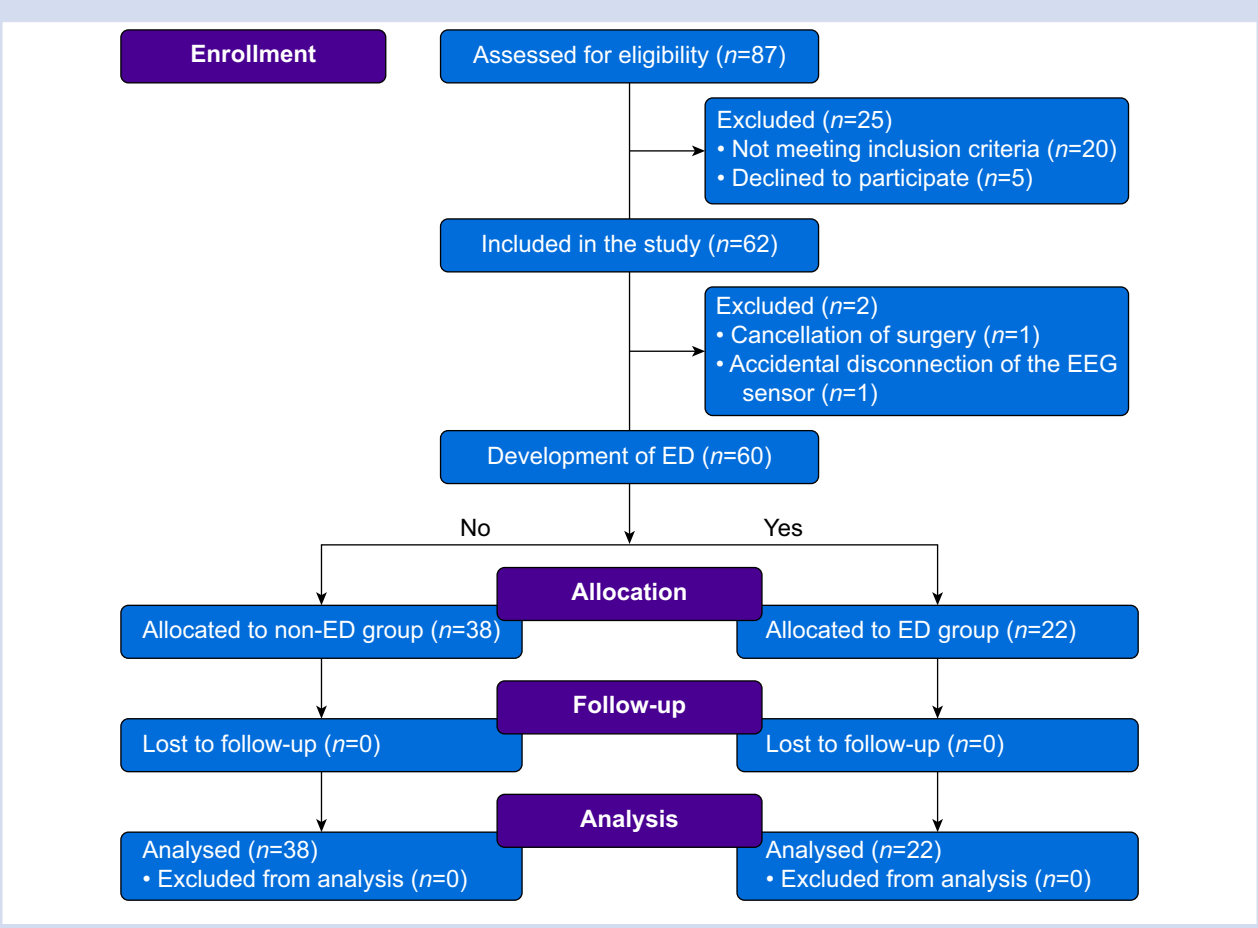

Fig 1. Flow diagram of patient disposition. ED, emergence delirium.

Table 1 Patient characteristics.

	ED group (*n*=22)	Non-ED group (*n*=38)	*P*-value
Age, yr	5.8 (3–8)	6.2 (3–8)	0.295
Female	9 (39.1)	13 (35.1)	0.755
Height, cm	115.8 (8.3)	120.0 (9.2)	0.091
Weight, kg	23.3 (6.3)	25.4 (7.0)	0.246
ASA physical status, 1/2	19/3	36/2	0.258
Surgical time, min	38.3 (16.5)	42.8 (18.7)	0.362
Anaesthesia time, min	70.2 (22.0)	72.8 (21.0)	0.659
Type of surgery			0.755
Ophthalmic	13 (59.1)	24 (63.2)	
Otorhinolaryngeal	9 (40.9)	14 (36.8)	
mYPAS	9.8 (4.9)	8.5 (4.2)	0.319
Premedication (midazolam/ketamine)	5/17	15/23	0.185
Use of neuromuscular blocking agents	14 (63.6)	29 (76.3)	0.294
Eye opening time, min	20.0 (5.8)	22.5 (8.0)	0.221
Emergence time, min	9.4 (3.9)	11.8 (4.4)	0.040
Type of emergence			0.087
ddSWA to adSWA to NSWA	6 (27.3)	9 (23.7)	
ddSWA to NSWA	7 (31.8)	5 (13.2)	
adSWA to NSWA	1 (4.5)	10 (26.3)	
ddSWA to adSWA	5 (22.7)	8 (21.1)	
ddSWA	3 (13.6)	2 (5.3)	
adSWA	0 (0)	4 (10.5)	
Peak PAED score	16.5 (3.1)	5.2 (3.2)	<0.001
Peak Watcha score	3.4 (0.7)	1.5 (0.6)	<0.001
Peak FLACC score	8.5 (1.9)	2.6 (2.3)	<0.001

