Anesthesiology 2003; 99:1072–7

Narcotrend® and Bispectral Index® Monitor Are Superior to Classic Electroencephalographic Parameters for the Assessment of Anesthetic States during Propofol–Remifentanil Anesthesia

Gunter N. Schmidt, M.D., Petra Bischoff, M.D.,† Thomas Standl, M.D.,‡ Kai Jensen, M.D.,§ Moritz Voigt, M.D.,‖ Jochen Schulte am Esch, M.D.#*

Background: **A new electroencephalogram monitor, the Narcotrend®, was developed to measure anesthetic depth. The authors compared the Narcotrend®, the Bispectral Index®, and classic electroencephalographic and hemodynamic parameters during anesthesia with propofol and remifentanil.**

Methods: **The authors investigated 25 patients undergoing laminectomy at different anesthetic states: awake, steady state anesthesia, first reaction during emergence, and extubation. Narcotrend® value; BIS; relative power (percent) in δ, θ, α, and β; median frequency; spectral edge frequency; and hemodynamic parameters were recorded simultaneously. The ability of the classic and processed electroencephalographic and hemodynamic parameters to predict the clinically relevant anesthetic states of awake, steady state anesthesia, first reaction, and extubation was tested using prediction probability.**

Results: **Only the Narcotrend® was able to differentiate between awake *versus* steady state anesthesia and steady state anesthesia *versus* first reaction/extubation with a prediction probability value of more than 0.90.**

Conclusions: **Modern electroencephalographic parameters, especially Narcotrend®, are more reliable indicators for the clinical assessment of anesthetic states than classic parameters.**

ASSESSMENT of the depth of anesthesia is of profound interest for anesthesiologists. However, measurement of depth of anesthesia is still an unsolved problem because there is no clear definition of what *depth of anesthesia* means.

The Narcotrend®, a new monitor displaying a derived electroencephalographic parameter (Narcotrend®; MonitorTechnik, Bad Bramstedt, Germany), automatically classifies the resting electroencephalogram into stages defined by Kugler during the 1980s.[1,2] Narcotic stages deescalate from the awake state (stage A) to isoelectric electroencephalogram using 14 distinct gradations (table 1).[1] Adequate depth of anesthesia is indicated by D0, D1, D2, E0, and E1, followed by F0 and F1, indicating burst suppression and isoelectric electroencephalogram, respectively. In a recent study, the Narcotrend® was compared with the Bispectral Index® (BIS®; Aspect Medical Systems, Newton, MA). Decreasing Narcotrend® stages during anesthesia were accompanied by decreasing BIS® values.[3] However, no validation of the predictive probability of these monitors to differentiate clinically relevant endpoints of anesthesia is available so far.

The goal of the current study was to compare the Narcotrend®, BIS®, and classic electroencephalographic and hemodynamic parameters by analyzing the accuracy of each parameter to distinguish between different states of anesthesia, such as awake, steady state anesthesia, and emergence/extubation. Our hypotheses are that there is no difference in performance between the Narcotrend® and the BIS® in differentiation of anesthetic states, and both monitors would be better than classic power spectral electroencephalographic or hemodynamic parameters in this issue.

Materials and Methods

After institutional review board approval (Ärztekammer Hamburg, Hamburg, Germany) and written informed consent, 25 elective patients were included in the study. Selection criteria were age between 18 and 75 yr, American Society of Anesthesiologists physical status classification I or II, and laminectomy surgery. No patient with any medication interacting with the central nervous or cardiopulmonary system was included in the study to avoid influences on the electroencephalographic and hemodynamic parameters.

