ORIGINAL CLINICAL RESEARCH REPORT

Monitoring Depth of Hypnosis: Mid-Latency Auditory Evoked Potentials Derived aepEX in Children Receiving Desflurane-Remifentanil Anesthesia

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BACKGROUND: The aepEXplus monitoring system, which uses mid-latency auditory evoked potentials to measure depth of hypnosis, was evaluated in pediatric patients receiving desflurane-remifentanil anesthesia.

METHODS: Seventy-five patients, 1–18 years of age (stratified for age; 1–3, 3–6, 6–18 years, for subgroup analyses), were included in this prospective observational study. The aepEX and the bispectral index (BIS) were recorded simultaneously, the latter serving as a reference. The ability of the aepEX to detect different levels of consciousness, defined according to the University of Michigan Sedation Scale, investigated using prediction probability (P_k), and receiver operating characteristic (ROC) analysis, served as the primary outcome parameter. As a secondary outcome parameter, the relationship between end-tidal desflurane and the aepEX and BIS values were calculated by fitting in a nonlinear regression model.

RESULTS: The P_k values for the aepEX and the BIS were, respectively, .68 (95% CI, 0.53–0.82) and .85 (95% CI, 0.73–0.96; P = .02). The aepEX and the BIS had an area under the ROC curve of, respectively, 0.89 (95% CI, 0.80–0.95) and 0.76 (95% CI, 0.68–0.84; P = .04). The maximized sensitivity and specificity were, respectively, 81% (95% CI, 61%–93%) and 86% (95% CI, 74%–94%) for the aepEX at a cutoff value of >52, and 69% (95% CI, 56%–81%) and 70% (95% CI, 57%–81%) for the BIS at a cutoff value of >65. The age-corrected end-tidal desflurane concentration associated with an index value of 50 (EC_{50}) was 0.59 minimum alveolar concentration (interquartile range: 0.38–0.85) and 0.58 minimum alveolar concentration (interquartile range: 0.41–0.70) for, respectively, the aepEX and BIS (P = .69). Age-group analysis showed no evidence of a difference regarding the area under the ROC curve or EC_{50}.

CONCLUSIONS: The aepEX can reliably differentiate between a conscious and an unconscious state in pediatric patients receiving desflurane-remifentanil anesthesia. (Anesth Analg 2020;130:194–200)

KEY POINTS

- **Question:** How does the aepEX monitor perform in detecting different depths of hypnosis in children during desflurane-remifentanil anesthesia?
- **Findings:** This study demonstrates that the aepEX monitor has reasonable sensitivity and high specificity to detect the return of consciousness while having a low prediction probability of distinguishing different depths of hypnosis.
- **Meaning:** The aepEX monitor can reliably be used as an additional parameter to detect the return of consciousness in children receiving desflurane-remifentanil anesthesia.

Monitoring the depth of hypnosis (DoH) in anesthetized patients provides the anesthesiologist with significant additional information, enabling one to adjust the dose of anesthetic agents more adequately, according to the needs of the patient. DoH monitoring in children has been shown to result in the use of lower doses of anesthetic drugs and a faster recovery.[1–3] Bearing in mind the ongoing discussion about potential neurotoxic effects of anesthetic drugs on the developing brain, this technology can help prevent anesthetic drug overdosing, adding safety to the conduct of pediatric anesthesia.

Mid-latency auditory evoked potentials (MLAEP) can be utilized to measure the DoH during anesthesia.[4–7] The developmental time of MLAEP extends through the first decade of life,[8] as opposed to the raw electroencephalogram (EEG), which is not mature before early adulthood. MLAEP are therefore a potentially more useful parameter to assess the DoH than EEG in children.

The aepEXplus monitor (aepEX) is a commercially available DoH monitor that utilizes MLAEP. In previous studies, the performance of the aepEX

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was evaluated in children during propofol and sevoflurane anesthesia.[9,10] Desflurane, due to its low blood-gas partition coefficient, has a unique pharmacokinetic profile, which, from a clinical perspective, can best be described as "fast in-fast out." Desflurane is a challenging drug for DoH monitors because they have to calculate their DoH indices in a clinical setting characterized by fast changes in hypnotic drug target concentration.

The current study was conducted to assess the performance of the aepEX monitor in children during desflurane-remifentanil anesthesia. For means of reference, bispectral index (BIS) values were also recorded simultaneously.