Data are presented as the mean (standard deviation) or number of patients (%). Age was expressed as the mean (range).
adSWA, alpha-dominant slow-wave anaesthesia; ASA, American Society of Anesthesiologists; ddSWA, delta-dominant slow-wave anaesthesia; ED, emergence delirium; FLACC, Face, Legs, Activity, Cry, and Consolability; mYPAS, modified Yale Preoperative Anxiety Scale; NSWA, non-slow-wave anaesthesia; PAED, Paediatric Assessment of Emergence Delirium.

The values of spectral powers and their ratios from the two channels were averaged, and the averaged values were used in the final analysis.

Using the bandpass-filtered channel 1 EEG waveforms for the emergence period, spectrograms, time-series plots of alpha and delta power, and hypnograms were generated. For spectrograms, the whole waveform was divided into 4-s-long segments overlapping adjacent segments by 90%. Each segment underwent fast Fourier transform, and the calculated amplitudes were log-transformed into decibel (dB) units [$20\times log_{10}$ (amplitude)]. The time-series plots of alpha and delta power were drawn by extracting their peak power from the spectrograms.[20] Hypnograms were plotted using three types of anaesthesia: non-slow-wave anaesthesia (NSWA), delta-dominant slow-wave anaesthesia (ddSWA), and alpha-dominant slow-wave anaesthesia (adSWA). NSWA was defined as both delta and alpha power ≤7 dB. Otherwise, (delta or alpha power >7 dB), ddSWA and adSWA were defined as delta power>alpha power and delta power≤alpha power, respectively.[21] Emergence trajectory was categorised by two independent investigators who were blinded to the development of ED based on longitudinal changes in the type of anaesthesia.

Study endpoints

The primary outcome was the delta RP during the emergence period. The secondary outcomes were the RP of other

Table 2 Relative and absolute power of brain waves during the emergence period.

	ED group (*n*=22)	Non-ED group (*n*=38)	*P*-value
Relative power			
Delta waves, 1–4 Hz	0.579 (0.083)	0.453 (0.090)	<0.001
Theta waves, 4–8 Hz	0.152 (0.041)	0.144 (0.035)	0.402
Alpha waves, 8–13 Hz	0.155 (0.063)	0.218 (0.088)	0.005
Beta waves, 13–30 Hz	0.114 (0.069)	0.186 (0.070)	<0.001
Absolute power (μV^2 Hz^{-1})			
Total power	1152.2 (734.9)	1038.2 (544.5)	0.495
Delta waves	695.2 (492.1)	485.8 (294.9)	0.043
Theta waves	176.5 (157.3)	155.0 (100.0)	0.519
Alpha waves	162.4 (86.5)	230.3 (176.5)	0.097
Beta waves	118.0 (69.5)	167.1 (69.3)	0.010

Data are presented as mean (standard deviation).
ED, emergence delirium.

