Comparability of Narcotrend™ index and bispectral index during propofol anaesthesia

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Background. The dimensionless Narcotrend™ (NCT) index (MonitorTechnik, Germany, version 4.0), from 100 (awake) to 0, is a new index based on electroencephalogram pattern recognition. Transferring guidelines for titrating the Bispectral Index™ (BIS, Aspect Medical Systems, USA, version XP) to the NCT index depends on their comparability. We compared the relationship between BIS and NCT values during propofol anaesthesia.

Methods. Eighteen adult patients about to have radical prostatectomy were investigated. An epidural catheter was placed in the lumbar space and electrodes for BIS and NCT were applied as recommended by the manufacturers. After i.v. fentanyl 0.1 mg, anaesthesia was induced with a propofol infusion. After intubation, patients received bupivacaine 0.5% 15 ml via the epidural catheter. Forty-five minutes after induction, the propofol concentration was increased to substantial burst suppression pattern and then decreased. This was done twice in each patient, and BIS and Narcotrend values were recorded at intervals of 5 s. The efficacy of NCT and BIS in predicting consciousness vs unconsciousness was evaluated using the prediction probability ($P_K$).

Results. We collected 38 629 artefact-free data pairs of BIS and NCT values from the respective 5-s epochs. Because of artefacts, another 5008 epochs had been excluded from data analysis (3855 epochs for the NCT index alone, 245 epochs for the BIS alone and 908 epochs for both indices). Mean (SD) values in awake patients were 94 (6) for Narcotrend and 91 (8) for BIS. With loss of the eyelash reflex, both values were significantly reduced, to 72 (9) for NCT ($P<0.001$) and to 77 (11) for the BIS index ($P<0.001$). The $P_K$ value for loss of eyelash reflex was similar for BIS (0.95) and NCT (0.93). Decreasing BIS values coincided with decreasing NCT values. A sigmoid model \[\text{NCT index} = 52.8 + 26.8 / (1 + \exp(- (\text{BIS} - 78.3) / 4.8))^{0.4}; r=0.52\] described the correlation between BIS and NCT index in a BIS range between 100 and 50. For BIS values lower than 50, a second sigmoid model with a correlation of $r=0.83$ was applied \[\text{NCT index} = 6.6 + 45.3 / (1 + \exp(- (\text{BIS} - 29.8) / 2.4))^{0.6}; r=0.83\]. The relationship between burst suppression ratio (BSR) and NCT index was best described by the following sigmoid model: \[\text{NCT index} = 265 / (1 + \exp(- (\text{BSR} + 108) / -49)); r=0.73\].

Conclusions. We found a sufficient correlation between BIS and NCT index, but deviations from the line of identity in some ranges require attention. Therefore, a simple 1:1 transfer from BIS to NCT values is not adequate. Our results might serve as a blueprint for the rational translation of BIS into NCT values.

Br J Anaesth 2004; 93: 235–40

Keywords: monitoring, bispectral index; monitoring, Narcotrend™

Accepted for publication: March 11, 2004

The effects of anaesthesia on the electroencephalogram (EEG) were described as early as in the first half of the last century, but it required the advances in computer and monitor technology of the last decade to enable widespread clinical application of the EEG to monitor the depth of anaesthesia. The introduction of the Bispectral Index™ (BIS; Aspect Medical Systems, Newton, MA, USA) for the parameterization of the EEG was a milestone. The BIS overcame several shortcomings of the spectral variables used previously, such as the median frequency and the spectral edge frequency, and especially the paradoxical increase in spectral variables which has been demonstrated for light sedation and burst suppression. EEG-guided anaesthesia with the BIS showed substantial clinical advantages.
compared with non-EEG-guided clinical groups: anaesthetic
drug consumption was reduced and recovery times short-
tened.5–9 Therefore, the BIS became the standard of EEG
monitoring in anaesthesia. However, in recent years several
reports revealing limitations of the BIS have been published,
indicating that a further search for EEG indices is
justified.10–12 Schmidt and colleagues13 investigated the
Narcotrend and BIS during emergence from propofol–
remifentanil anaesthesia. Both variables indicated changes
in the propofol infusion but not the remifentanil infusion.
In another investigation with propofol–remifentanil anae-
thesia, the Narcotrend was able to differentiate awake vs
steady-state anaesthesia and steady-state anaesthesia vs the
first reaction and extubation with a prediction probability
greater than 0.90.14 The Narcotrend index (MonitorTechnik,
Bad Bramstedt, Germany) is a new EEG index, which
has been developed at the University Medical School of
Hanover, Germany, and is now available commercially.15
The Narcotrend algorithm is based on pattern recognition
of the raw EEG and classifies the EEG epochs into different
stages from A (awake) to F (increasing burst suppression
to electrical silence). The newest Narcotrend software version
additionally includes a dimensionless Narcotrend index from
100 (awake) to 0 (electrical silence), similar to the BIS.
However, while much information is available for the BIS,
the amount of study data on the Narcotrend and its index
is very limited. Therefore, transferring guidelines from the BIS
to Narcotrend would make it possible to extrapolate BIS data
to Narcotrend applications and would therefore be of interest
for the clinical use of the Narcotrend monitor. We compared
the relationship between the BIS and Narcotrend index during
anaesthesia with propofol.

