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Narcotrend® Does Not Adequately Detect the Transition between Awareness and Unconsciousness in Surgical Patients

Gerhard Schneider, M.D., Eberhard F. Kochs, M.D.,† Bettina Horn, M.D.,‡ Matthias Kreuzer, M.Sc.,§ Michael Ningler, M.Sc.§*

Background: **The Narcotrend® index (MonitorTechnik, Bad Bramstedt, Germany) is a dimensionless number between 0 and 100 that is calculated from the electroencephalogram and inversely correlates with depth of hypnosis. The current study evaluates the capability of the Narcotrend® to separate awareness from unconsciousness at the transition between these levels.**

Methods: **Electroencephalographic recordings of 40 unpremedicated patients undergoing elective surgery were analyzed. Patients were randomly assigned to receive (1) sevoflurane–remifentanil ($\leq 0.1\ \mu g \cdot kg^{-1} \cdot min^{-1}$), (2) sevoflurane–remifentanil ($\geq 0.2\ \mu g \cdot kg^{-1} \cdot min^{-1}$), (3) propofol–remifentanil ($\leq 0.1\ \mu g \cdot kg^{-1} \cdot min^{-1}$), or (4) propofol–remifentanil ($\geq 0.2\ \mu g \cdot kg^{-1} \cdot min^{-1}$). Remifentanil and sevoflurane or propofol were given until loss of consciousness. After tracheal intubation, propofol or sevoflurane was stopped until return of consciousness and then restarted to induce loss of consciousness. After surgery, drugs were discontinued. Narcotrend® values at loss and return of consciousness were compared with each other, and anesthetic groups were compared. Prediction probability was calculated from values at the last command before and at loss and return of consciousness.**

Results: **At 105 of 316 analyzed time points, the Narcotrend® did not calculate an index, and the closest calculated value was analyzed. No significant differences between loss and return of consciousness were found. In group 1, Narcotrend® values were significantly higher than in group 3. Prediction probability was 0.501.**

Conclusions: **In these challenging data, the Narcotrend® did not differentiate between awareness and unconsciousness. In addition, Narcotrend® values were not independent from the anesthetic regimen.**

DURING the past decade, an increasing number of monitors have been developed for a direct assessment of anesthetic depth or the hypnotic component of anesthesia. This goal may be reached by observation of the spontaneous or evoked electrical activity of the brain, *i.e.*, the electroencephalogram, or (auditory) evoked potentials. The Narcotrend® (MonitorTechnik, Bad Bramstedt, Germany) is one of the newer electroencephalogram-based monitors that promises quantification of the hypnotic component of anesthesia. Using a multivariate statistical algorithm, the Narcotrend® monitor quantifies anesthesia-induced electroencephalographic changes. This classification system is based on electroencephalographic changes induced by sleep and was developed by Loomis *et al.*[1] The psychiatrist Kugler[2] adapted this classification for anesthesia-induced electroencephalographic changes, and this was further modified by Schultz *et al.*[3] Originally, classification results are given in a six-letter system with a total of 14 substages[3]:

A: awareness
B_{0-2}: sedation
C_{0-2}: light anesthesia
D_{0-2}: general anesthesia
E_{0-1}: general anesthesia with deep hypnosis
F_{0-1}: general anesthesia with increasing burst suppression.