The primary objective of this prospective observational study was to assess the ability of the aepEX to detect the return of consciousness during emergence from anesthesia. Our secondary objective was to assess the relationship between the aepEX and different end-tidal desflurane concentrations.

METHODS

This article adheres to the applicable STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guideline. The study was reviewed and approved on May 12, 2011 by the Institutional Review Board of the Erasmus MC, Rotterdam, the Netherlands (MEC 2011–104, NL 35976.078.11) and registered in the Dutch trial register before inclusion of the first patient (http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=2983, NTR2983, principal investigator: Y. M. Cheung, date of registration: July 12, 2011). Written informed consent was obtained from the participants' parents or guardians. According to the Dutch law, additional written informed assent was collected from children ≥12 years of age.

Patients scheduled in the Erasmus MC, Sophia children's hospital for elective general, urologic, plastic, or orthopedic surgery were eligible for inclusion. The entire cohort of 75 patients was stratified for age into 3 groups of 25 children each (group 1: 1–3 years; group 2: 3–6 years; and group 3: 6–18 years) to detect possible age-related effects. Exclusion criteria consisted of known allergies to any medication in the study protocol (remifentanil, desflurane, sevoflurane, and/or propofol), the presence of a clinically significant hearing impairment, the use of medication (eg, premedication, antiepileptics), having a condition affecting the EEG (to prevent bias), and a planned postoperative admittance to the pediatric intensive care unit.

Conduct of Anesthesia

After arrival at the operating room, an intravenous cannula was inserted and remifentanil 0.5 $\mu g \cdot kg^{-1}$ was administered over 15 seconds followed by a continuous infusion of 0.1 $\mu g \cdot kg^{-1} \cdot minute^{-1}$. General anesthesia was induced with propofol 3.0–5.0 $mg \cdot kg^{-1}$.

When it was not possible to obtain intravenous access in the awake child, induction was performed with sevoflurane by facemask, after which an intravenous access was obtained in the anesthetized child. Immediately after an intravenous cannula was in place, remifentanil was administered according to the same scheme as in awake children. After insertion of a laryngeal mask, airway desflurane was slowly washed in to an end-tidal desflurane concentration (Et_{des}) of approximately 1 minimum alveolar concentration (MAC), adjusted for age.[11]

Once the airway was secured, locoregional analgesia was given whenever possible and appropriate. Ropivacaine 0.2% was used for low-volume ultrasound-guided peripheral locoregional techniques and caudal blocks. Penile nerve blocks were performed with bupivacaine 0.5%. When locoregional analgesia was not an option, for whatever reason, remifentanil was increased to a dose of 0.3–0.4 $\mu g \cdot kg^{-1} \cdot minute^{-1}$ during the surgery.

During anesthesia, all patients were monitored with our standard equipment, which consists of electrocardiogram, pulse oximetry, noninvasive blood pressure measurement, temperature, capnography, and inspired and end-tidal concentrations of oxygen, sevoflurane, and desflurane.

aepEX and BIS Monitoring

After induction of general anesthesia, the skin on the forehead was swabbed with alcohol and abraded with Sensor Prep (Medical Device Management, Essex, United Kingdom) to decrease the impedance to a low enough level to allow for both aepEX and BIS monitoring. aepEX and BIS electrodes were then attached, respectively, on the left and right sides of the patient's forehead according to the manufacturer's recommendation. A commercially available over-the-ear headphone (MDR-V150; Sony Europe, London, United Kingdom) was connected to the aepEX because standard earplugs are unsuitable for small children. aepEX index values were transferred to a personal computer at 5-second intervals using the aepEX's logger software (version 1.3, Medical Device Management, Essex, United Kingdom). aepEX data labeled with "artefact," as shown by the aepEX logger software, were excluded from subsequent analysis.

The BIS Vista monitoring system (version 2.02, Aspect Systems International, de Meern, the Netherlands) was used, with a smoothing rate of 15 seconds. BIS data were directly transferred at 1-second intervals to a USB stick plugged into the monitor. BIS values with a signal quality <50%, as indicated by the BIS signal quality index, were excluded from subsequent analysis.