After premedication with 7.5 mg oral midazolam (30 min before induction), anesthesia was induced with 0.7 $\mu g \cdot kg^{-1} \cdot min^{-1}$ remifentanil continued after 2 min with additional target-controlled infusion (TCI) of 5.0 μg/ml propofol over 10 min. Rocuronium bromide (0.6 mg/kg) was used to facilitate tracheal intubation. After intubation, anesthesia was maintained with 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ remifentanil and 3.0 μg/ml propofol (Diprifusor, Graseby 3500; Graseby Medical Limited, Hertfordshire, Watford, United Kingdom). After the end of surgery, remifentanil infusion was stopped, and 10 min later, propofol was reduced step by step (0.2 μg/ml) every 3 min. Extubation criteria were sufficient spontaneous breathing and spontaneous eye opening. We defined different anesthetic states: awake, steady state anesthesia, first reaction, and extubation (table 2). Com-

* Anesthesia Fellow, † Associate Professor in Anesthesiology, ‡ Professor in Anesthesiology, § Staff Anesthesiologist, ‖ Research Fellow, # Professor in Anesthesiology and Chairman.

Received from the Department of Anesthesiology, University Hospital Hamburg-Eppendorf, Hamburg, Germany. Submitted for publication October 29, 2002. Accepted for publication June 11, 2003. Support was provided solely from department sources. Presented in part at the Annual Meeting of the American Society of Anesthesiologists, Orlando, Florida, October 15, 2002.

Address reprint requests to Dr. Schmidt: Department of Anesthesiology, University Hospital Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany. Address electronic mail to: guschmid@uke.uni-hamburg.de.

Table 1. Narcotrend® Stages and Corresponding Electroencephalogram and Clinical Description

No.	Narcotrend® Stages	Electroencephalogram Description	Clinical Description
1	A	α Activity	Awake
2	B0	↓	↓
3	B1	β Activity	
4	B2	↓	
5	C0		
6	C1	θ Activity	
7	C2	↓	
8	D0		
9	D1		
10	D2	↓	
11	E0		
12	E1	δ Activity	
		↓	
13	F0	Burst suppression	
14	F1	Isoelectric electroencephalogram	Very deep anesthesia

parisons were performed for awake *versus* steady state anesthesia, steady state anesthesia *versus* first reaction, and steady state anesthesia *versus* extubation.

The electroencephalogram was registered by seven adhesive silver–silver chloride gel-filled electrocardiogram electrodes (Blue-Sensor; Medicotest, Olstykke, Denmark) on carefully prepared skin (Arbo-Prep; Tyco Healthcare, Neustadt, Germany). Electrode placement was performed according to the instructions of the manufacturers of BIS® (two-channel reference, At1-Fpz and At2-Fpz, ground Fp2) and Narcotrend® (one-channel bipolar at the hairless skin of the forehead). Electrode impedance was kept below 5 kΩ. BIS® (version 3.3), relative power in δ (%δ: 0.5–3.75 Hz), θ (%θ: 4.0–7.75 Hz), α (%α: 8.0–13.5 Hz), β (%β: 13.75–30.0 Hz), spectral edge frequency, and median frequency were recorded by the Aspect A-1000 monitor (Aspect Medical Systems). The signals were bandpass filtered between 0.5 and 30 Hz. Bispectral and spectral smoothing rates were 30 s. For artifact detection, "slow rate, suppression, motion, and height frequency" were enabled. Narcotrend® stages (version 2.0 AF/F) were registered by the Narcotrend® electroencephalographic system (MonitorTechnik). All data were stored on disk.

Hemodynamic parameters such as heart rate, noninvasive mean arterial pressure (MAP), and oxygen saturation were measured and registered at every point of measurement (Solar 8000; Marquette Hellige Medical Systems, Milwaukee, WI). End-expiratory carbon dioxide concentrations were maintained between 35–40 mmHg during the whole observation time.