A recent study showed that Bispectral Index (BIS) values between 40 and 64 predominantly correspond with Narcotrend® stages D and E, representing general anesthesia.[4] In the latest version of the Narcotrend®, the alphanumerical classification was transformed into a numerical index that spans the range from 0 to 100. The transform was performed in such a way that Narcotrend® ranges correspond to BIS ranges. Recently, it has been shown that Narcotrend® guidance of anesthesia may lead to reduced drug consumption and faster recovery from anesthesia.[5] However, few studies have been published that examined whether the Narcotrend® index correctly indicates depth of hypnosis and anesthesia. Differentiation of a fully conscious from a deeply anesthetized patient may be achieved by routine clinical assessment. Differentiation between a patient with awareness under sedation and a patient who is just unconscious is by far more difficult. If a monitor of consciousness was able to identify the patient status at the transition between awareness and unconsciousness, it would clearly improve clinical assessment of sedation and hypnosis. The current study uses the challenging period of transition at loss of consciousness (LOC) and return of consciousness (ROC) to test the ability of Narcotrend® to differentiate between patients just aware and patients just unconscious. This analysis uses previously recorded electroencephalographic data and examines response to command as a clinical measure of anesthetic depth. How well the Narcotrend® differentiates between electroencephalographic data that were recorded during awareness and data that were recorded during unconsciousness in surgical patients is examined.

* Assistant Professor, † Professor, Director, and Chair, ‡ Resident, § Research Fellow.

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Address reprint requests to Dr. Schneider: Department of Anesthesiology, Klinikum rechts der Isar, Technische Universität München, Ismaningerstr. 22, 81675 Munich, Germany. Address electronic mail to: Gerhard.Schneider@LRZ.tum.de.

Materials and Methods

The current study is a reanalysis of previously recorded electroencephalographic data. Electroencephalographic recordings were from induction of anesthesia until emergence and included a period of intended awareness after intubation. Patients gave informed written consent to the protocol that was approved by the university's ethics committee (Technische Universität München, Munich, Germany)[6] and involved a reduction of the hypnotic agent until patients followed command after tracheal intubation. Digitally recorded electroencephalograms were replayed on a specifically designed digital/analog signal converter. This converter allows replay of recorded electroencephalographic data as analog signals, *i.e.*, electric activity at the electrode recording sites. This signal may be used to test new electroencephalographic monitors (or updated versions of electroencephalographic monitors) with previously recorded electroencephalographic data.[7] For the present analysis, electroencephalographic data from 40 adult patients with American Society of Anesthesiologists physical status I or II who underwent elective surgery during general anesthesia were used. Exclusion criteria were rapid sequence induction, medication with drugs affecting the central nervous system, pregnancy, psychiatric, or neurologic diseases. Patients were randomly assigned to receive anesthesia with one of the following drug combinations: (1) sevoflurane–remifentanil ($\leq 0.1\ \mu g \cdot kg^{-1} \cdot min^{-1}$), (2) sevoflurane–remifentanil ($\geq 0.2\ \mu g \cdot kg^{-1} \cdot min^{-1}$), (3) propofol–remifentanil ($\leq 0.1\ \mu g \cdot kg^{-1} \cdot min^{-1}$), or (4) propofol–remifentanil ($\geq 0.2\ \mu g \cdot kg^{-1} \cdot min^{-1}$). Monitoring included noninvasive blood pressure; heart rate; oxygen saturation; oxygen, carbon dioxide, and sevoflurane concentrations; and respiratory parameters. All data were stored on a personal computer. At electroencephalographic electrode positions, the skin was prepared with alcohol to maintain impedances of less than 5 kΩ. Two-channel referential electroencephalogram was recorded from electrode positions AT1, AT2, Fz (reference), and Fp1 (ground) using the A-1000 electroencephalographic monitor (BIS® version 3.3; Aspect Medical Systems Inc., Newton, MA). The high pass was set to 0.25 Hz, no low pass was used, and the notch filter (50 Hz) was enabled. The electroencephalogram was continuously digitized at 256 Hz/channel and simultaneously recorded on the personal computer. Unpremedicated patients received remifentanil infusion at either 0.1 or 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ according to the group assignment. Every 30 s, patients were asked to squeeze the investigator's hand. To verify this response, the command was immediately repeated, and the patient was required to squeeze the hand also to this repeated command. Anesthesia was started with sevoflurane mask induction (groups 1 and 2) or propofol injections (0.7 mg/kg, followed by 20 mg every 30 s, groups 3 and 4). Loss of consciousness (LOC1) was defined as the time when the patient stopped squeezing hand to command. After LOC1, additional propofol or sevoflurane was given to increase the level of hypnosis. A blood pressure cuff was inflated on the right arm and maintained for 5 min to occlude the circulation of the right forearm and retain the ability to move the arm to command while succinylcholine (1.0 mg/kg) was given for intubation (isolated forearm technique of Tunstall).[8] Then, while remifentanil infusion was continued, sevoflurane or propofol was stopped until patients gave a verified response to command (return of consciousness [ROC1]). Sevoflurane or propofol bolus injection, followed by continuous infusion, was recommenced. Loss of consciousness 2 (LOC2) was noted when patients stopped following commands and commands to squeeze the hand were stopped. Remifentanil was administered within the predefined remifentanil infusion rates. Sevoflurane and propofol were maintained according to clinical practice. At the end of surgery, commands to squeeze the hand were given every 30 s. Sevoflurane, propofol, and remifentanil were discontinued, and return of consciousness (ROC2) was noted at the first verified (*i.e.*, repeated) response to command.