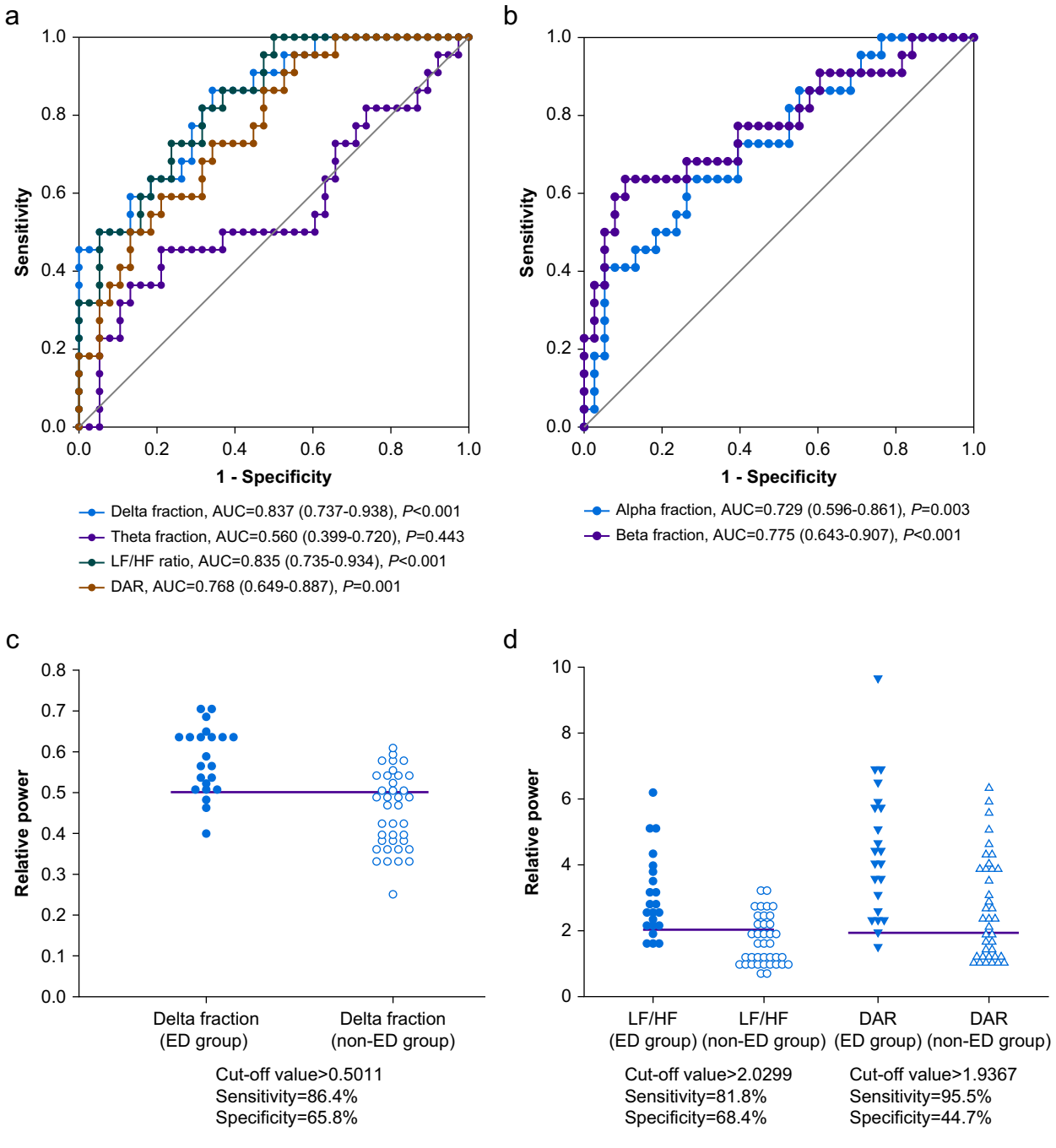

Fig 2. Receiver operating characteristic (ROC) curves of (a) the relative power of delta and theta waves, LF/HF ratio, DAR, and (b) the relative power of alpha and beta waves with dot histograms of (c) the relative power of delta waves, (d) LF/HF ratio, and DAR. Area under the curve (AUC) values are presented as the AUC (lower bound–upper bound of 95% confidence interval). Red lines represent the cut-off values. DAR, delta-to-alpha ratio; ED, emergence delirium; RP, relative power; LF/HF ratio, ratio of low-frequency (from delta and theta waves) to high-frequency (from alpha and beta waves) power.

waves, the ratio of low (delta and theta waves) to high frequency (alpha and beta waves) waves (LF/HF ratio), delta-to-alpha ratio (DAR), emergence time (interval from the cessation of anaesthetics to the discharge from the operating theatre), eye opening time (interval from the cessation of anaesthetics to eye opening or hand squeezing on verbal command), PACU stay time, total consumption of analgesics, pain scores in the PACU, and patterns of emergence trajectory.

Sample size calculation

Sample size was calculated using PASS software (version 15.0, NCSS statistical software, Kaysville, UT, USA) based on the

data from our pilot study. In the pilot study of 13 patients (out of whom three patients developed ED), the difference in mean delta RP between the ED and non-ED group was 0.12 with standard deviations of 0.1 for the ED group and 0.11 for the non-ED group. To achieve 90% statistical power at a significance level of 0.05 in Student's *t*-test, 55 patients were required. Considering a dropout rate of 10%, the final sample size was 62 patients. The data from the pilot study were not included in the main study.

Statistical analysis

After determining normality with the Kolmogorov–Smirnov test, normally and non-normally distributed data were presented as the mean (standard deviation) and median (1st–3rd quartiles), respectively. Categorical data are presented as the number of patients (percentage). The student's *t*-test and Mann–Whitney U test were used to compare the normally and non-normally distributed data, respectively. Categorical data were compared using Pearson's χ^2 test.

Receiver operating characteristic (ROC) curves were generated for all RPs of each EEG wave, LF/HF ratio, and DAR during the emergence period. Their area under the curve (AUC) was presented with a 95% confidence interval. The closer to 1 the AUC of the ROC curve is, the better the variable of the ROC curve determines ED. The maximum value of Youden's index (sensitivity+specificity−1) was regarded as the cut-off value of the variable of the ROC curve. To assess the linear relationship of the RPs of each brain wave, LF/HF ratio, and DAR with the peak PAED scores, simple linear regression analysis was performed.