Table 2. Evaluated States during Anesthesia with Propofol and Remifentanil

Evaluated States	Drugs
Awake	—
Steady state anesthesia	0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ remifentanil, 3.0 μg/ml propofol
First reaction	Step-wise reduction of propofol
Extubation	—

Statistical Analysis

For all parameters, the 95%, 90%, 75%, 50%, 25%, 10%, and 5% percentiles were calculated for the investigated states. The accuracy to distinguish between the anesthetic states awake *versus* steady state anesthesia, steady state anesthesia *versus* first reaction, and steady state anesthesia *versus* extubation were analyzed with the prediction probability (P_K). P_K was calculated for all parameters using a custom spreadsheet macro, P_KMACRO, as described by Smith *et al.*[4] The jackknife method was used to compute the SE of the estimate. Comparisons of the P_K values were performed with the P_KDMACRO.[4] A value of P_K of 0.5 means that the parameter predicts the states not better than a 50:50 chance. A value of P_K of 1.0 means that the parameter predicts the states correctly 100% of the time. A value less than 0.5 means that discordance is more likely than concordance. To enable comparison of P_K, we used $1 - P_K$ when the P_K value was less than 0.5.[4] Logistic regression was used to analyze the probability for first reaction in comparison with steady state anesthesia for the Narcotrend® and BIS®. Correlations between the Narcotrend® and BIS® were evaluated by nonparametric Spearman rank correlation coefficient and linear regression analysis for all data pairs from awake through extubation. Statistical analysis were performed using the SPSS package (version 9; SPSS, Chicago, IL), P_KMACRO, and P_KDMAKRO.[4]

Results

Data evaluation was performed in 25 patients (12 female, 13 male; age, 51 ± 13 [SD] yr; weight, 73 ± 13 kg; height, 171 ± 10 cm) with almost artifact-free signal registration. Length of laminectomy was 98 ± 34 min without unusual perturbations such as blood loss or hypothermia. Patients were extubated at a propofol TCI of 1.5 ± 0.2 μg/ml without complications.

Because the information of separation measures (such as the Wilcoxon test) is limited for the evaluation of a depth of anesthesia parameter,[4] we investigated P_K values for the comparison of anesthetic states (fig. 1). Only the Narcotrend® was able to differentiate between awake *versus* steady state anesthesia, steady state anesthesia *versus* first reaction, and steady state anesthesia *versus* extubation with a P_K value of more than 0.90 (table 3 and fig. 2). Logistic regression analysis indicated a 95% probability that the patients would show a first reaction during emergence from propofol anesthesia for the Narcotrend® stages D0/C2 (fig. 3). The BIS® showed high P_K values for awake *versus* steady state anesthesia

