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Electroencephalogram dynamics in children during different levels of anaesthetic depth

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HIGHLIGHTS

- EEG dynamics in children are strongly influenced by anaesthetic depth and to a lesser extent by age.
- For children under deep anaesthesia, age dependency of EEG parameters is only seen for total power.
- In children under light anaesthesia relative beta band power increases linearly with age.

ABSTRACT

Objective: Anaesthesia-induced dynamics in EEG are dependent on age and level of anaesthesia, but distinct characterisation in children is incomplete. Here we analyse EEG dynamics in children related to age and level of anaesthesia.
Methods: Frontal EEG recordings were obtained from 93 children (0–19 years) during routine clinical anaesthesia. EEG segments were selected at four different levels of anaesthesia: emergence, light anaesthesia, deep anaesthesia, and very deep anaesthesia.
Results: Total power differed significantly over age at deep ($R^2 = 0.314$; $p < 0.0001$) and very deep anaesthesia ($R^2 = 0.403$; $p < 0.0001$). Relative beta band power at light anaesthesia increased linearly with age ($R^2 = 0.239$; $p < 0.0001$).
Results: Level of anaesthesia caused significant differences for relative delta band power (increasing with anaesthetic depth), for relative beta band power and for spectral edge frequency (decreasing with anaesthetic depth) for all children ($p < 0.0001$).
Conclusions: EEG parameter in children were primary dependent on anaesthetic depth, where beta band power, delta band power and spectral edge frequency showed a linear relation. Age-dependency during anaesthesia procedure were only seen for single EEG parameters.
Significance: Different levels of anaesthesia can be identified by relative beta band power, relative delta band power and spectral edge frequency irrespective of the children's age.

1. Introduction

Loss of consciousness induced by general anaesthetic agents has been proposed to be related to disruptions of connectivity between neuronal networks of the thalamus and the cerebral cortex (Alkire et al., 2000). Accordingly, the electroencephalogram (EEG), as a tool to measure synchronicity of network connectivity, has gained a position as the de facto standard to monitor the depth of anaesthesia. However, EEG signatures used to identify different levels of anaesthesia are not well characterized in children, and still need to be properly described before implementation in clinical practice.

EEG dynamics during anaesthesia and sleep are strongly dependent on age (Schmitt and Wohlrab, 2012; Akeju et al., 2015; Davidson et al., 2008). The period from birth to adolescence is marked by a particularly rapid development and fundamental changes in brain connectivity, which are reflected in the different effects of anaesthetics on EEG oscillations during this period (Akeju et al., 2015; Davidson et al., 2008; Constant and Sabourdin, 2012; Cornelissen et al., 2015). This development is seen in EEG activity of awake children, which shows characteristic

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changes in baseline oscillation: theta and delta oscillations are observed in infants of up to one year of age, increasing in frequency towards slow alpha activity for toddlers, and reaching a baseline alpha activity around the age of 6 years (Schmitt and Wohlrab, 2012). However, age-related EEG characteristics in children during different levels of anaesthesia are still not well established.

Previous studies on children have demonstrated an age-dependence for total EEG power and spectral parameters during deep anaesthesia, as well as during emergence from anaesthesia (Akeju et al., 2015; Davidson et al., 2008; Constant and Sabourdin, 2012; Cornelissen et al., 2015). However, it is still unknown whether this age-dependence can be found consistently during other levels of anaesthetic depth, and how EEG relative band power parameters can be used for monitoring depth of anaesthesia.

Characterizing EEG dynamics during different levels of anaesthesia, as well as their dependence on age, might help to establish a foundation for the development of age-appropriate monitoring of general anaesthesia and sedation in children.

The aim of this study was to determine the effect of age on basic EEG power spectrum parameters during different levels of routine anaesthesia. We conducted this study as an observational, retrospective analysis of EEG data recorded during routine clinical anaesthesia in children. We hypothesized that during routine anaesthesia, depth of anaesthesia, as well as age, will cause changes in EEG power, spectral edge frequency, and in the relative band-power of alpha-, beta-, theta-, and delta- bands.

2. Methods

2.1. Study population and anaesthetic procedure

This study was performed as a retrospective observational trail (NCT03066024). After approval by the local ethics committee (EA2/027/15; Ethikkommission der Charité – Universitätsmedizin Berlin), frontal EEG recordings of 95 children that underwent general anaesthesia between April and November 2015 were obtained from our clinical database. Children with pre-existing neurological conditions (one child), as well as children undergoing neurosurgical procedures (one child), were excluded. All the remaining 93 cases underwent general anaesthesia induced by propofol bolus application, and maintained with sevoflurane as the sole anaesthetic agent, supplemented with opioids, in accordance with our standard operating procedures.