A two-tailed $P<0.05$ was considered statistically significant. IBM SPSS version 25 (IBM Corp., Armonk, NY, USA) and NCSS software version 12.0 (NCSS statistical software) were used to perform the statistical analyses.

Results

After enrolment, two patients were excluded from the study. Out of the remaining 60 patients, 22 patients developed ED (ED group), whereas the other 38 patients did not (non-ED group; Fig. 1). ED occurred 14.9 (4.8) min after the cessation of sevoflurane. No significant difference was found in baseline characteristics or intraoperative variables between the two groups (Table 1). The emergence time was shorter in the ED group than in the non-ED group (9.4 [3.9] *vs* 11.8 [4.4] min, $P=0.040$], whereas eye opening time was comparable between the two groups. There was no difference in the incidence of ED between patients receiving midazolam and ketamine as premedication (25.0% *vs* 42.5%, $P=0.185$). The peak PAED, Watcha, and FLACC scores were higher in the ED group than in the non-ED group (Table 1).

During the emergence period, the delta RP of each channel and their averaged values were significantly higher, while those of the alpha and beta waves were lower in the ED group than in the non-ED group (Table 2). The absolute

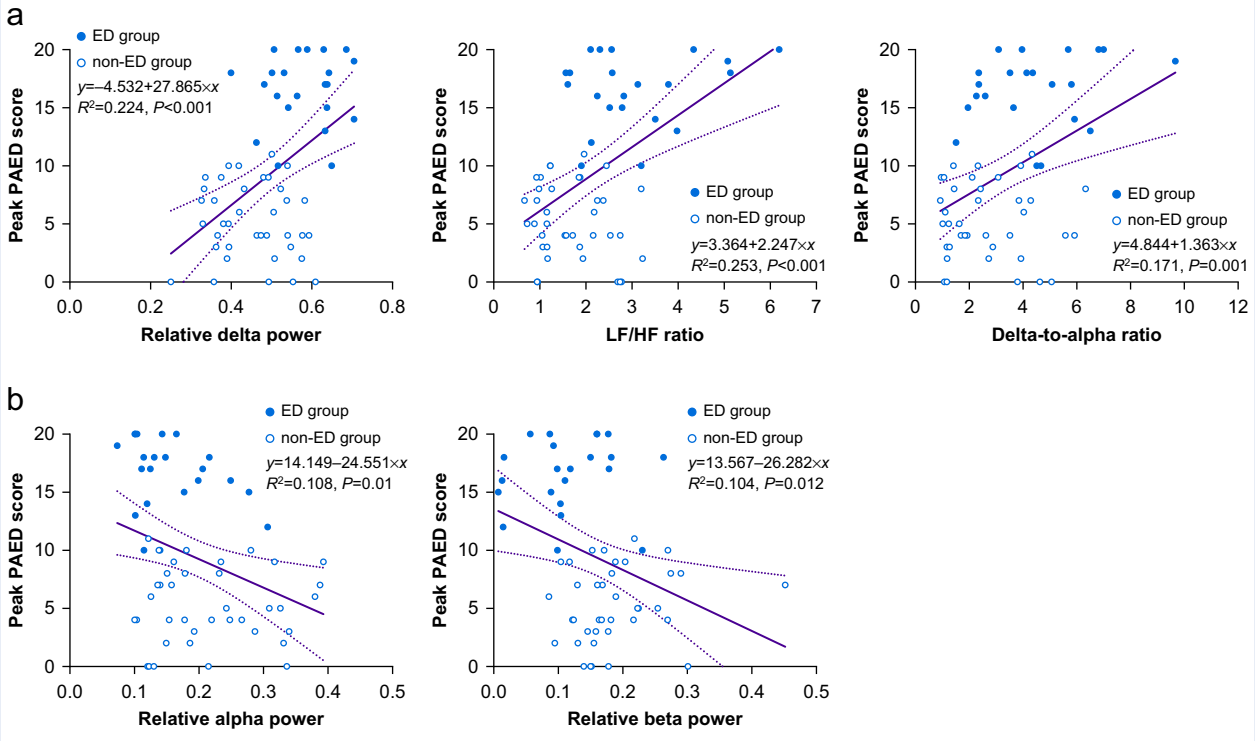

Fig 3. Linear relationships of PAED score to (a) relative delta power, LF/HF ratio, delta-to-alpha ratio, and (b) relative alpha and beta powers. ED, emergence delirium; LF/HF ratio, ratio of low-frequency (from delta and theta waves) to high-frequency (from alpha and beta waves) power; PAED, Paediatric Assessment of Emergence Delirium. The solid line and two dotted lines represent the predicted values of linear regression models and 95% confidence intervals of each predicted value, respectively.

powers of the delta and beta waves were higher and lower, respectively, in the ED group than in the non-ED group. However, the RPs were comparable between the two groups after anaesthesia induction and at the end of surgery (Supplementary Table S1).