Data Analysis

To assess the ability of the Narcotrend® to differentiate between responsiveness and nonresponsiveness, the transition between these conditions was analyzed. The following Narcotrend® values were analyzed: at LOC1 and LOC2, the last value with a patient response (*i.e.*, 30 s before LOC) for "awareness" and the first value without patient response for "unconsciousness," and accordingly at ROC1 and ROC2, the last value without a patient response (*i.e.*, 30 s before ROC) for "unconsciousness" and the first value with patient response for "awareness." Because one data file was corrupted, this resulted in a total of 316 Narcotrend® index values. The Narcotrend® monitor did not always calculate index values at these times. In these instances, the closest value that had been calculated was selected, *i.e.*, the last index value that was calculated during responsiveness before LOC (or unconsciousness before ROC) and the first value that was obtained during unconsciousness after LOC (or responsiveness after ROC), and the according time delay was noted. Median and ranges of the time intervals between the last obtained and required Narcotrend® index during the transition between awareness and unconsciousness were calculated. The Narcotrend® values were used to calculate prediction probability (Pk) for discrimination between awareness and unconsciousness as described by Smith *et al.*[9] In addition, statistical analysis was performed using a general linear model for repeated measurements. Narcotrend® values were compared among LOC1, ROC1, LOC2, and ROC2 (within-subject factors). Narcotrend® values of the different

groups (1–4) were compared with each other (between-subject factor). Bonferroni corrections were used for *post hoc* tests of within-subject and between-subject factors. Overall significance was set at $P < 0.05$ (Bonferroni correction). Statistical analysis was performed with SPSS (SPSS Inc., Chicago, IL). Pk values were calculated with an Excel (Microsoft®, Redmond, WA) Macro (PK-MACRO). Values are mean (SD) unless stated otherwise.

After analysis, we were concerned that our method of data recording and presentation to the Narcotrend® monitor may have influenced the data in such a way that Narcotrend® values may have been influenced. In particular, aliasing noise may have been produced. Therefore, with approval from the local ethics committee, we performed an additional measurement in a volunteer receiving remifentanil–propofol anesthesia. In this volunteer, 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ remifentanil was administered, and propofol target-controlled infusion was started. Every 5 min, the propofol target was increased until LOC occurred. This level was maintained for 15 min. Next, the target level was increased until electroencephalographic burst suppression occurred. This level was also maintained for 15 min, and then propofol was stopped. After ROC, remifentanil infusion was stopped. During this period, the electroencephalogram was recorded with the identical method (Aspect A-1000 with a sample rate of 256 Hz). Synchronously, the Narcotrend® was applied, and the Narcotrend® index was recorded with the Windows HyperTerminal program (Hilgraeve, Monroe, MI). Subsequently, recorded electroencephalographic data were replayed three times, and during each replay, the Narcotrend® index was calculated from the digitized electroencephalogram. Recalculated Narcotrend® results were compared to the directly recorded Narcotrend® values.