Data collection for study purposes started 15 minutes after administration of propofol or when the end-tidal

sevoflurane concentration, in the case of an inhalation induction, was 0% as measured by our anesthesia machine (Primus, Draeger, Lübeck, Germany). Patients were primarily allowed to breathe spontaneously during the surgical procedure. In case of hypoventilation (end-tidal CO_2 >6.0 kPa), mechanical ventilation was used to reestablish and maintain normocapnia (end-tidal CO_2 of 4.5–6.0 kPa). During the surgical procedure, Et_{des} was initially titrated to 1.5 MAC and decreased every 3 minutes by 1 vol% to a minimum of 0.7 MAC, corrected for age. According to Taylor and Lerman,[11] we defined 1 MAC as 8.7%, 8.6%, 8.0%, and 7.5% for children 1–3, 3–5, 5–12, and ≥12 years of age. At the start of wound closure, Et_{des} was decreased to 0.5 MAC. After completion of the surgical procedure, the administration of desflurane was discontinued, and the fresh-gas flow was set to 10 L·minute^{-1} using 100% oxygen.

During the emergency period, the DoH was assessed according to the University of Michigan Sedation Scale (UMSS)[12] until the patient had a UMSS ≤1. The UMSS consists of 5 levels, including "awake/alert," "minimally sedated," "moderately sedated," "deeply sedated," and "unarousable," which correspond, respectively, to a UMSS of 0, 1, 2, 3, and 4.

Data analyses were performed with the average index value over 10 seconds before the intended time points as described previously.

Statistical Analysis

Primary Outcome. The relationship between the index values and different DoH (UMSS) were analyzed by calculating the prediction probability value (P_k), which was described by Smith et al.[13] A P_k value and the area under the curve (AUC) derived from a receiver operating characteristic (ROC) analysis are both measures of the discriminative ability of a predictor; to set it more precisely, P_k is a generalization of the AUC. ROC analyses can only be performed with dichotomous outcome parameters, whereas P_k also allows assessment of the discriminative power of a predictor when there are >2 states. A P_k of 1.0 corresponds with a DoH monitor that always predicts the correct UMSS. If a DoH monitor predicts the correct UMSS in only 50% of the cases, then it will have a P_k of .5. A P_k <.5 describes an inverse relationship. An inverse relationship will be expressed as $1 - P_k$ for a better understanding. P_k values were only computed when ≥3 different UMSS values were observed because computing this for only 2 different values would be the same as a ROC with its corresponding AUC. For each individual patient, the P_k value would be computed, after which the mean P_k value for its corresponding age group would be calculated.

ROC analyses and its corresponding AUC were performed to investigate the predictive capabilities of the DoH monitor to distinguish consciousness from unconsciousness using MedCalc for Windows, version 5.6.1 (MedCalc Software, Mariakerke, Belgium). The cutoff index value at which both the sensitivity and the specificity was the highest was defined as the maximized combination. For analysis, we defined consciousness and unconsciousness as a UMSS of, respectively, ≤1 and ≥2.

Secondary Outcome. aepEX and BIS data were fitted in a nonlinear regression model to analyze the relationship between index values and different Et_{des}. An inhibitory sigmoid E_{max} model was used for this purpose:

$$E = E_0 + \frac{(E_{max} - E_0)}{1 + 10^{(\log EC_{50} - \log x)\gamma}}$$

E_0 and E_{max} are, respectively, the minimum and maximum value of the index values, which were 0 and 100. The EC_{50} is the Et_{des} at which an index value of 50 was reached on the DoH monitors. E is the predicted index value during the administration of an Et_{des} of x, whereas γ is the Hillslope, which was variable to optimize the best fit for this model. The EC_{50} of each individual patient was first computed after which the median of the corresponding group was calculated.

Continuous data were tested for normality by visual inspection and the D'Agostino & Pearson omnibus normality test. To compare the EC_{50} between the aepEX and BIS (of the cohort and different age groups), the Wilcoxon matched-pairs signed rank test was used. When comparing the EC_{50} among different age groups, a Kruskal-Wallis test was used. P_k values of the aepEX and BIS (of the cohort and different age groups) were compared with a paired t test, while P_k values among different age groups were analyzed with an unpaired t test. These tests were computed and analyzed with GraphPad Prism for Windows, version 6.04 (GraphPad Software, San Diego, CA). The method of DeLong et al[14] was applied for analysis of the (paired) AUC between the aepEX and BIS monitor. The comparison of the AUC of different age groups was made according to the method of Hanley and McNeil.[15] All analyses among or within the 3 age groups were corrected for multiple testing with the Bonferroni correction, except for the Kruskal-Wallis test, for which Dunn's post hoc analysis was applied.

