The effects of electromyographic activity on the accuracy of the Narcotrend® monitor compared with the Bispectral Index during combined anaesthesia

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Summary

The Narcotrend® is a monitor system for the assessment of depth of anaesthesia. The objective of this trial was to investigate the susceptibility of the Narcotrend to electromyographic (EMG) activity when compared with the Bispectral Index (BIS). We enrolled 33 patients undergoing major urological procedures under combined anaesthesia (thoracic epidural analgesia and general anaesthesia). Anaesthetic depth was assessed simultaneously by the BIS XP and Narcotrend. The intended anaesthetic depth ranged between 40 and 55 in the BIS and between D2 and D0 in the Narcotrend. BIS, but not Narcotrend, values correlated significantly ($p < 0.0001$) with EMG. BIS values between 70 and 80 occurred intermittently above an EMG activity of 35 dB, whereas the Narcotrend and the clinical signs remained unchanged during the period of elevated BIS values. None of the patients reported intra-operative awareness. Increased electromyographic activity does not affect Narcotrend values. Under combined anaesthesia, the Narcotrend monitor is more reliable when compared with the BIS regarding susceptibility to increased EMG activity.

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Epidural administration of local anaesthetics during combined anaesthesia (thoracic epidural analgesia and general anaesthesia) reduces the amount of inhaled and intravenous anaesthetics required for maintenance of an adequate anaesthetic depth [1–3]. To quantify the anaesthetic depth and to avoid intra-operative awareness and recall, some investigators used Bispectral Index-guided administration of the anaesthetic agents. The individual adjustment of the anaesthetic depth to its actual demand led to a significant decrease in the requirement for isoflurane [1], sevoflurane [2] and propofol [3].

However, an increasing number of case reports [4–6] and randomised controlled trials [7–10] have pointed out the inaccuracies of the BIS which result from warming devices, vasoactive drugs and, most of all, from increased electromyographic activity. A monitor system (BIS) that has been actually designed to optimise the dosage of anaesthetic agents, fails to assess the anaesthetic depth accurately when EMG activity increases as a sign of recovery from neuromuscular blockade. This may mislead the anaesthetist to increase the dosage of anaesthetics in an attempt to re-adjust the anaesthetic depth, resulting in a possible haemodynamic deterioration or a prolonged recovery due to inadequate deep anaesthesia and unnecessary additional muscular paralysis.

The Narcotrend® (MonitorTechnik, Bad Bramstedt, Germany) is an electroencephalographic device which has been commercially available in Europe since 2000 and recently received US Food and Drug Administration approval.

Up to now, there is a lack of data regarding possible interactions between the Narcotrend and EMG activity. This is the first study designed to investigate the effects of EMG activity on the accuracy of the Narcotrend values under combined anaesthesia when compared to BIS.

Methods

Patients

After institutional approval and written informed consent, 33 consecutive patients, aged 26–81 years, ASA physical state II and III, scheduled for major urological surgery

(retropubic radical prostatectomy or nephrectomy) under a combination of thoracic epidural analgesia and general anaesthesia were enrolled in the investigation.

Exclusion criteria were patient's refusal for the peri-operative use of epidural analgesia, a history of drug and/or alcohol abuse, cerebrovascular and central nervous diseases, bleeding or coagulation disorders, concomitant antiplatelet therapy, known allergic diathesis to anaesthetic drugs or pregnancy.

Pre-operative arrangements/monitoring

Patients received 0.1 $mg.kg^{-1}$ midazolam orally 45 min prior to induction of general anaesthesia. Concomitant medication was continued as indicated. A five-lead electrocardiogram (ECG) including measurement of segmental ST depression (II, aVF, V5), and pulse oximetry were recorded. Arterial pressure was monitored continuously in the left radial artery (CMS Monitor®, model M1092A, Hewlett-Packard GmbH, Böblingen, Germany). A central venous catheter was placed in the internal jugular vein to obtain continuous monitoring of the central venous pressure. Anaesthetic depth was assessed simultaneously by the BIS XP monitor (BIS® sensor, Aspect Medical Systems Natick, MA) and the Narcotrend (version 4.0).

After careful preparation of the skin, three silver/silver-chloride gel-filled electrodes (Blue Sensor; Medicotest, Olstykke, Denmark) were placed on the forehead for Narcotrend recordings. The BIS XP compatible electrode, BIS-Quattro, containing four silver/silver-chloride gel-filled adhesive electrodes, was placed according to the instructions of the manufacturers. Electrode impedance of both monitor systems was kept below 5 kΩ. The smoothing rate for the BIS XP was 15 s.