Results

Analysis was planned for Narcotrend® values at the transition between awareness and unconsciousness at induction (LOC1), the awareness period (ROC1 and LOC2), and return of consciousness after surgery (ROC2). At each of these events, the last value before and the first value after the transition (*i.e.*, at LOC, the last value with and the first value without response to command, and at ROC, the last value without and the first value with response to command) were considered for analysis. One data file was corrupted, and ROC1 and LOC2 could not be analyzed. At 105 of the remaining 316 time points, the Narcotrend® did not calculate index values. As a consequence, the closest calculated Narcotrend® value was analyzed. This reduced the number of missing data to 15, *i.e.*, for 15 measurements, no calculated index value was available despite of an extended time window. The remaining 15 values were only from patients with a low remifentanil infusion rate (groups 1 and 3) at LOC1. Here, the Narcotrend® did not calculate an index and often indicated high-frequency artifacts. Table 1 shows the time interval between the clinical event and the closest time when the Narcotrend® gave an index value. This time interval was between 3 and 563 s. Pk for the differentiation between awareness and unconsciousness was 0.501 (SE = 0.033). A repeated-measurement general linear model did not find significant differences between LOC or ROC (fig. 1). Analysis of between-subject factors revealed that Narcotrend® values were not independent from the drug combination. In group 1, Narcotrend® values at LOC and ROC were significantly higher than in group 3.

Table 1. Missing Narcotrend® Index Values

	No Index, n	Time Interval Without Index, s, Median (Range)
LOC1	59	32 (3–515)
ROC1	18	73 (6–563)
LOC2	32	47 (4–345)
ROC2	4	8.5 (5–90)

Number of scheduled analysis times where Narcotrend® did not calculate an index (no index) and the time intervals to the closest calculated Narotrend® index value at loss of consciousness (LOC1), awareness reaction (ROC1), loss of consciousness after the awareness reaction (LOC2), and return of consciousness at the end of anesthesia (ROC2).

The additional comparison of recalculated Narcotrend® values with the directly recorded Narcotrend® found that no index was calculated in 28% in the direct measurement and between 22% and 28% of the recalculated data. During most of the periods with missing

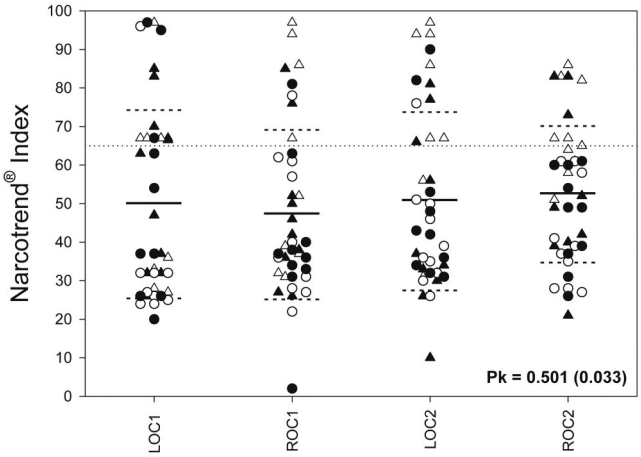

Fig. 1. Narcotrend® index at loss of consciousness (LOC1), awareness reaction (ROC1), loss of consciousness after the awareness reaction (LOC2), and return of consciousness at the end of anesthesia (ROC2). The figure shows individual values, mean (*solid lines*) and SD (*dashed lines*) of all patients in groups: (1) "low" remifentanil (0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$)–sevoflurane (△), (2) "high" remifentanil (0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$)–sevoflurane (▲), (3) "low" remifentanil–propofol (○), and (4) "high" remifentanil–propofol (●). Prediction probability (Pk) (SE) of the Narcotrend® for detection of consciousness is given. The *dotted line* shows the recommended upper level of Narcotrend® for general anesthesia.

values, the monitor indicated high-frequency (muscle) artifacts. A minor part of missing values was from periods of automated electrode impedance check. Seventy-five percent of the reanalyzed Narcotrend® values were identical or did not differ by more than 5; an additional 17% showed a difference between 6 and 10. Only 8% of the recalculated values showed index values that differed by more than 10. These differences also existed between each of the reanalyzed values.