Methods
We obtained institutional review board (Ärztekammer des
Saarländes, Saarbrücken, Saarland, Germany) approval and
written informed consent, and studied 18 adult male patients,
ASA physical status II, who were about to have radical pro-
statectomy. We excluded patients with disabling central ner-
vous or cerebrovascular disease, a history of hypersensitivity
to opioids or substance abuse, and those receiving treatment
with opioids or any psychoactive medication.

All patients were premedicated with midazolam 7.5 mg kg\(^{-1}\)
only orally on the morning of surgery. An i.v. catheter was inserted
into a large forearm vein and standard monitors were applied.
An epidural catheter was placed in the lumbar space. The EEG
was recorded continuously using an Aspect A-2000 BIS mon-
tor (version XP) and a Narcotrend monitor (version 4.0). After
skin preparation with isopropyl alcohol 70%, the BIS (BIS-XP
sensor; Aspect Medical Systems) and the Narcotrend (Blue
sensor; Medicotest, Olstykke, Denmark) electrodes were
positioned as recommended by the manufacturers. For the
Narcotrend, two commercially available ECG electrodes
were placed on the patient’s forehead separated by a minimum
distance of 8 cm, and a third electrode was positioned laterally
and served as a reference electrode. Finally, impedances were
measured for each set of electrodes to ensure optimal electrode
contact, defined as ≤6 kΩ for the Narcotrend and ≤7.5 kΩ for
the BIS, as required by the manufacturers.

Fentanyl 0.1 mg i.v. was given and anaesthesia was
induced 5 min later with a propofol infusion system (Graseby
3400; Graseby Medical, Watford, UK) initially started at a
delivery rate of 36 mg kg\(^{-1}\) h\(^{-1}\). After loss of the eyelash
reflex, oxygen was given by face mask, the propofol infusion
was reduced to a delivery rate of 16 mg kg\(^{-1}\) h\(^{-1}\), patients
were given atracurium 0.5 mg kg\(^{-1}\), the trachea was intubated
3 min later, and the lungs were ventilated to obtain an end-
tidal carbon dioxide partial pressure of 35 mm Hg. After
intubation, patients received bupivacaine 0.5% 15 ml via
the epidural catheter; the propofol infusion was adjusted
according to clinical needs. Complete neuromuscular block-
ade during the investigation was ensured by further atracur-
ium 0.25 mg kg\(^{-1}\).

Forty-five minutes after induction of anaesthesia, the
propofol infusion rate was increased to 26 mg kg\(^{-1}\) h\(^{-1}\) until a
substantial burst suppression pattern was recognized in the
raw EEG. Thereafter, the propofol infusion rate was reduced
to 0.5 mg kg\(^{-1}\) h\(^{-1}\) until a BIS value of 50 was reached. After
this procedure had been completed twice, propofol infusion
rates were again adjusted to clinical needs. At the time of the
final surgical suture, the propofol infusion was stopped.

BIS, Narcotrend index values and the respective Narco-
trend stages were automatically recorded at intervals of 5 s
during the investigation. The times of loss of verbal response,
loss of eyelash reflex, spontaneous opening of eyes and extu-
bation were recorded.

Statistics
Statistical comparisons used the paired \(t\)-test for BIS and
Narcotrend data at loss of verbal response or loss of eyelash
reflex vs baseline; the test was two-tailed and statistical sig-
nificance was defined as \(P<0.05\). Correlation calculations
between the Narcotrend index and BIS and between the
Narcotrend index or BIS and the burst suppression ratio were
performed as linear or non-linear regression analysis as appro-
priate. Data are presented as mean and standard deviation (SD)
or (in Fig. 1) as median and the 10th and the 90th centiles.

The efficacy of Narcotrend and BIS in predicting loss of
verbal response and the eyelash reflex, opening of the eyes
and extubation was evaluated using the prediction probability
\(P_K\). As described by Smith and colleagues,16 a \(P_K\) value of
1 means that the value of the predicting variable always
correctly predicts the variable to be predicted. A \(P_K\) value of
0.5 means that the indicator prediction is no better than
chance alone. Using a spreadsheet macro, the \(P_K\) value was
computed (Excel 2000; Microsoft, Redmond, VA, USA),
for example, for the assessments made while awake and
immediately after loss of verbal response.