Thoracic epidural analgesia

Before induction of anaesthesia, an epidural catheter was inserted through an 18-gauge Tuohy needle (Perisafe® Plus, BD, Bidford-on-Avon, UK) with the loss-of-resistance method in the sitting position at a midthoracic level with the bevel facing in a cephalad direction. The catheter was inserted 3–4 cm into the epidural space. After a negative aspiration test, a test dose of 3 ml of lidocaine 2% was administered for detection of intrathecal misplacement of the catheter. Intra-operative analgesia was performed by application of 10 ml ropivacaine 0.3% and 1.0 $\mu g.ml^{-1}$ sufentanil via the epidural catheter every 60 min.

General anaesthesia

Anaesthesia was induced with 1.5 $mg.kg^{-1}$ propofol and 0.5 $\mu g.kg^{-1}$ sufentanil. Tracheal intubation was facilitated by 0.5 $mg.kg^{-1}$ rocuronium. General anaesthesia was maintained by desflurane in oxygen/nitrous oxide (35%/65%). Patients were mechanically ventilated to an end-tidal carbon dioxide of 4.8–5.3 kPa at a fresh gas flow of 1 $l.min^{-1}$. (Primus, Dräger, Lübeck, Germany). Body temperature was maintained at a minimum of 36 °C with warmed infusions.

Study protocol

Electromyographic activity was indicated continuously on the BIS XP platform and compared with electrical stimulation of the ulnar nerve at the wrist by the nerve stimulator (Innervator® NS 252, Fisher & Paykel, Healthcare, Auckland, New Zealand) using the train-of-four stimuli (TOF, 2 Hz for 2 s). Anaesthetic depth, haemodynamic parameters (heart rate and mean arterial pressure) and clinical signs (lacrimation, diaphoresis and patient's movements) were recorded continuously and documented at 5-min intervals. Increases in the EEG values (BIS and/or Narcotrend), indicating an inadequate anaesthetic depth, were treated only if they were accompanied by simultaneous changes of the haemodynamic parameters for more than 20% of baseline values and/or changes of the clinical signs. Insufficient intra-operative analgesia was determined as increase of mean arterial pressure and/or heart rate for more than 20% of baseline values following surgical stimulation in the presence of normovolaemia (central venous pressure 8–12 mmHg). In the case of insufficient intra-operative analgesia, continuous administration of remifentanil starting with 0.2 $\mu g.kg^{-1}.min^{-1}$ was allowed. When haemodynamic measures returned to baseline values and clinical signs indicated sufficient analgesia, remifentanil administration was tapered until it reached zero.

Desflurane adjustment for maintenance of BIS and Narcotrend within the intended range was performed continuously during surgery with an allowed stabilisation phase of 5 min following changes in the desflurane administration.

Postoperative follow-up

After skin closure, the volatile anaesthetic was discontinued and following extubation of the trachea in the operating room, patients were monitored for at least 60 min in the post anaesthesia care unit (PACU). To detect intra-operative awareness or recall, patients were interviewed immediately and 2 weeks after surgery using the Brice [11] questionnaire:

1 What is the last thing you remember, before you fell sleep?
2 What was the first thing you remember, waking up?
3 Do you remember anything else between those two points?
4 Did you have dreams?
5 Were they pleasant or frightening?

Statistics

Linear regression was used to assess the relation between EMG activity and EEG readings. For both BIS and Narcotrend, a linear model was fitted with EMG as predictor variable. As the data come from repeated measurements of the same subjects, a random intercept term was included in the model. As the observations are taken longitudinally, within-subject errors are likely to be autocorrelated. A first-order autoregressive process was employed to account for this special covariance structure.

Because of different durations of anaesthesia, missing values occurred after the 90th min in a number of subjects. Individual plots of observed and fitted values over time showed an increasing lack of fit after that time. Therefore, analysis was restricted to the first 90 min.

After allowing for different variances in each subject, normal probability plots (Q-Q-plots) approximated a straight line through the origin, thus indicating normal distribution of the residuals.

p values were calculated for the effect of EMG. The goodness of fit of the resulting models was evaluated by the squared correlation between fitted and observed values as a substitute for r-squared in linear models without repeated measures.

The statistical analysis was performed using GNU R [12] with the NLME package [13].