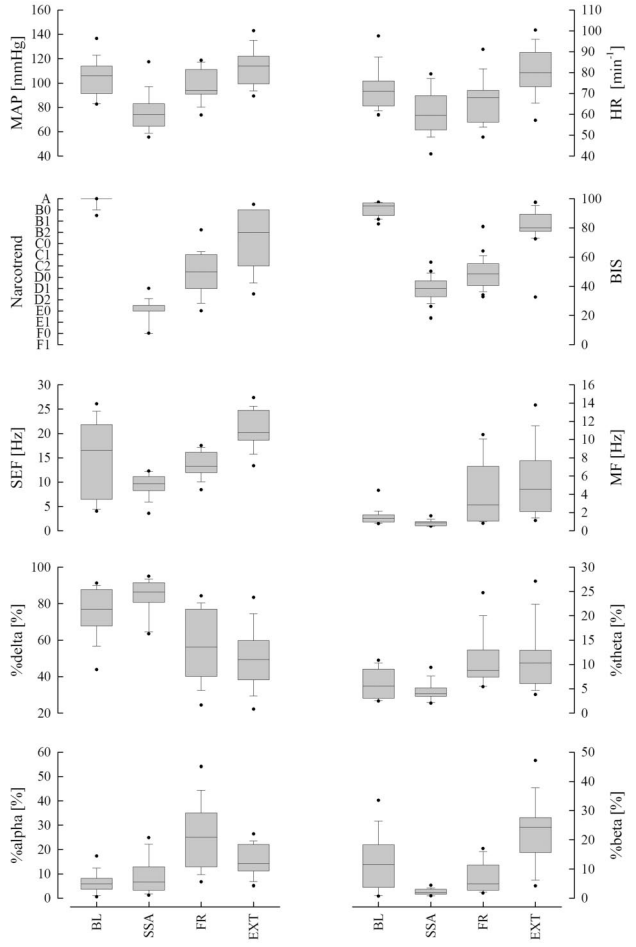

Fig. 1. Parameters during investigated anesthetic states. Shown are mean arterial blood pressure (MAP); heart rate (HR); Narcotrend®; Bispectral Index® (BIS®); spectral edge frequency (SEF); median frequency (MF); and relative (percent) power in δ, θ, α, and β during the investigated states: awake, steady state anesthesia, first reaction, and extubation. To demonstrate the scatter of the data, 95%, 90%, 75%, 50%, 25%, 10%, and 5% percentiles are represented. BL = awake; EXT = extubation; FR = first reaction; SSA = steady state anesthesia.

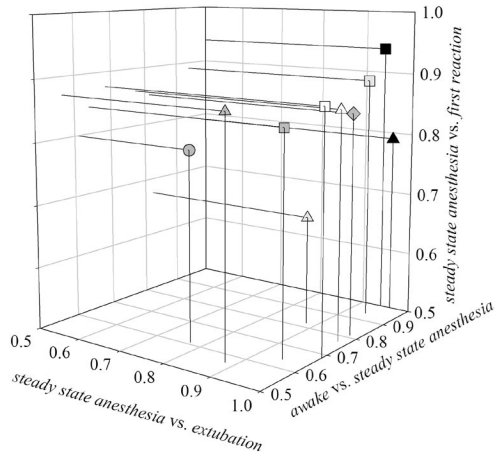

Fig. 2. Prediction probability (P_K) for the comparison of the investigated states. Results are shown for awake *versus* steady state anesthesia, steady state anesthesia *versus* first reaction, and steady state anesthesia *versus* extubation. A three-dimensional scatter plot is presented with data for mean arterial blood pressure (MAP; *light gray square*); heart rate (HR; *light gray triangle*); Narcotrend® (*filled square*); Bispectral Index® (BIS®; *filled triangle*); spectral edge frequency (SEF; *open square*); median frequency (MF; *open triangle*); and relative (%) power in δ (*dark gray square*), θ (*dark gray triangle*), α (*dark gray circle*), and β (*dark gray diamond*). A P_K value of 1.0 means that the parameter predicts the states correctly 100% of the time. A P_K of 0.5 means that the parameter predicts not better than a 50:50 chance.

and steady state anesthesia *versus* extubation (P_K > 0.90), whereas the P_K value for steady state anesthesia *versus* first reaction was 0.79 (table 3).

Because of the different algorithms of the Narcotrend® and BIS® to evaluate the spontaneous electroencephalogram, we were interested in the relation of both parameters. A high correlation coefficient ($r = -0.85$, $P < 0.001$) of both was found (fig. 4). Linear regression was able to predict BIS® by Narcotrend® (BIS = Narcotrend® × (−5.397 + 99.318); $P < 0.001$) and Narcotrend® by BIS® (Narcotrend® = BIS × (−0.149) + 16.478, $P <$

Table 3. Comparison of the States Awake *vs.* Steady State Anesthesia, Steady State Anesthesia *vs.* First Response, and Steady State Anesthesia *vs.* Extubation

	Awake *vs.* Steady State Anesthesia		Steady State Anesthesia *vs.* First Reaction		Steady State Anesthesia *vs.* Extubation	
	P_K	SE	P_K	SE	P_K	SE
MAP	*0.94*	0.03	0.89	0.05	*0.94*	0.04
HR	0.82	0.06	0.67	0.08	0.88	0.05
Narcotrend®	*1.00*	NE	*0.94*	0.03	*0.94*	0.05
BIS®	*1.00*	NE	0.79	0.07	*0.96*	0.04
SEF	0.68	0.10	0.88	0.06	*1.00*	NE
MF	0.77	0.08	0.86	0.06	*0.98*	0.01
% δ	0.64	0.09	0.85	0.06	*0.95*	0.03
% θ	0.57	0.10	0.87	0.05	0.88	0.05
% α	0.61	0.09	0.80	0.07	0.77	0.07
% β	0.81	0.09	0.85	0.06	*0.98*	0.02