Descriptive analyses were performed with IBM SPSS Statistics for Windows, version 21.0 (IBM Corp, Armonk, NY). Variables were presented as mean ± standard deviation unless stated otherwise. P values <.05 were considered statistically significant.

A sample size of 25 children per age group and the defined age groups correspond to similar published studies concerning DoH monitors.[6,16,17] Previous studies have assumed that a reliable P_k value can be computed with a sample size of >20 patients.[18–20]

Table 1. Baseline Characteristics

Characteristics	1–3 y (N = 20)	3–6 y (N = 24)	6–18 y (N = 24)	Entire Cohort (N = 68)
Female, no. (%)	1 (5)	2 (8)	7 (29)	10 (15)
Age, median [range] (mo)	22 [12–35]	54 [37–70]	139 [73–210]	74 [12–210]
Weight, median (IQR) (kg)	12 (10–15)	17 (15–21)	44 (26–59)	17 (14–26)
Procedure, no. (%)				
Upper extremity	3 (15)	3 (13)	5 (21)	11 (16)
Subumbilical	17 (85)	20 (83)	19 (79)	56 (82)
Upper and lower extremity	0 (0)	1 (4)	0 (0)	1 (1)
Locoregional analgesia technique, no. (%)				
Caudal	17 (85)	16 (67)	9 (38)	42 (62)
Brachial plexus	1 (5)	2 (8)	2 (8)	5 (7)
Lumbosacral plexus	0 (0)	2 (8)	10 (42)	12 (18)
Epidural	0 (0)	1 (4)	0 (0)	1 (1)
None	2 (10)	3 (13)	3 (13)	8 (12)

Abbreviation: IQR, interquartile range.

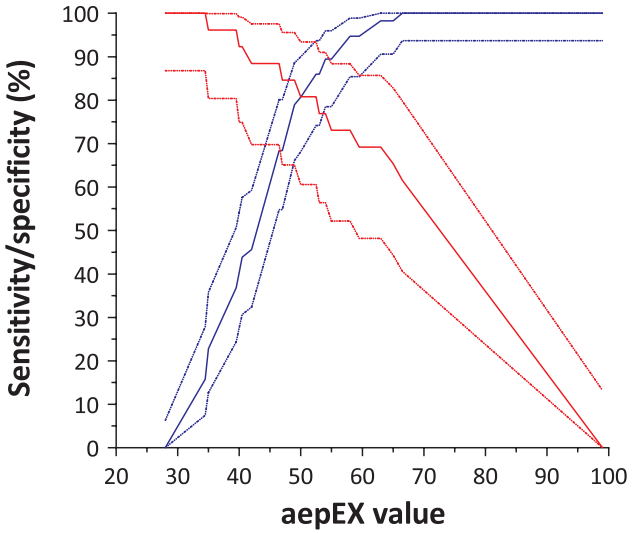

Figure 1. aepEXplus monitor's (aepEX) receiver operating characteristic. Sensitivity (solid red lines) and specificity (solid blue lines) at different aepEX cutoff values with their respective 95% CIs (dotted red and blue lines).

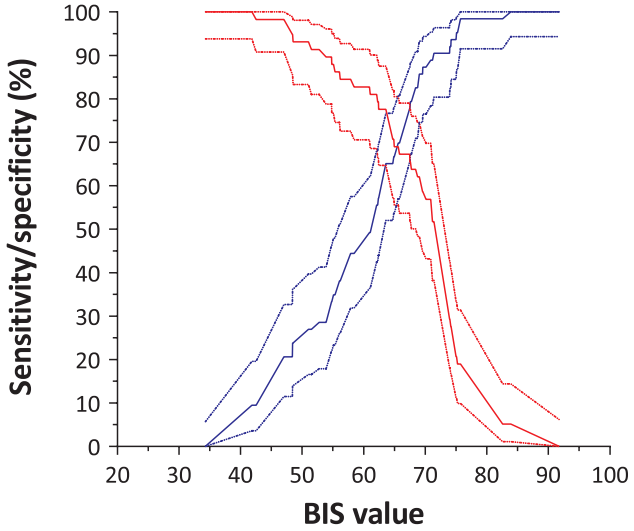

Figure 2. Bispectral index's (BIS) receiver operating characteristic. Sensitivity (solid red lines) and specificity (solid blue lines) at different BIS cutoff values with their respective 95% CIs (dotted red and blue lines).