Results

Measurements could be performed in all 33 patients. None of the patients had to be removed from evaluation due to violations of the study protocol or inappropriate signal quality due to artefacts in both monitor systems. Patients' characteristics, type and duration of surgery are presented in Table 1.

Combined anaesthesia could be performed in all patients. Epidural administration of ropivacaine 0.3% + sufentanil 1 $\mu g.ml^{-1}$ led to sufficient intra-operative analgesia, and additional remifentanil administration due to signs of inadequate intra-operative analgesia was not necessary. Neuromuscular blockade diminished within 40 ($\pm$ 10) min after injection of rocuronium for facilitation of tracheal intubation as indicated by the EMG value on the BIS XP monitor and the stimulation of the ulnar nerve by means of the nerve stimulator (TOF = 4). During the further course of surgery, no repeated administration of neuromuscular blocking agents was necessary.

There were no intra- or postoperative complications related to the anaesthetic regimen. All epidural catheters were removed within a mean (SD) of 5 (1) days after surgery and all patients were discharged within 15 days after surgery. During the interviews (Brice questionnaire), no patient reported intra-operative awareness or recall.

Mean (SD) duration of surgery was 170 (29) min without complications, such as extensive blood loss, haemodynamic deterioration, hypothermia, or prolonged neuromuscular blockade. End-tidal concentration of desflurane during surgery ranged between 2.7% and 2.3%, equal to 1–0.8 minimum alveolar concentration (MAC) in nitrous oxide, respectively.

Of 990 possible measurements (33 patients and 30 time points of documentation in 5-min intervals), data of 625 measurements could be obtained due to the shorter duration of surgery among some patients. For BIS, but not for Narcotrend, there was a strong positive correlation with EMG ($p < 0.0001$). This correlation holds true for both subject means and individual mean centred readings with $R^2 = 0.385$ for the BIS and $R^2 = 0.008$ for the Narcotrend, respectively (Figs 1 and 2).

High BIS values (> 70) occurred among 16 (48.4% of all cases) patients at EMG activity level > 30 dB as indicated by the BIS XP platform and verified by electrical stimulation of the ulnar nerve (TOF = 4)

Table 1 Patients' characteristics, duration and type of surgery.

	Age; year	Sex; F/M	Height; cm	Weight; kg	Duration; min	Surgery; type
Mean (SD)	65 (10)	4/29	177 (7)	82 (13)	170 (29)	10 NE/23 RPE

F, female; M, male; RPE, radical prostatectomy; NE, nephrectomy.

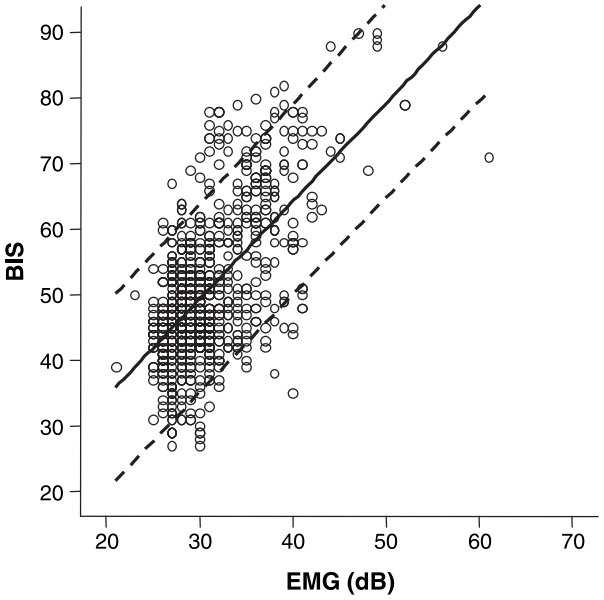

Figure 1 Scatterplot of BIS values vs EMG. Significant correlation, $p < 0.0001$, between BIS and EMG, $R^2 = 0.39$, equation: $y = 1.49x + 4.56$.