Prediction probability (P_K) and SE for mean arterial blood pressure (MAP), heart rate (HR), Narcotrend®, Bispectral index® (BIS®), spectral edge frequency (SEF), median frequency (MF), relative (%), δ, θ, α, and β. P_K value of 1.0 means that the parameter predicts the conditions correctly 100% of the time. P_K of 0.5 means that the parameter predicts the conditions no better than 50:50 chance. Values in italics indicate $P_K > 0.90$.

NE = not estimated.

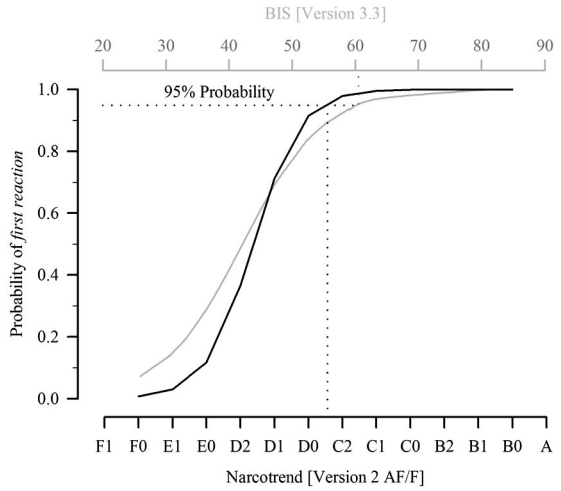

Fig. 3. Probability of the first reaction during emergence as a function of Narcotrend® and Bispectral Index® (BIS®). Logistic probability response curve for the model of Narcotrend® and BIS® for state steady state anesthesia *versus* first reaction. *Dotted lines* indicate the 95% probability of the first reaction for both parameters.

0.001). The results of the linear regression for Narcotrend® are shown in table 4.

Discussion

In the current study, we confirmed the advantage of modern over classic electroencephalographic parameters. The classic electroencephalographic parameters were unsatisfying to distinguish between the awake and anesthetized state, but they provided useful information during emergence from anesthesia. Interestingly, also hemodynamic parameters, especially MAP, seemed to be a reliable parameter to differentiate between the investigated states in healthy patients during propofol and remifentanil anesthesia.

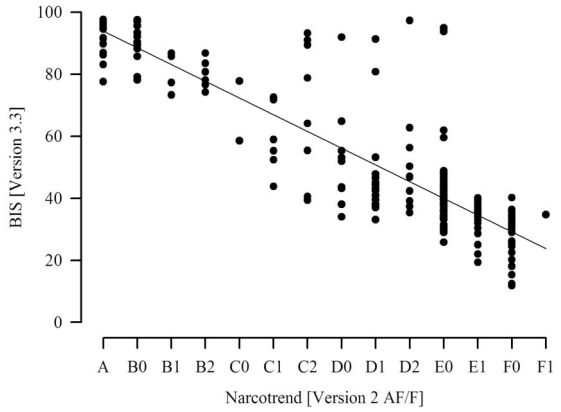

Fig. 4. Comparison of Narcotrend® and Bispectral Index® (BIS®). Scatter plot and linear regression line (Narcotrend® = BIS × (−0.149) + 16.478; BIS = Narcotrend® × (−5.397) + 99.318). Shown are all data pairs from awake through extubation (n = 350). The cluster of points well off the regression line, with BIS® values greater than 80 and Narcotrend® values between C2 and E0 are due to data pairs during induction of anesthesia. Narcotrend® was associated with a faster decrease than BIS®.