Discussion

These data show that in this challenging data set from loss and return of consciousness, the Narcotrend® was not able to differentiate between awareness and unconsciousness. Narcotrend® values showed considerable variation at specific levels of anesthesia (*i.e.*, loss and return of consciousness). Such index variability has been described for the BIS[6,10–13] and the patient state index (PSI).[6] As the current study shows, this problem also exists for the Narcotrend®. In an editorial, Drummond[14] defined requirements for a depth-of-anesthesia monitor. Not only must the average values of an index be statistically different between different levels of anesthesia or sedation, but the measurement of an individual patient must indicate his or her current level of anesthesia. An overlap between the range of values for different stages of sedation and anesthesia must be avoided.[15] As our data show, none of these requirements was achieved by the Narcotrend®. In contrast to the BIS and the PSI, where for the identical data sets the mean values of unconsciousness and awareness showed a statistically significant difference,[6] this difference was not measured by the Narcotrend®. This is also reflected by a low Pk. Pk has been recommended to measure the performance of an index of anesthetic depth. Pk is not influenced by a selected threshold value and can be used to quantify the ability of an index to discriminate different levels of anesthesia.[9] A Pk of 0 is obtained when an monitor indicates exactly the opposite of the clinical status, *i.e.*, every conscious patient is classified as unconscious and *vice versa*. A Pk of 1 means correct classification for every measurement, and a Pk of 0.5 is obtained when the index is as good as chance (*e.g.*, flipping a coin). In the current study, Pk for the Narcotrend® was only 0.501, *i.e.*, not much better than a random process. A potential drawback of the current approach is the use of pooled data from four transitions between awareness and unconsciousness. If the Narcotrend® value at the transition between awareness and unconsciousness is relatively stable in the individual patient, the use of pooled data may inadequately increase the overall Pk. We have, as have others before us,[16,17] accepted the limitation of this approach. The results of the current analysis revealed high intraindividual variability, *i.e.*, in the individual patient, ROC1 occurred at index values that were different from values at ROC2 (fig. 2), which reduces the risk of inappropriately high Pk values. In addition, Pk was not much higher than chance (Pk = 0.5), which makes an inadequate increase of Pk unlikely.

Sixty-two of the 79 Narcotrend® values that were measured during ROC were below 65. Therefore, Narcotrend® indicated moderate or even (excessively) deep anesthesia, whereas the patient showed an awareness reaction, *i.e.*, responded adequately to the command to squeeze the investigator's hand. Mean Narcotrend® values at both LOC and ROC were between 45 and 50, suggesting a deeper level of hypnosis.