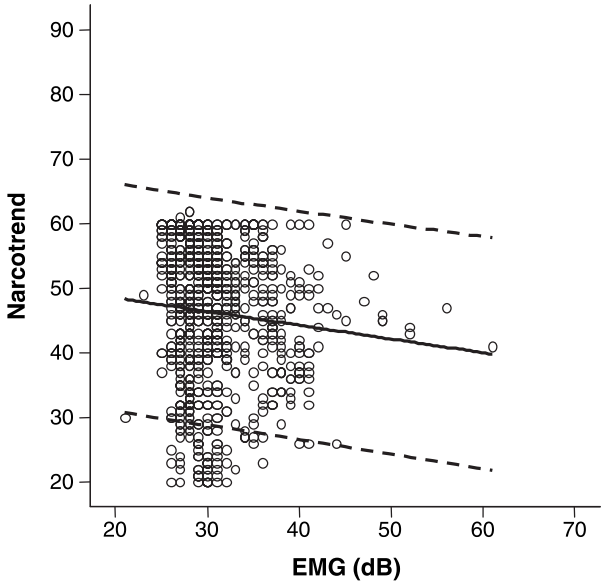

Figure 2 Scatterplot of Narcotrend values vs EMG. No statistical significance, p = 0.101, between Narcotrend and EMG, $R^2 = 0.008$, equation: $y = -0.213x + 52.79$.

without simultaneous increases in the Narcotrend values or changes in the clinical signs (Fig. 3). During that period, patients were asked to squeeze the investigator's hand to reproduce intra-operative consciousness, but none of the patients responded. Even after painful squeezing of the M. trapezius, there was no indication of inadequate anaesthetic depth. For these patients, the median BIS value was 75 and the median EMG activity 38 dB. A regression model revealed an R^2 of 0.179 with $p < 0.001$.

In contrast to the BIS, there were no increases in the Narcotrend values throughout surgery due to interaction with increased EMG activity.

Discussion

In the present study, the BIS and Narcotrend monitor systems were evaluated regarding their susceptibility to electromyographic activity during major urological procedures under the combination of thoracic epidural analgesia and general anaesthesia. Our results demonstrate a significant correlation between EMG and BIS, but not between EMG and Narcotrend under constant anaesthetic depth and sufficient intra-operative analgesia, as indicated by the haemodynamic parameters, the clinical signs and the lack of patients' response to tactile and verbal stimuli during elevated BIS values.

The development of the Narcotrend algorithm is based on descriptions of EEG pattern changes during human sleep, first described by Loomis in 1937 [14]. Loomis defined five stages, A–E, to distinguish the different hypnotic stages. In the late 1990s, Schultz developed the Narcotrend, a monitor device for the assessment of anaesthetic depth, using the Loomis classification of five different hypnotic stages, adding 15 substages for a more precise classification of the EEG (Table 2). Briefly, the signals are sampled at 128 samples per second with a 12-bit resolution, and are bandpass filtered to 0.5–45 Hz. The power spectrum is calculated by means of a Fast Fourier Transformation (FFT), allowing enormous visual compression of spectral data by stacking and thus simplified recognition of time-related changes in the EEG. Impedances and electrode potentials are continuously tested at defined time intervals to ensure a high EEG signal quality. Trace segments with a length of 20 s, the so-called epochs, are the units of classification. Following filtering of artefacts, the EEG parameters that are relevant for the detection of suppression and that contribute to the discriminant functions are calculated and updated. Finally, a smoothing value of the Narcotrend classification is calculated as a weighted mean (weights depending on the background parameters) [15].

The BIS algorithm includes three EEG subparameters, depending on the depth of anaesthesia: 'Burst suppression', the 'SynchFastSlow' and the 'BetaRatio'. Burst suppression has a greater weight in the calculation of BIS values during general anaesthesia when compared to sedation. The SynchFastSlow is defined as the logarithm of the following ratio: the sum of bispectrum peaks in the 0.5–47 Hz range divided by the sum of the bispectrum peaks in the 40–47 Hz range. The weight of SynchFastSlow in the BIS index calculation relates to the degree of EEG activity during general anaesthesia. The weight of BetaRatio is greatest at light sedation. The BetaRatio is calculated as the log of the ratio of power in two empirically derived frequency bands: $\log(P_{30-40\,Hz}/P_{11-20\,Hz})$ [16].

Both Narcotrend and BIS algorithms use frequencies between 0.5 and 47 Hz to compute the raw EEG into a narcotic stage. Regarding EMG activity creating frequencies from 25 to 300 Hz [17], this might be a source of interference between the two monitor systems and the muscle activity, due to an overlap between the frequencies generated by increased muscular activity and the frequencies originating from the EEG. The BIS XP platform contains an EMG activity bar that indicates the muscle activity throughout the measure, and the manufacturers point out the improvements in the software of the BIS in combination with the new BIS Quattro® electrode as regards indicating and filtering artefacts, like electromyographic activity. However, the results of our investigation do not confirm the expectations of these improvements.