Table 4. Linear Regression Analysis

		95% Confidence Interval	
	BIS®	Lower Bound	Upper Bound
A	94	90	98
B0	89	85	92
B1	83	79	87
B2	78	73	82
C0	72	67	77
C1	67	62	72
C2	62	56	67
D0	56	50	62
D1	51	44	57
D2	45	39	52
E0	40	33	47
E1	35	27	42
F0	29	21	37
F1	24	16	32

Evaluation of the relation of the Narcotrend® and Bispectral Index® (BIS®) for all data pairs (n = 350) in the current study.

The measurement of depth of anesthesia is still an unsolved problem because there is no definition of exactly what *depth of anesthesia* means. However, a depth of anesthesia monitor would be of enormous clinical and experimental interest to increase the safety of the patient and to reduce costs by avoiding drug overdosing. A gold standard for the measurement of depth of anesthesia is missing. One strategy is to investigate the relation of a potential parameter to anesthetic effect-site concentrations. However, it is well known that sensitivity to anesthetics is associated with interindividual variations.[5] Another strategy is to compare clinically measured depth of anesthesia with a parameter such as the Observer's Assessment of Alertness and Sedation Score.[6] In this case, the interindividually sensitivity of anesthetics could be minimized.

The present study was performed using a propofol and remifentanil anesthetic, often used in our hospital. We were aware that anesthetic depth could be different between the patients (interindividual), especially during steady state anesthesia. With the detection of first reaction and the extubation state, we also investigated individual and not drug-dosing regimen–dependent anesthetic states. It should be mentioned that we did not measure propofol blood/plasma concentrations but used a calculated professional pharmacokinetic model, the Diprifusor system.[7] Previous studies with the Diprifusor system have shown variations between measured and calculated concentrations. The bias of systemic overprediction and underprediction of the measured plasma concentrations (median performance error) has been reported to be −7%,[8] 16%,[9] and 21%.[10] However, because the real plasma concentrations were not analyzed in the current study, potential relevant differences from the TCI data remain unclear.

In the current study, only the Narcotrend® was able to distinguish all investigated states of anesthesia accurately. To our knowledge, no other investigations of the ability of the Narcotrend® to predict anesthetic state have been conducted. Data on the Narcotrend® in the literature are very rare.[3,11] In a previous study, our group found significant increases in Narcotrend® stages during emergence from propofol when TCI doses of propofol were reduced.[11] Also, a significant correlation between the Narcotrend® and TCI of propofol was found. However, a high correlation does not necessarily mean a good distinction between anesthetic states such as steady state anesthesia *versus* first reaction. Kreuer *et al.*[3] investigated the relation between the Narcotrend® and BIS® during anesthesia with propofol and remifentanil with time intervals of 1 min during induction and emergence and every 5 min during maintenance of anesthesia by descriptive analysis. When BIS® values were 64–40, indicating general anesthesia,[12] in 94% of the cases, the Narcotrend® stage was D or E. The authors concluded that increasing depth of anesthesia as indicated by the BIS® is accompanied by corresponding effects as displayed by the Narcotrend®.[3] These findings are in concordance with results from the current study using the statistical method of linear regression to analyze the relation of Narcotrend® and BIS®. A Narcotrend® stage of D or E was highly significantly correlated with BIS® values between 56 and 35. Interestingly, figure 4 show a cluster of points well off the regression line, with BIS® values greater than 80 and Narcotrend® values between C2 and E0. This cluster is due to the data pairs during induction of anesthesia. Narcotrend® was associated with a faster decrease than BIS®. The evaluation of the spontaneous electroencephalogram by different mathematic strategies (Narcotrend® and BIS®) resulted in similar information during anesthesia with propofol and remifentanil.