RESULTS

Between December 2012 and September 2014, a total of 75 patients were included, of whom 7 had to be excluded secondarily due to the following reasons: administration of premedication (N = 1, group 2), tracheal intubation (N = 1, group 1), and ventilation difficulties before or during the data collection (N = 4, group 1; N = 1, group 3). Details concerning baseline characteristics of the patient are shown in Table 1.

During the wash-in period of desflurane, 28 patients (N = 11, group 1; N = 8, group 2; N = 9, group 3) had difficulties maintaining normocapnia, despite mechanical ventilation. In these patients, a further increase of desflurane was avoided, and intraoperative measurements were started at an end-tidal desflurane concentration <1.5 MAC. In another 3 patients (N = 1, group 1; N = 2, group 2), the target MAC of 1.5 could not be reached due to an unexpected short surgical procedure. Furthermore, we were unable to collect data until a UMSS of 1 was reached in 3 patients (N = 2, group 2; N = 1, group 3) due to patient agitation during emergence. In 1 patient (group 3), the aepEX could not compute any index values due to excessive artifact contamination of the signal. From this patient, only BIS values from the emergency period were available for analysis.

Data during emergence were available in 45 patients in which ≥3 UMSS values could be observed. The

Table 2. Receiver Operator Characteristics Analysis of the aepEX and BIS Monitor

Age Group	AUC of the aepEX (Mean: 95% CI)	AUC of the BIS (Mean: 95% CI)	*P* Value
Group 1	0.76 (0.55–0.90)	0.63 (0.42–0.81)	.31[a]
Group 2	0.95 (0.79–1.00)	0.84 (0.64–0.95)	.05[a]
Group 3	0.99 (0.85–1.00)	0.98 (0.84–1.00)	.87[a]
Entire cohort	0.89 (0.80–0.95)	0.76 (0.68–0.84)	.04

Abbreviations: aepEX, aepEXplus monitor; AUC, area under the curve; BIS, bispectral index; CI, confidence interval.
[a]Uncorrected *P* value for multiple testing.

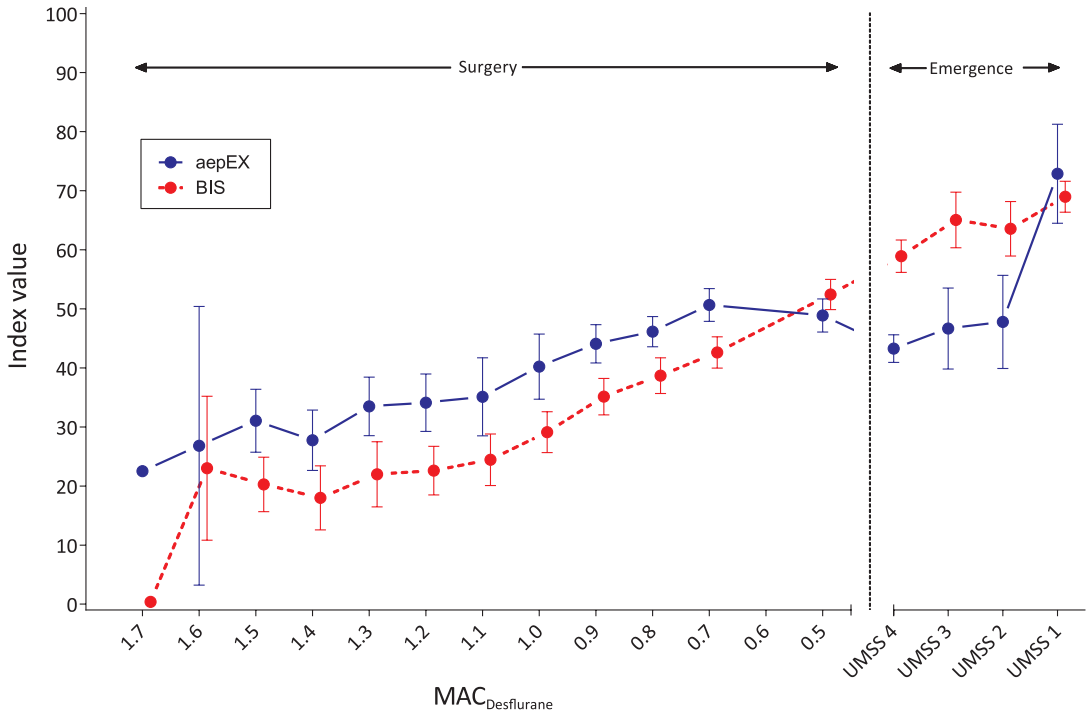

Figure 3. Trend of aepEXplus monitor (aepEX) and bispectral index (BIS). Mean index values of the aepEX (solid lines) and BIS (dashed lines) with their respective 95% CIs related to different end-tidal desflurane concentrations and University of Michigan Sedation Scale (UMSS) values. MAC indicates minimum alveolar concentration.