Figure 2a shows the ROC curves of the variables, the high values of which are associated with ED (delta RP, LF/HF ratio, and DAR), whereas Figure 2b shows the ROC curves of the variables, the low values of which are associated with ED (RPs of the alpha and beta waves). The delta RP and the LF/HF ratio had the highest areas under their ROC curves, which were 0.837 (0.737–0.938) and 0.835 (0.735–0.934) (Fig. 2a), respectively. Their cut-off values were 0.5011 at a sensitivity of 86.4% and a specificity of 65.8% and 2.0299 at a sensitivity of 81.8% and a specificity of 68.4%, respectively (Fig. 2c and d).

The delta RP, LF/HF ratio, and DAR had a significant positive linear relationship with the peak PAED score (R^2=0.224, 0.253, and 0.171, P<0.001, P<0.001, and P=0.001, respectively, Fig. 3a). In contrast, a significant negative linear relationship was found between the RPs of the alpha and beta waves and the peak PAED score (R^2=0.108 and 0.104, P=0.01 and P=0.012, respectively, Fig. 3b).

The spectrograms, time-series plots of alpha and delta power, and hypnograms were categorised into six types of emergence trajectories, which include (A) ddSWA to adSWA to NSWA, (B) ddSWA to NSWA, (C) adSWA to NSWA, (D) ddSWA to adSWA, (E) ddSWA, and (F) adSWA (Fig. 4). Despite no difference in the pattern of emergence trajectory between the two groups (P=0.087, Table 1), the trend of a lack of adSWA was observed in the non-ED group.

Discussion

There is growing evidence that EEG provides information on thalamo-cortical function during the maintenance of anaesthesia. In older adults whose thalamo-cortical synaptic transmission declines,[22] reduced alpha power and coherence are observed with an increased probability of burst suppression.[23] At very early ages (≤3 months), when thalamo-cortical