The BIS® is the most evaluated parameter derived from the spontaneous electroencephalogram. In the current study, the BIS® showed a perfect division of the awake *versus* steady state anesthesia states. However, BIS® was a poor detector of the states of steady state anesthesia *versus* first reaction during emergence. One possibility for the poor detection could be the well-known delay of BIS® during the fast changes of propofol emergence. Baker *et al.*[13] observed that BIS® most accurately reflects the level of consciousness of the patient approximately 60 s previously. This seems to be realistic because the total update delay of BIS® is approximately 30 s.[14] This would also explain the results from the current study with the high P_K value for steady state anesthesia *versus* extubation. Extubation was executed more than 60 s after the first reaction period in all cases. However, we were not able to use the newest version of BIS® (version 3.3 instead of version xp) in the current study, which may restrict our results in this issue. We used the Aspect A-1000 monitor because of the possibility to calculate the classic electroencephalographic parameters. Moreover, the delay of BIS® as described by Baker was also performed for the new Aspect-2000 monitor.

The value of hemodynamics to assess depth of anesthesia is still controversial.[15–19] MAP can be only an indirect parameter to estimate the hypnotic effects. Changes in MAP are mediated by the cardiodepressive side effects of propofol and remifentanil. MAP was therefore far more likely to predict increasing and decreasing concentrations of propofol and remifentanil rather than any particular stages of depth of anesthesia. However, our study underlined the experience of many anesthesiologists to estimate the drug-dosing regimen by hemodynamics.

The median frequency, representative of the classic electroencephalographic parameters, had been reported to be a useful tool to measure depth of anesthesia. Median frequency was used by Schwilden *et al.*[20,21] to confirm a closed-loop feedback system to control propofol and methohexital anesthesia. In contrast, other studies showed that classic electroencephalographic parameters did not correlate with depth of anesthesia.[22–24] In the current study, we found limitations of the classic electroencephalographic parameters to monitor depth of anesthesia. Our findings confirm that it seems to be difficult to assess depth of anesthesia using only classic electroencephalographic parameters. Otherwise, the classic parameters, especially spectral edge frequency and $\%\beta$, mediated important information during emergence from anesthesia. Further studies should evaluate whether these data are useful to create a subparameter improving Narcotrend® or BIS® during emergence from anesthesia.

In the current study, we used the P_KMACRO to estimates the P_K and SE based on the given data of the 25 patients. It should be mentioned that these estimates are not the true values of P_K and SE, but the estimates can be used for statistical hypothesis testing.[4] For example, the estimates of $P_K = 1.0$ for awake *versus* steady state anesthesia in the current study may be estimates of $P_K < 1.0$ if more patients are investigated.

The results of the current study underline our hypothesis that the Narcotrend® and BIS® show nearly similar changes during the investigated periods of anesthesia. The Narcotrend® was superior to BIS® to detect emergence from anesthesia, most probably because of the known time delay of 60 s for BIS®. Both are superior to classic electroencephalographic parameters in monitoring and differentiating different states of anesthesia.

References

1. Kugler J: Elektroenzephalographie in Klinik und Praxis. Stuttgart, New York, Thieme, 1981
2. Schultz B, Grouven U, Schultz A: Automatic classification algorithms of the

EEG monitor Narcotrend for routinely recorded EEG data from general anaesthesia: A validation study. Biomed Tech 2002; 47:9–13

3. Kreuer S, Biedler A, Larsen R, Schoth S, Altmann S, Wilhelm W: The Narcotrend: A new EEG monitor designed to measure the depth of anaesthesia: A comparison with Bispectral Index monitoring during propofol-remifentanil-anaesthesia. Anaesthesist 2001; 50:921–5

4. Smith WD, Dutton RC, Smith NT: Measuring the performance of anesthetic depth indicators. ANESTHESIOLOGY 1996; 84:38–51

5. Schnider TW, Minto CF, Shafer SL, Gambus PL, Andresen C, Goodale DB, Youngs EJ: The influence of age on propofol pharmacodynamics. ANESTHESIOLOGY 1999; 90:1502–16

6. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, Schwam EM, Siegel JL: Validity and reliability of the observer's assessment of alertness/sedation scale: Study with intravenous midazolam. J Clin Psychopharmacol 1990; 10:244–51