Statistical analysis was performed using SigmaStat 2.03
and SigmaPlot 2000 computer software (SPSS, Erkrath,
Germany).
Comparison of Narcotrend and bispectral index

Results

Eighteen ASA II patients were enrolled in this study. The mean age (range) was 62 (45–71) yr, mean (SD) weight 80 (9) kg and height 174 (5) cm.

A total of 38 629 data pairs of BIS and Narcotrend index from artefact-free 5-s EEG epochs were collected. The average number of epochs included per patient was 2146 (353). Because of artefacts, no variable value could be calculated for the Narcotrend or the BIS or for both indices in another 5008 epochs, which were therefore excluded from data analysis; these were 3855 epochs for the Narcotrend index alone, 245 epochs, which were therefore excluded from data analysis; the Narcotrend or the BIS or for both indices in another 5008 epochs, which were therefore excluded from data analysis; these were 3855 epochs for the Narcotrend index alone, 245 epochs for the BIS alone, and 908 epochs for both indices.

Because of artefacts, no variable value could be calculated for any epochs for the BIS alone, and 908 epochs for both indices.

Fig 1 Relationship between Narcotrend index and bispectral index. For each Narcotrend index value from 1 to 99, the median (thick line) and the 10th and the 90th quartiles (thin lines) of the respective BIS values are shown. The dotted line represents the line of identity.

For BIS values lower than 50, a second sigmoid model with a correlation of $r=0.83$ was applied:

Narcotrend index

$$= 6.6+45.3/(1+\exp(-(\text{BIS}–29.8)/2.4))^{0.6}; r=0.83 \text{ (Fig. 2).}$$

However, as shown in Fig. 2, a plateau of BIS values, in contrast to the Narcotrend index, was observed. Because of this plateau the individual correlation curves between the BIS and the Narcotrend index are additionally shown in Fig. 3 ($r=0.43\pm0.20; \text{ range } 0.73–0.11$).

In 5389 epochs, a burst suppression ratio (BSR) of >5% was indicated by the A-2000 BIS monitor. The relationship between the BSR and BIS and between the BSR and the Narcotrend index differed substantially. The relationship between the BSR and the Narcotrend index was best described by the following sigmoid model (Fig. 4):

Narcotrend index

$$=265/(1+\exp(-(\text{BSR}+108)/-49)); r=0.73.$$

For a BSR between 5 and 40%, no relevant change in BIS ($r=0.1$) values was observed, whereas at BSR >40% the BIS linearly decreased: BIS = 42.14–0.4217×BSR ($r=−1$).

Discussion

According to a Medline analysis performed in October 2003, more than 440 publications are available for BIS. These cover
a huge range of information of clinical interest, e.g. titration guidelines for anaesthetics in different procedures and different patient populations. At the same time there were only 11 studies available for the Narcotrend, another monitor designed to assess the depth of anaesthesia. A comparison of these numbers clearly shows that transferring guidelines from BIS to Narcotrend index values would make it possible to extrapolate BIS data to Narcotrend applications and would therefore be of interest for the clinical use of the Narcotrend monitor.

In the present study we compared BIS and Narcotrend index data from 38 629 artefact-free EEG epochs during propofol anaesthesia, covering the whole scale of both indices from 99 to 1. We found a good correlation between the BIS and Narcotrend index values, with little space between the 10th and the 90th centiles (Fig. 1), but deviations from the line of identity in some ranges require attention. The efficacy of the Narcotrend and BIS in predicting the transition from consciousness to unconsciousness with the induction of anaesthesia or from unconsciousness to consciousness during emergence from anaesthesia was similar, as measured by the prediction probability (Table 1).

Some methodical limitations must be considered. For the comparison between BIS and Narcotrend index values, we chose a non-steady-state approach with changing propofol concentrations. This is in contrast to possible study designs using either constant effect compartment concentrations of the anaesthetic drug, e.g. via target-controlled infusion, or keeping one EEG parameter value constant and recording the parameter values of the second EEG parameter at that specific value of the first parameter. This latter approach has been used previously in comparisons between the BIS and the Alaris auditory evoked potential (AEP) index, in which the AEP index values were recorded after titrating the anaesthetic drug to BIS values of 30, 40, 50 or 60.17

The non-steady-state approach we chose has the advantage that a larger range of values is covered; in the present investigation we were able to study the whole scale of both indices from 99 to 1. In addition, the non-steady-state approach is closer to daily clinical practice in anaesthesia. As the period needed for data averaging and smoothing of one 5-s parameter value was 30 s for the BIS and was therefore different from that for the Narcotrend index value (20 s),18 the comparability of the values during periods with fast-changing drug concentrations, such as during induction of anaesthesia, bears some uncertainty.