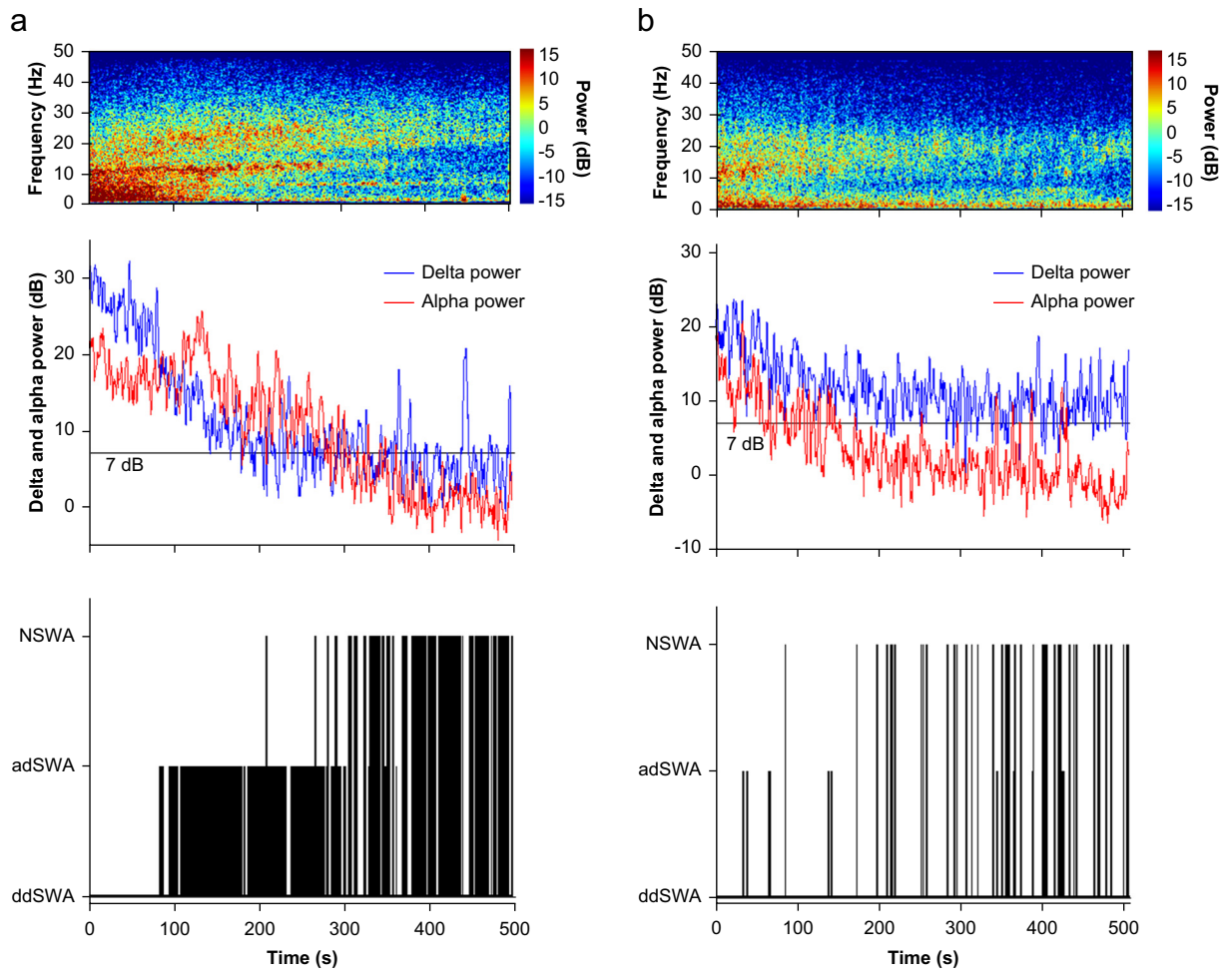

Fig 4. Spectrograms, time-series plots of alpha and delta power, and hypnograms according to EEG patterns during emergence from anaesthesia, which include (a) ddSWA to adSWA to NSWA, (b) ddSWA to NSWA, (c) adSWA to NSWA, (d) ddSWA to adSWA, (e) ddSWA, and (f) adSWA. The plots without adSWA were obtained from children with ED, and vice versa. adSWA, alpha-dominant slow-wave anaesthesia; ddSWA, delta-dominant slow-wave anaesthesia; ED, emergence delirium; NSWA, non-slow-wave anaesthesia.

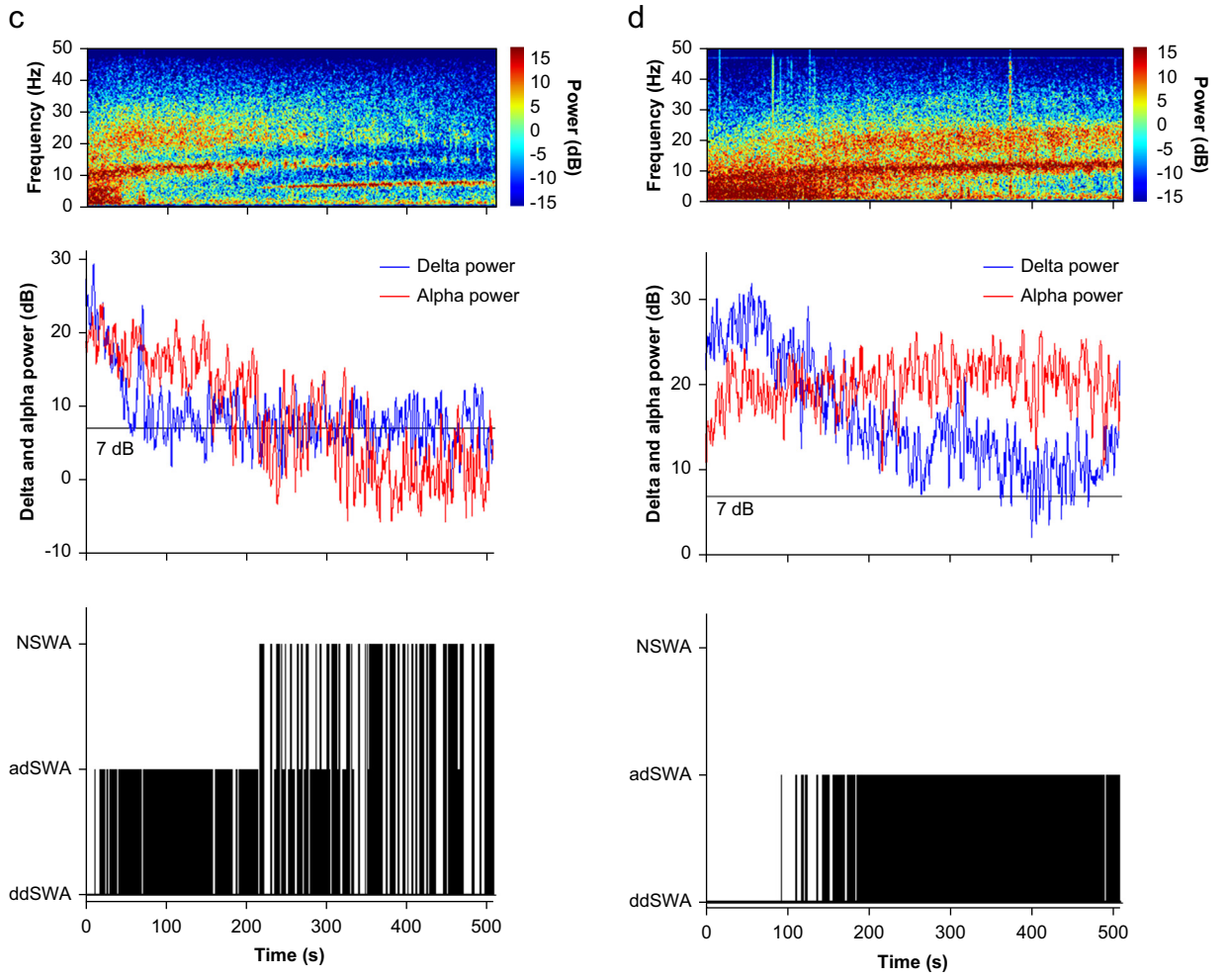

Fig 4. (*continued*)

and cortico-thalamic connections are not fully mature, slow and delta (0.1–4 Hz) oscillations are dominant.[24] Until 10 months old, the connections become weakly established with minimal or absent coherence in the alpha band. Afterwards, the more strengthened connections are accompanied by highly coherent alpha oscillation. In line with the EEG changes, anatomical changes develop as children grow according to a structural magnetic resonance imaging (MRI) study.[25]