quality of the EEG signal was sufficient to compute 13 P_k values for the aepEX and 37 for the BIS. A paired *t* test was possible in 12 P_k data pairs, resulting in a P_k value of .68 (95% CI, 0.53–0.82) for the aepEX and 0.85 (95% CI, 0.73–0.96) for the BIS ($P = .02$). Because only 12 pairs of P_k values were available for analysis, a subsequent age-group analysis was abandoned.

The maximized combination of sensitivity and specificity of the aepEX was 81% (95% CI, 61%–93%) and 86% (95% CI, 74%–94%) at an index value >52. This was for the BIS at an index value of >65, during which the sensitivity was 69% (95% CI, 56%–81%) and the specificity 70% (95% CI, 57%–81%). A detailed relationship between index value and sensitivity and specificity are plotted in Figures 1 and 2.

Paired comparisons of the AUC of the aepEX and BIS monitor showed no evidence for a difference between the entire cohort or the different age groups. Details are shown in Table 2. We also found no evidence of a difference when comparing AUCs of the 3 age groups with each other after correction for multiple testing.

A total of 569 aepEX values qualified for subsequent analysis (having no artifacts), while the BIS provided 632 index values with a signal quality of >50%. These values are plotted in Figure 3, describing the relationship between the index values of both DoH monitors during different Et_{des} and UMSS.

The age-corrected EC_{50} for the aepEX ($EC_{50aepEX}$) was 0.59 MAC (interquartile range: 0.38–0.85; N = 57) and for the BIS (EC_{50BIS}) 0.58 MAC (interquartile range: 0.41–0.70; N = 63). Eleven $EC_{50aepEX}$ could not be computed due to software limitations (unable to converge data; N = 2, group 1; N = 1, group 2; N = 1, group 3), too few intraoperative data (N = 1, group 1; N = 1, group 2; N = 1, group 3), and data with too many artifacts (N = 3, group 2; N = 1, group 3). Software limitations accounted for 2 missing EC_{50BIS} (N = 1, group 1; N = 1, group 3) and 3 for having too few intraoperative data (N = 1, group 1; N = 1, group 2; N = 1, group 3). Both monitors had a comparable r^2: 0.62 (95% CI, 0.54–0.71) for the aepEX and 0.69 (95% CI, 0.63–0.76) for the BIS. The Kruskal-Wallis tests comparing the EC_{50} among different age groups also showed no evidence of a difference ($P = .27$ for the aepEX and $P = .12$ for the BIS). Paired comparison (N = 57) between the $EC_{50aepEX}$ and EC_{50BIS} resulted in a *P* value of .69. The same comparison for age groups 1, 2, and 3 revealed *P* values of, respectively, .38, .14, and .84.

DISCUSSION

Our study demonstrates that the aepEX monitor differentiates between unconscious and conscious pediatric patients with a 10% higher sensitivity and specificity than the BIS monitor. As opposed to this finding, the aepEX performs inferiorly to the BIS to correctly predict different UMSS. We found no evidence of an age-related difference in performance of the aepEX, suggesting that the aepEX performs equally in all patients from 1 to 18 years of age.

The results of this study are consistent with our findings from the previous study investigating the

aepEX in children during propofol and sevoflurane anesthesia.[9,10] This finding implies that the aepEX monitor also performs equally during different commonly used anesthetics in children, that is, propofol, sevoflurane, and desflurane.

As proposed by Smith et al,[13] the P_k approach to measure the performance of an anesthetic depth indicator is aimed to include different levels of anesthetic depth in the analysis. We could, however, only measure 2 levels of anesthetic depth in the majority of our patients, which is probably attributable to the properties of desflurane, for example, its low blood-gas partition coefficient. Nonetheless, we found evidence of the superiority of the BIS over the aepEX in discriminating different UMSS levels.