Only in five patients did the awareness reaction occur within 5 min after succinylcholine administration. The median time interval between succinylcholine administration and awareness was 14 min 4 s (minimum, 1 min 43 s; maximum, 32 min 47 s). The Narcotrend® had problems calculating index values and often showed an error warning that high-frequency (muscle) artifacts were present. As a consequence of these problems, no index value was calculated in 105 of 316 transition periods, where the level of hypnosis substantially changed, *i.e.*, the transition between awareness and unconsciousness occurred. A complete absence of information was noted for 15 of the 80 planned measurements during LOC1 at induction. This complete failure of the monitor only occurred in patients receiving the low infusion rate of remifentanil. The electroencephalogram of these patients often showed high-frequency activity (> 30 Hz). This activity may mainly reflect muscle activity (electromyography) rather than electroencephalographic activity and often caused the Narcotrend® not to calculate an index value. In contrast to the Narcotrend®, this high-frequency activity did not stop the BIS or the PSI from calculating index values in the same patients.[6] This observation may indicate a clinically relevant difference between the Narcotrend® and the BIS or the PSI, illustrating a limitation for the clinical application of Narcotrend®. In most instances where Narcotrend® had not calculated an index value, there was at least a preceding (or following) value for the same patient state. There was a remarkable duration of periods without index calculation, especially during LOC (79 and 68 s) but also during the awareness reaction (96 s), with maxima up to almost 10 min. During these dynamic phases, such a time interval may mean that the patient state has substantially changed in the meantime. This also has consequences for the current data analysis. Numerous index values were not taken directly from the transition between awareness and unconsciousness or *vice versa*, and there was a remarkable distance to the clinical endpoint LOC or ROC. The analyzed Narcotrend® values are a longer time interval away from the transition periods, *i.e.*, the measured index values are also further away from the index range of transition