In the context of delirium, various studies have analysed perioperative EEG in adults and found EEG patterns in delirious patients that are similar to those observed in the degraded or immature thalamo-cortical system. A recent multicentre study found a lack of spindle alpha power during emergence from anaesthesia in adult patients developing postoperative delirium.[20] In addition, the analyses of postoperative EEG obtained from adult patients with postoperative delirium revealed high delta RP.[5,6] However, the studies that have investigated EEG patterns in children with ED have not analysed EEG in this regard, and have some limitations. One study reported that interictal epileptiform discharges occurring during anaesthesia induction were associated with ED. However, the residual effects of premedication (midazolam) might confound their results obtained during anaesthesia induction. Even after anaesthesia induction, other confounding factors causing neuroinflammation, such as surgical stress and the effects of anaesthetics on the maintenance of anaesthesia,[9] might promote the development of ED.

Another study shed some light on the mechanisms for ED.[10] In all cases, after the cessation of sevoflurane, delta activity was attenuated, followed by an indeterminate state that was characterised by diffuse, mixed alpha and beta activity. The control group awoke from sleep or drowsy states (theta activity or delta activity with spindles) after this indeterminate state. In contrast, the ED group aroused from the indeterminate state before the onset of sleep-like EEG patterns. Because residual anaesthetic effects may cause the indeterminate state, it can be assumed that children with ED awake under anaesthetic effects that are not fully eliminated. In adults, patients with postoperative delirium awake from anaesthesia not passing through adSWA, whereas those without postoperative delirium undergo ddSWA followed by adSWA and NSWA.[20] Likewise, in