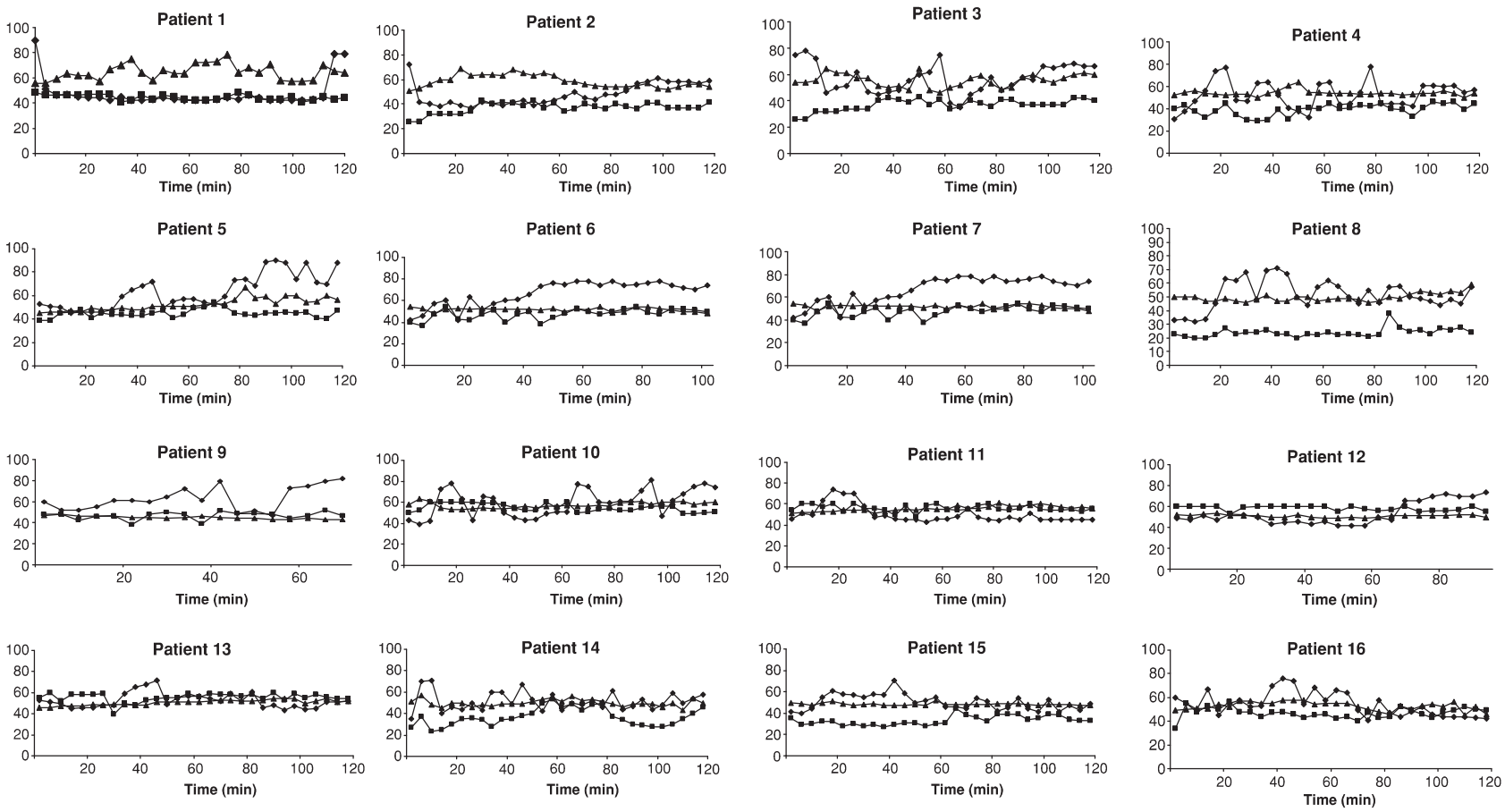

Figure 3 Intra-operative course of BIS and Narcotrend values and heart rate among patients with BIS elevations during surgery. ◆, BIS; ■, Narcotrend; ▲, heart rate.

Table 2 Narcotrend stages and the respective Narcotrend index ranges (version 4.0).