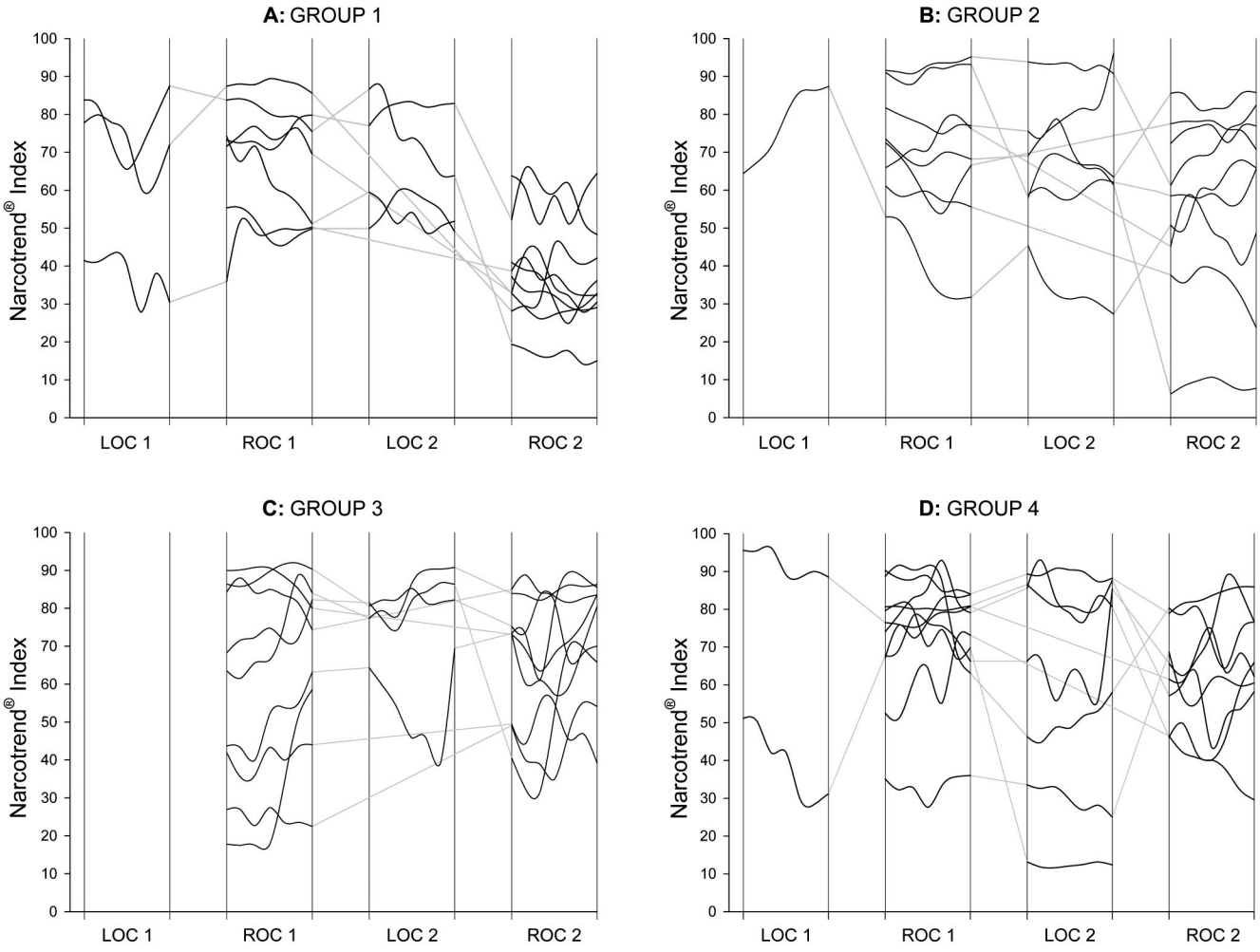

Fig. 2. Narcotrend® index at loss of consciousness (LOC1), awareness reaction (ROC1), loss of consciousness after the awareness reaction (LOC2), and return of consciousness at the end of anesthesia (ROC2). The graphs show the 30-s transition intervals from the last response to command to the first command to which the patient did not respond ("squeeze hand") (LOC) and *vice versa* (ROC). Individual patient curves are shown for group 1 (*A*), sevoflurane/remifentanil ($\leq 0.1\ \mu g \cdot kg^{-1} \cdot min^{-1}$); group 2 (*B*), sevoflurane–remifentanil ($\geq 0.2\ \mu g \cdot kg^{-1} \cdot min^{-1}$); group 3 (*C*), propofol–remifentanil ($\leq 0.1\ \mu g \cdot kg^{-1} \cdot min^{-1}$); and group 4 (*D*), propofol–remifentanil ($\geq 0.2\ \mu g \cdot kg^{-1} \cdot min^{-1}$). At the transition intervals, numerous values were not calculated by the Narcotrend®. The figure shows between- and within-patient variability.

between awareness and unconsciousness. Therefore, separation between these data should be easier, and Pk values should be higher than Pk values that were derived directly from the transition points. In contrast to these expectations, Pk values of the Narcotrend® were lower than Pk values of the BIS or the PSI, even though for the BIS and the PSI the data from the transitions (a more challenging data set) had been used.

In a previous study that examined the separation between steady state anesthesia and responsiveness during emergence from anesthesia, Pk of the BIS was lower than Pk of the Narcotrend®. The authors stated that the lower Pk of the BIS may result from the facts that BIS calculation requires approximately 30 s and that they did not compensate for this calculation interval.[18] In our data analysis, where this time compensation had been performed,[6] Pk of the BIS was higher than Pk of the Narcotrend®.

Electroencephalographic data were collected with the Aspect A-1000 monitor. Results show that the BIS, the index value that is calculated by this monitor, separates between unconsciousness and awareness better than the Narcotrend® when the same raw electroencephalographic data are used. Results of the current analysis support the use of the monitor that had originally been used to collect the electroencephalographic data. This may reflect a potential bias. Therefore, the comparison of direct Narcotrend® measurement from a volunteer and subsequent measurement from the volunteer's electroencephalogram was performed. In this volunteer, all levels from light sedation to deep hypnosis (reflected by electroencephalographic burst suppression) were measured. Both the original Narcotrend® recordings and the analysis of the replayed electroencephalogram contained comparable time intervals with high-frequency artifacts. This excludes the hypothesis that in the re-

played electroencephalographic data, aliasing artifacts had led to additional high-frequency noise, which could have induced additional artifact periods. Only 8% of Narcotrend® values showed a difference greater than 10 between the original recording and the reanalysis from the recorded electroencephalographic data. This difference existed not only between the on-line Narcotrend® recording and each of the three off-line measurements, but also between the off-line measurements. These differences are most likely due to minimal time differences: Five-second segments of the electroencephalogram are used to calculate a Narcotrend® value. Small differences (in the range of milliseconds) in start times of the Narcotrend® monitor lead to different 5-s segments. This explains why a small percentage of Narcotrend® values are different not only between the original recording and the recalculated index, but also between the three off-line calculations of Narcotrend® values.