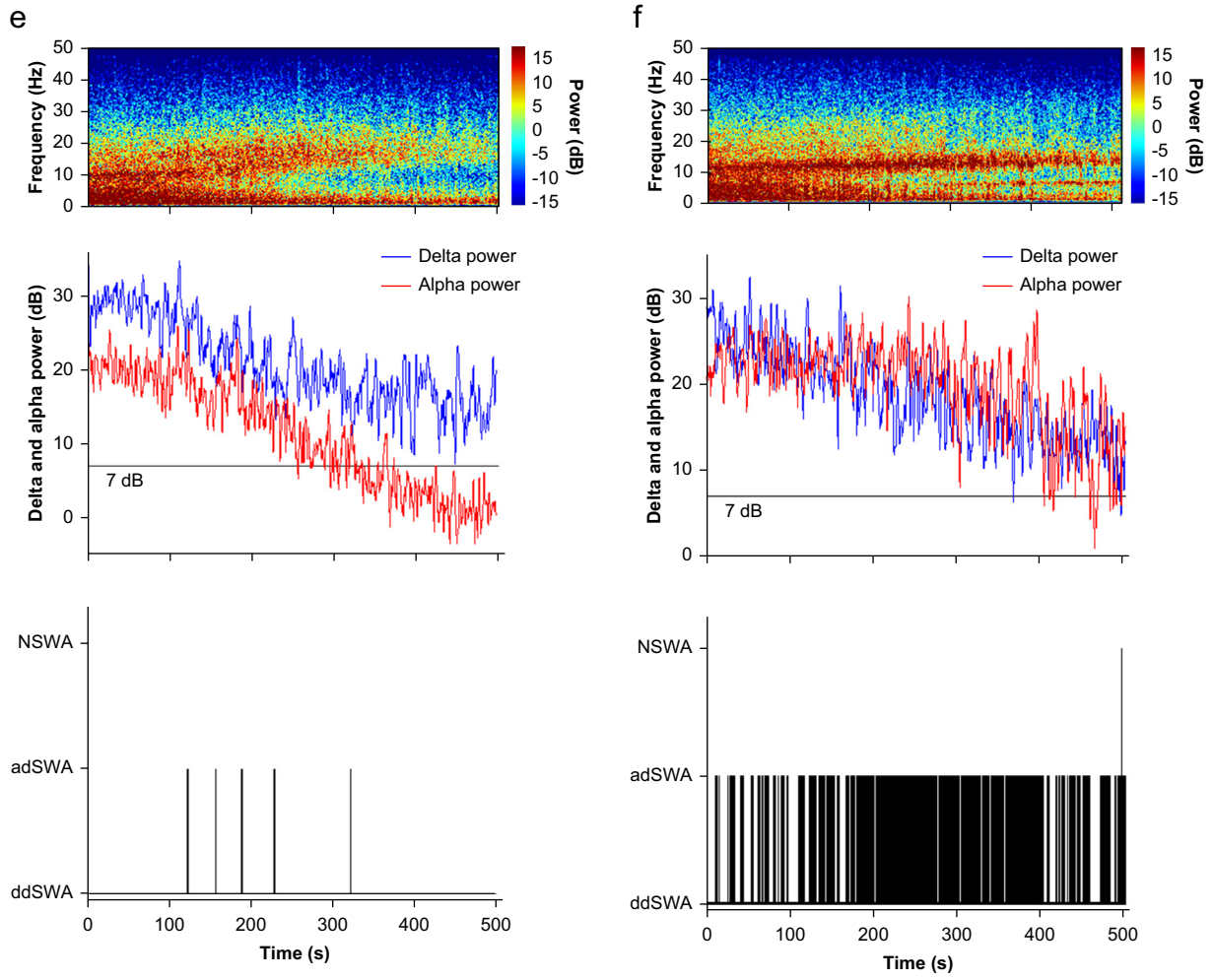

Fig 4. (*continued*)

this study, although the difference was not statistically significant, ddSWA was more predominant than adSWA in children with ED. In agreement with this finding, enhanced delta activity with reduced alpha activity was observed in children with ED. The RPs of each wave, LF/HF ratio, and DAR also had a linear relationship with the severity of ED. Because alpha frequency indicates cognitive and memory performance of the cortex in the thalamo-cortical feedback loops in awake subjects,[26] we speculate that the low alpha RP with high delta RP (predominant ddSWA compared with adSWA) observed during emergence from anaesthesia might impair cognitive and memory functions, thereby leading to ED.

Although natural sleep and anaesthesia are inherently different, they share common neurotransmitters, circuitry, and electrical patterns.[27,28] Gamma-aminobutyric acid type A receptors mediate loss of consciousness in both natural sleep and anaesthesia.[29,30] In addition, alpha frequency in the frontal EEG is generated by hyperpolarising neurons of the thalamus during sleep and anaesthesia.[31] Accordingly, ddSWA, adSWA, and NSWA correspond to non-rapid eye movement (NREM) stage 3 sleep, NREM stage 2 sleep, and REM sleep, respectively.[21] In line with the common characteristics between sleep and anaesthesia, the transition from deep sleep to wakefulness is also observed in some NREM parasomnias, such as night terror or sleepwalking.[32–35] The interruption of the continuity of delta activity (impaired arousal) during NREM sleep causes night terror, which shares common characteristics with paediatric ED, such as predominance in preadolescent children, behavioural patterns including sudden cry or loud scream as a result of intense fear, and resolution within several minutes.[32,35] Sleepwalking, which presents with ambulation under impaired consciousness after arousal from sleep,[32] occurs immediately after a significant increase in slow-wave (delta) activity.[33,34]

Some limitations should be considered in this study. Although our previous study used the PAED and Watcha scores to determine ED,[15] these scales have inherent limitations, such as inability to distinguish ED from pain and no valid cut-off value for the determination of ED. To overcome these limitations, ED was qualitatively determined using the DSM IV or 5 criteria[16] under the consensus of two independent

assessors. To quantify the severity of ED, we used the PAED score. Next, high delta RP, LF/HF ratio, and DAR do not always indicate ED because of the relatively low specificity. Some patients with higher delta RP did not show agitated behaviour despite the difficulties in recovering their orientation at admission to the PACU. This pattern is similar to hypoactive delirium in older patients after general anaesthesia,[5] but the current diagnostic tools do not allow for definite diagnosis of hypoactive delirium in children. Although the two-channel EEG used in this study is portable and affordable and reduces time, effort, and cost, it cannot provide information about the effects of location that multichannel EEG can do. Another limitation was that we could not record EEG preoperatively and postoperatively because of excessive artifacts induced by the movement of children who were mostly uncooperative. Additionally, because the sample size was not estimated for patterns of the spectrogram during the emergence period and the EEG power after anaesthesia induction and at the end of surgery, a lack of statistical power might preclude significant findings. The amplitude threshold to determine the type of anaesthesia in adult patients (7 dB) was used in this study. However, the threshold has not been validated in the paediatric population. Finally, the ED incidence of this study is higher than that of other studies.[10,36] The higher incidence is consistent with the results of a previous study that reported a higher incidence in patients undergoing otorhinolaryngologic and ophthalmological procedures compared with those undergoing other procedures.[36] Therefore, the generalisation of our results should be made with caution.

In summary, ED in children is associated with EEG patterns (high delta RP with low alpha RP, LF/HF ratio, and DAR) derived from frontal EEG recorded during emergence from sevoflurane anaesthesia. Our findings may contribute to predicting the development of ED in children. However, at present, no commercial EEG device provides the values of the predictive EEG parameters in clinical settings. Therefore, further studies are warranted to validate our results and make them clinically applicable.

Authors' contributions

Writing of the first draft: JK, EK
Interpretation of data: JK, HCL, SHB, EK
Acquisition of data: JK, HL, ML, YC
Analysis of data: JK
Analysis of EEG data and results: HCL
Revision of the draft: HCL, SHB, HL, ML, YC
Design of the study concepts, and final revision of the draft: EK
Read and approved the final manuscript: all authors.

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Declarations of interest

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.07.060.

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