The Narcotrend monitor performs an automatic analysis of the EEG during anaesthesia. The methods for automatic classification were developed on the basis of a visual assessment of the EEG which, in origin, is related to sleep classification. Loomis and colleagues19 described systematic changes of the EEG during human sleep and defined five stages, A–E, to distinguish different EEG patterns. Subsequently, the
Narcotrend scale was extended; it was refined by the definition of substages, and was applied to the classification of EEGs recorded during anaesthesia, stage A representing the awake state and stage F representing a very deep level of anaesthesia with increasing burst suppression. Several subparameters of the EEG, which were found to be best suited to discriminating between the different visually determined substages, were combined in multivariate discriminant functions to classify an epoch into one of the substages between A and E. Discriminant analysis yields probabilities for the degree of similarity of an EEG epoch with the typical stages A–E during anaesthesia. In addition, algorithms for the classification of stage F were developed which are based on the proportion and intensity of very flat EEG segments. The newest version of the Narcotrend software (version 4.0) introduced a dimensionless Narcotrend index from 100 (awake) to 0 (electrical silence), which is similar to the BIS. The relationship between the Narcotrend substages and the Narcotrend index, as obtained from this study, is given in Table 2.

The Narcotrend algorithm excluded more epochs because of artefacts than the BIS algorithm. This indicates that the artefact detection algorithm of the Narcotrend is more sensitive, but not necessarily better, than that of the BIS monitor. By evaluating characteristic artefacts in the EEG, caused by muscle activity, eye movements, and electrocautery, the Narcotrend algorithm includes the development of functions for the automatic identification and exclusion of artefacts from subsequent data processing. Especially this last dynamic approach for the detection of artefacts, relying on comparison with the EEG parameter values of surrounding epochs, seems theoretically favourable, but data proving the superiority of this approach are still lacking. Unfortunately, no exact and detailed artefact detection algorithm has been published for either index.

In contrast to the BIS ranges recommended for general anaesthesia, i.e. BIS between 40 and 65, the relationship between the Narcotrend index and the BIS deviates substantially from the line of identity (Figs 2 and 3). On the basis of a previous study, with an older version of the Narcotrend software before the introduction of the Narcotrend index, Narcotrend stage C1 was proposed as equivalent to a BIS of 60 and Narcotrend stage D0 was proposed as equivalent to a BIS of 50. With these guidelines, Narcotrend-guided anaesthesia was shown to result in the same reduction in anaesthetic drug consumption and in the same shortening of recovery time as BIS-guided anaesthesia. According to the results of our present study, Narcotrend stage C1 can be translated into Narcotrend index values from 70 to 74, corresponding to median BIS values from 59 to 64. Narcotrend stage D0 can be translated into Narcotrend index values from 57 to 64, corresponding to median BIS values from 41 to 46. This underlines that a simple 1:1 transfer from BIS to Narcotrend index values in this range would not be adequate. Our present results therefore support the institution of rational guidelines for targeting Narcotrend index ranges during general anaesthesia.

In the presence of a burst suppression pattern, the relationship between the Narcotrend index and the BIS deviates substantially from the line of identity. For example, a burst suppression ratio of 40% is related to a median BIS value of 25 but to a median Narcotrend index value of 12. Recently, the non-optimal relationship between burst suppression ratio and BIS version 3.22 has been reported. An increasing anesthetic drug effect, resulting in an increase in the duration of suppression to a suppression ratio of up to 40%, was not adequately reflected by the BIS, whereas beyond a suppression ratio of 40% the BIS and the suppression ratio invariably showed a linear correlation ($r=−1$). Unfortunately, the new BIS version XP behaves in a nearly unchanged manner, in addition to the slightly lower BIS values at the respective suppression ratios. In contrast, Narcotrend index values are substantially lower than BIS values at the respective suppression ratios. The Narcotrend index decreases with increasing suppression ratio even at low suppression ratios, but the relationship between suppression ratio and Narcotrend index at suppression ratios $>40\%$ is less steep than that between suppression ratio and BIS. These differences should be taken into account if titrating barbiturates in patients to obtain a burst suppression pattern.

The BIS has been reported to reach a pharmacodynamic plateau at values of approximately 40 and near or at the beginning of burst suppression. Interestingly, unchanged mean BIS values in these ranges are related to substantial changes in the respective Narcotrend index, promising a possibly better reflection of the pharmacodynamic effect of anaesthetic drugs in these ranges by the Narcotrend index than by the BIS.

In conclusion, we found a sufficient correlation between BIS and Narcotrend index values with a small gap between the 10th and the 90th centiles, whereas deviations from the line of identity in some ranges require attention. Therefore, a simple 1:1 transfer from BIS values to Narcotrend index values is not adequate. Our results might serve as a blueprint for a rational ‘translation’ of BIS into Narcotrend index values.

Acknowledgement
This study was supported solely by departmental funding.

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