Interestingly, Narcotrend® values were not independent from the anesthetic regimen at identical clinical endpoints. Narcotrend® values of patients receiving sevoflurane anesthesia with a low infusion rate of remifentanil (0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$, group 1) were significantly higher than values measured in patients with propofol and a low infusion rate of remifentanil (group 3). This difference suggests that the use of identical Narcotrend® ranges as a guide for anesthesia would induce different levels of hypnosis depending on the anesthetic drug combination, and the Narcotrend® index may be drug specific.

In the current study, *awareness* was defined as the adequate response to a verbal command (awareness reaction). To exclude the possibility that randomly occurring movements of the hand are erroneously counted as awareness reaction, an obeyed command was immediately repeated, and a response was only counted as response when the patient squeezed hand again. The ability to respond to a command indicates intact short-term or working memory, a memory function of limited capacity that spans a few seconds. This must not be confused with explicit long-term memory, which is usually thought of when the term *memory* is used. The difference between short-term and explicit long-term memory explains why none of our patients remembered being aware (long-term explicit memory) even though this had occurred in all patients (short-term memory). Absence of a response to a command may be a conservative measure of an adequate level of hypnosis, because the ability to respond to a command does not cause recall of the period. However, absence of explicit long-term memory may not be not sufficient for general anesthesia, because implicit (unconscious) memory may be present[19] and associated with wakefulness and could have long-term consequences.[20,21] In addition, it has been demonstrated that increased duration of responsiveness increases the risk of explicit memory.[22]

Few validation data have been published for the Narcotrend® index. A previous study compared parallel recordings of the BIS and the Narcotrend® and found a decrease of BIS values with decreases of Narcotrend® index values.[4] However, there were several data pairs where one index did not confirm the results of the other index. There was no explanation for this disagreement, and the authors concluded that there should be "further investigations on sensitivity and specificity of the displayed monitor results."[4] Two publications examined Narcotrend® values during propofol–remifentanil anesthesia and found conflicting results. Analysis of data recorded during emergence from anesthesia resulted in the conclusion that "modern EEG variables did not provide an adequate assessment of depth of anesthesia when remifentanil was used."[23] However, analysis of intraoperatively recorded data suggested that "modern electroencephalographic parameters, especially Narcotrend®, are more reliable indicators for the clinical assessment of anesthetic states than classic parameters."[18] In this previous study, Narcotrend® values allowed a good separation between steady state anesthesia and the first response during emergence (Pk = 0.9), and performance of the Narcotrend® was superior to the BIS® monitor.[18] In the current analysis, Pk was only 0.5 for Narcotrend®. This is because two very similar signals were used for analysis, electroencephalograms from patients that were just unresponsive and from patients who were just following command at the transition from awareness to unconsciousness, which represents a challenging data set.

To the best of our knowledge, no other articles have been published that have tried to correlate Narcotrend® values with clinical measurements of the sedative or hypnotic component of anesthesia. We suggest that a thorough validation of the Narcotrend® must be performed before it is used to guide the administration of anesthetic agents. Otherwise, the index may falsely suggest inadequate levels of anesthesia, *e.g.*, excessively deep anesthesia during adequate levels. This in turn would result in a reduction of anesthesia and possibly increase the risk of awareness. In an editorial about the use of the BIS in pediatric patients, Watcha[24] explained the importance of a thorough validation of a hypnosis monitor before its use as a guide for the administration of anesthetic agents. The same principles are relevant for every monitor of sedation and hypnosis, because "in clinical investigations, as in other matters, first things should come first."[24]

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