Narcotrend stage	Narcotrend index
Awake	
A	95–100
B_0	90–94
Sedated	
B_1	85–89
B_2	80–84
Light anaesthesia	
C_0	75–79
C_1	70–74
C_2	65–69
General anaesthesia	
D_0	57–64
D_1	47–56
D_2	37–46
General anaesthesia with deep hypnosis	
E_0	27–36
E_1	20–26
E_2	13–19
General anaesthesia with increasing burst suppression	
F_0	5–12
F_1	1–4

None of the Narcotrend versions contains an indicator about EMG activity. Considering that the Narcotrend algorithm includes frequencies between 0.5 and 47 Hz, one would assume that increased EMG activity would also interfere with the EEG recordings and thereby affect the accuracy of the values. However, during the measures in all our patients we did not observe an increase in the Narcotrend values similar to the BIS values during enhanced EMG activity.

The exact algorithm of both monitor systems has not yet been published in detail. Regarding the BIS monitor, the possible explanation about sudden and/or periodical increases of the values in the presence of enhanced EMG activity could be the overlapping frequencies of EMG and EEG. Although the Narcotrend algorithm and EMG activity 'share' the same frequency band, increased EMG activity did not lead to any change in the Narcotrend values. A possible explanation of this observation could be that the Narcotrend algorithm does not process EMG activity. As long as the exact algorithm is not published, this explanation remains speculative.

Recently, Schneider et al. [18] and Russell [19] presented challenging data about the accuracy of the Narcotrend. Schneider and colleagues investigated the reliability of the Narcotrend during induction of anaesthesia regarding an adequate detection of the transition between awareness and unconsciousness. The Narcotrend failed to detect accurately changes in the consciousness of surgical patients during induction of general anaesthesia and regained consciousness after interruption of propofol administration following tracheal intubation. Russell used the isolated forearm technique to assess the reliability of the Narcotrend at a defined anaesthetic depth and concluded that the Narcotrend is unable to detect consciousness during general anaesthesia due to the fact that patients responded to verbal commands.

The main difference between our study design and that of Schneider et al. is that we performed our measures during a steady state. We evaluated the Narcotrend during surgery at a defined anaesthetic depth, without changes in the administration of desflurane, to provoke transient awake phases.

In contrast to the study of Russell, who examined 12 patients, we did not observe any periods during our investigation in which the monitor of the Narcotrend was blank due to malfunction or inappropriate signal quality. Based on Russell's findings, we asked the patients to squeeze the anaesthesiologist's hand at BIS values > 60; none of the patients responded. Another contrast to the above-mentioned study was the fact that we targeted a 'deeper' anaesthetic depth as indicated by the Narcotrend (D2-D0) in contrast to Russell who intended C-levels, which is comparable with deep sedation or light anaesthesia.

Processed EEG monitors are applied increasingly in anaesthetic practice. Patients undergoing major abdominal or urological surgery in a combination of epidural analgesia and general anaesthesia may benefit from the individual adjustment of the anaesthetic depth. The synergistic effects of these techniques decrease the requirement of inhaled and intravenous anaesthetic agents with consecutive faster emergence from anaesthesia and recovery from surgery [20]. Epidural analgesia decreases not only the requirement of anaesthetic agents, but also reduces the amount of neuromuscular blocking agents (NMBA) required for an optimal surgical field [3, 21]. Patients require fewer NMBAs as the afferents from the surgical field are blocked at spinal level. Conclusively, EMG activity is relatively high in the absence of NMBAs and this might be a source of interference with the p-EEG devices, affecting thereby their reliability in assessing accurately the anaesthetic depth. As shown for the BIS [4–10], EMG activity influences its accuracy, in the manner that adequately anaesthetised patients appear more awake than they in fact are. A possible (unnecessary) increase of the anaesthetic depth and a simultaneous administration of NMBAs with consecutive haemodynamic deterioration, or prolonged emergence may counterbalance the advantages of a p-EEG, individually adjusted administration of the anaesthetic agents.

Ever since it was stated that p-EEG monitoring may influence patient outcome [22], clinicians expect p-EEG

monitor systems to be robust against interferences throughout surgery and provide data which are reliable and comparable with the clinical signs.

This is the first study investigating the effects of EMG activity on the accuracy of the Narcotrend during combined anaesthetic procedures. Among our 33 patients, unlike the BIS XP, the Narcotrend was not affected by enhanced electromyographic activity.

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