2.2. EEG recording

The EEG of each child was recorded continuously during the anaesthesia. In most children, the EEG was recorded for the complete length of anaesthesia, with few exceptions where the recording started after induction or ended before emergence from anaesthesia. Frontal EEG recordings were performed using the Narcotrend Monitor (MT Monitor Technik, Bad Bramstedt, Germany; software 4.0). Single use surface EEG electrodes (Ambu BlueSensor N/Bad Nauheim Germany) were placed immediately after induction of anaesthesia at the positions Fp1 and F7 or Fp2 and F8, with a ground electrode at Fpz. The skin was prepared with alcohol to reduce impedance. Electrode impedance was <8 kΩ in each channel, and differences between each channel were below 5 kΩ. Sampling frequency was 1024/s, down-sampled to 128/s. A band-pass filter was used to limit the frequency range to 0.5–45 Hz. The frequency resolution of the fast Fourier transformation (FFT) was 0.5 Hz. The power band values were summed for each frequency band range.

2.3. EEG data analysis

Two-minute EEG data segments were selected from each child during four different levels of anaesthesia: (1) "emergence", defined as a time-span around 5 min after anaesthesia was discontinued at the end of surgery; data were only included if Narcotrend Stadium B was reached during postoperative EEG recording; (2) "light aesthesia", defined as an end tidal sevoflurane concentration below 0.7 MAC (minimal alveolar concentration); primarily indicated by the Narcotrend Stadium C; (3) "deep anaesthesia", defined as an end tidal sevoflurane concentration above 0.8 MAC; primarily indicated by the Narcotrend Stadium D; and (4) "very deep anaesthesia", defined as a time-span 2–5 min after anaesthesia induction with a propofol bolus. Data were only included if Narcotrend Stadium E was reached within 5 min after anaesthesia induction. Data segments were selected by visual inspection, to ensure that they were noise- and artefact-free. Data segments were put in order from emergence to very deep anaesthesia, to point out the influence of depth of anaesthesia on the EEG parameters, even though this is not in line with the time order of the data segments evaluated. For each segment, we calculated the mean value from the chosen two-minute EEG data segments, to define overall power (μV^2), the relative beta (12.5–30 Hz), alpha (7.5–12.5 Hz), theta (3.5–7.5 Hz), and delta (0.5–3.5 Hz) band powers (%), as well as the spectral edge frequency 95% (SEF/Hz), using the EEG viewer software (MT Monitor Technik, Bad Bramstedt, Germany, Version1.6). Analyses were performed based on the signals from the Fp1-F7 and Fp2-F8 electrodes with the Fpz electrode as reference.

2.4. Statistical analysis

Results are expressed as arithmetic mean ± SD for patient characteristics, as well as for age-related and level of anaesthesia-related EEG parameters. Statistical tests were conducted as follows: non-parametric test via Mann-Whitney U for two independent samples, Kruskal-Wallis test for three or more independent samples, and the Fisher exact test for qualitative data. To illustrate the age-dependence of the investigated parameters, plots of the total power (μV^2), the relative band powers (%) for the beta-, alpha-, theta-, delta-spectrum, and the spectral edge frequency (Hz) over age for each level of anaesthesia were created. The best-fit regression model was obtained to describe the relationship between age and EEG parameters using regression analysis in SPSS Version 23. Total power was best analysed by a third-degree polynomial regression model, whereas relative band powers in the beta-, alpha-, theta-, delta-spectrum, and spectral edge frequency were analysed by linear regression model. The significance threshold was set at $p < 0.001$. To define the sensitivity, specificity and the cut off values to differentiate in between emergence versus light anaesthesia, light anaesthesia versus deep anaesthesia and deep anaesthesia versus very deep anaesthesia we calculated ROC curve analyses. Statistical testing was performed using SPSS, Version 23, Copyright© SPSS, Inc., Chicago, Illinois 60606, USA.

3. Results

Data was collected over a period of 6 months, from April until November 2015. Patient characteristics and the dosages of the administered drugs are summarized in Table 1. Anaesthesia duration was longer in the <1-year-old age group, as there was a higher proportion of cleft-lip-palate surgery in this age group, which mainly involves a surgery duration of 3–5 h. Due to routine clinical practice, the administered propofol concentration was significantly elevated in age group <1 year.