7. Gray JM, Kenny GNC: Development of the technology for "Diprifusor" TCI systems. Anaesthesia 1998; 53(suppl):22–7

8. Coetze JF, Glen JB, Wium CA, Boshoff P: Pharmacokinetic model selection for target-controlled infusion of propofol. ANESTHESIOLOGY 1995; 82:1328–45

9. Swinhoe CF, Peacock JE, Glen JB, Reilly CS: Evaluation of predictive performance of a "Diprifusor" TCI system. Anaesthesia 1998; 53:61–7

10. Davidson JA, Macleod AD, Howie JC, White M, Kenny GN: Effective concentration 50 for propofol with and without 67% nitrous oxide. Acta Anaesthesiol Scand 1993; 37:458–64

11. Schmidt GN, Bischoff P, Standl Th, Voigt M, Papavero L, Schulte am Esch J: Narcotrend, Bispectral Index, and classical electroencephalogram variables during emergence from propofol/remifentanil anesthesia. Anesth Analg 2002; 95:1324–30

12. Johansen J, Sebel P: Development and clinical application of electroencephalographic bispectrum monitoring. ANESTHESIOLOGY 2000; 93:1336–44

13. Baker GW, Sleigh JW, Smith P: Electroencephalographic indices related to hypnosis and amnesia during propofol anaesthesia for cardioversion. Anaesth Intensive Care 2000; 28:386–91

14. Jensen EW, Litvan H: Rapid extraction of middle-latency auditory-evoked potentials (letter). ANESTHESIOLOGY 2001; 94:718

15. White PF, Boyle WA: Relationship between hemodynamic and electroencephalographic changes during general anesthesia. Anesth Analg 1989; 68:177–81

16. Kato M, Komatsu T, Kimura T, Sugiyama F, Nakashima K, Shimada Y: Spectral analysis of heart rate variability during isoflurane anesthesia. ANESTHESIOLOGY 1992; 77:669–74

17. Leslie K, Sessler DI, Smith WD, Larson MD, Ozaki M, Blanchard D, Crankshaw DP: Prediction of movement during propofol/ nitrous oxide anesthesia. ANESTHESIOLOGY 1996; 84:52–63

18. Mantzaridis H, Kenny GN: Auditory evoked potential index: A quantitative measure of changes in auditory evoked potentials during general anaesthesia. Anaesthesia 1997; 52:1030–6

19. Struys MM, Jensen EW, Smith W, Smith NT, Rampil I, Dumortier FJ, Mestach C, Mortier EP: Performance of the ARX-derived auditory evoked potential index as an indicator of anesthetic depth: A comparison with Bispectral Index and hemodynamic measures during propofol administration. ANESTHESIOLOGY 2002; 96:803–16

20. Schwilden H, Schüttler J, Stoeckel H: Closed-loop feedback control of methohexital anesthesia by quantitative EEG analysis in humans. ANESTHESIOLOGY 1987; 67:341–7

21. Schwilden H, Stoeckel H, Schüttler J: Closed-loop feedback control of propofol anesthesia by quantitative EEG analysis in humans. Br J Anaesth 1989; 62:290–6

22. Drummond JC, Brann CA, Perkins DE, Wolfe DE: A comparison of median frequency, spectral edge frequency, a frequency band power ratio, total power, and dominance shift in the determination of depth of anesthesia. Acta Anesthesiol Scand 1991; 35:693–9

23. Dwyer RC, Rampil IJ, Eger E, Benett HL: The electroencephalogram does not predict depth of isoflurane anesthesia. ANESTHESIOLOGY 1994; 81:403–9

24. Chen CL, Liu CC, Chen TL, Wu GJ, Huang CH, Lin SY, Chao CC: Recovery from propofol anesthesia: A quantitative electroencephalographic analysis. Acta Anesthesiol Sin 1994; 32:77–82