The concept that consciousness has levels has been accepted for decades. Many different clinical observational scales have been designed, validated, and used to assess the level of consciousness, among them the Observer's Assessment of Alertness/Sedation scale and the UMSS. All of these scales assume that DoH is graded and that, beginning with a fully awake subject, each step of the scale reflects a "lower level of consciousness," or, in the context of anesthesia research, "depth of hypnosis." By now we are still not sure about the true underlying mechanism(s) of our mental states named consciousness and unconsciousness. Regarding unconsciousness, it is even possible that the concept of "hypnotic depth" is not correct at all, in other words, that we are either conscious or unconscious.[21] Therefore, we also performed an ROC analysis as an alternative approach to quantify the monitors' performance. An ROC analysis requires only 2 different states ("conscious" and "unconscious") for analysis. Beside this, it also gives a more clinically applicable result, that is, a clear cutoff value with its corresponding sensitivity and specificity. In our current study, we found that when choosing the maximal sensitivity and specificity, the aepEX is superior to the BIS. Choosing the clinically most relevant combination of the sensitivity and specificity of the monitors depends on personal preferences regarding the most important monitoring target. When prevention of intraoperative awareness is of paramount importance, a DoH monitor with a higher sensitivity is favorable. However, if the sensitivity is chosen too high, the resulting low specificity would render the monitor useless (Figures 2–3).

By definition, the EC_{50} is the drug concentration needed to achieve 50% of the drug's maximum effect. In our current study, we fitted our intraoperative data in a nonlinear regression model to compute the EC_{50}. However, the EC_{50} can also be measured by recording the end-tidal desflurane concentration while maintaining an index value of 50. Fletcher et al[17] performed such a study by maintaining a BIS of 60 during pediatric scoliosis surgery under desflurane anesthesia. The end-tidal concentration desflurane needed to maintain a BIS of 60 can be described as an EC_{60} for the BIS monitor. Although an EC_{60} is different from an EC_{50} and our study designs are not comparable, we found a similar MAC of 0.58. Caution is needed when comparing both studies; despite the aforementioned, their EC_{60} comes close to the EC_{50BIS} we observed.

Although processed EEG and MLAEP have strong relationships with consciousness level, we should not solely rely on computed DoH index values. A recent study by Schneider et al[22] supports this concept. They demonstrated that the combination of the BIS monitor with other standard monitoring parameters, for example, heart rate and blood pressure, resulted in a P_k of 1.0 to detect the return of consciousness in adult patients, emphasizing the importance of observing the patient as a whole.

Almost all patients in our study received additional locoregional analgesia before the surgical procedure, most often a caudal block. Davidson et al[16] demonstrated that a caudal block resulted in a decrease in BIS value of 5 points. The effect of a caudal block on the aepEX has not yet been studied. Although remifentanil decreases the MAC of volatile anesthetics, the DoH seems to be unaffected by it, which was demonstrated by Schraag et al and Guignard et al.[23,24] Both studies observed no effect of remifentanil on the aepEX and BIS index values, and we assume that this also applies for our study.

Other studies have revealed a P_k BIS value of .82 and .89, which is similar to our observed P_k value of .85.[25,26] However, these results were observed in the adult population and concerned P_k values detecting different end-tidal desflurane concentrations or eye opening after general anesthesia. Because our observed P_k BIS value is not comparable to other studies and only 13 paired P_k values could be computed in our study, interpretations of the P_k values of the aepEX and BIS are limited.

The age stratification applied in this study was designed to match similar studies for comparison purposes. However, concerns can be made due to the broad range of group 3 (6–18 years of age). Because the MLAEP is still developing until the first decade of life,[8] this group consisted of children with developing MLAEP and fully developed MLAEP pathways. However, because the development of the MLAEP is a continuous process, we would at least expect to find a difference between group 1 (fully undeveloped MLAEP) and group 3 (MLAEP in final development combined with fully developed MLAEP) if an age-dependent performance for the aepEX exists. It would be interesting to compare group 3 with adult data, but unfortunately no such comparable study was published.

Our study population consisted predominantly of male children. However, we believe it is unlikely that this factor affected our study.

In conclusion, our current study observed that the aepEX monitor could reliably differentiate unconsciousness from consciousness in pediatric patients during remifentanil-desflurane anesthesia combined with a locoregional technique. ■

DISCLOSURES

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