British Journal of Anaesthesia **93 (2)**: 235–40 (2004)
DOI: 10.1093/bja/aeh182 Advance Access publication June 11, 2004

BJA

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 [NCT index=52.8+26.8/(1+exp(−(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 [NCT index=6.6+45.3/(1+exp(−(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: NCT index=265/(1+exp((−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,[1] 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.[2] 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[3] and burst suppression.[4] 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 shortened.[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 colleagues[13] 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 anaesthesia, 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 Saarlandes, Saarbrücken, Saarland, Germany) approval and written informed consent, and studied 18 adult male patients, ASA physical staus II, who were about to have radical prostatectomy. We excluded patients with disabling central nervous 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} 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 monitor (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 $\leqslant 6\ k\Omega$ for the Narcotrend and $\leqslant 7.5\ k\Omega$ 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 blockade during the investigation was ensured by further atracurium 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 Narcotrend 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 extubation 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 significance 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 appropriate. 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).

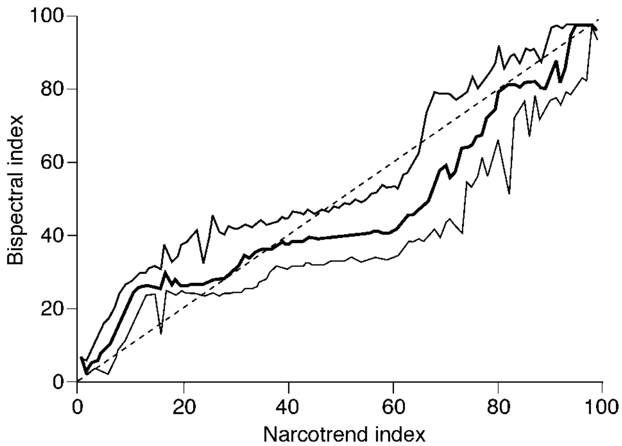

Fig 1 Relationship between Narcotrend index and bispectral index. For each Narcotrend index value from 1 to 99, the median (thick line) and the 10th and the 90th quartiles (thin lines) of the respective BIS values are shown. The dotted line represents the line of identity.

Table 1 Narcotrend and BIS index at clinical end-points of a propofol anaesthetic. Values are mean (SD). P_K=prediction probability

	Narcotrend		BIS-XP	
	Index	P_K	**Index**	P_K
Baseline	94 (6)		91 (8)	
Loss of verbal response	80 (7)	0.97	82 (10)	0.97
Loss of eyelash reflex	72 (9)	0.93	77 (11)	0.95
Open eyes spontaneously	80 (6)	0.97	77 (9)	0.95
Extubation	87 (7)	0.98	82 (5)	0.98

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

	Narcotrend stage	Narcotrend index
Awake	A	95–100
Sedated	B_0	90–94
	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

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 for the BIS alone, and 908 epochs for both indices.

Mean (SD) baseline values were 94 (6) for the Narcotrend and 91 (8) for the BIS. Compared with baseline, loss of verbal response and loss of the eyelash reflex were accompanied by a significant reduction in mean Narcotrend index values to 80 (7) and 72 (9) respectively (P<0.001) and of BIS values to 82 (10) and 77 (11) (P<0.001). The prediction probability (P_K) for loss of the eyelash reflex was similar for the BIS (P_K=0.95) and the Narcotrend (P_K=0.93). During emergence from anaesthesia, opening of eyes was associated with a BIS value of 77 (9) and a Narcotrend index of 80 (6); the corresponding P_K values were P_K=0.97 and P_K=0.95 (Table 1).

As displayed in Table 2, we were able to identify the classification of Narcotrend index values with the respective Narcotrend stages and substages from A to F.

Increasing BIS values coincided with increasing Narcotrend index values. In Fig. 1 the median and 10th and the 90th centiles of the BIS and the corresponding Narcotrend index values are shown. A sigmoid model was used to describe the correlation between the BIS and the Narcotrend index in the BIS range between 100 and 50:

$$\text{Narcotrendindex} = 52.8 + 26.8/(1+\exp(-(\text{BIS}-78.3)/4.8))^{0.4}; r=0.52.$$

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

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

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±0.20; 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):

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

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

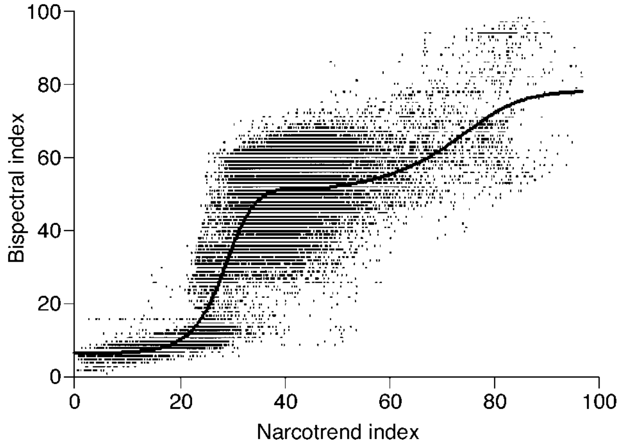

Fig 2 A sigmoid model (Narcotrend index=52.8+26.8/(1+exp(−(BIS−78.3)/4.8))$^{0.4}$; *r*=0.52) described the correlation between all BIS and Narcotrend index values in a BIS range between 100 and 50. For BIS values lower than 50 a second sigmoid model with a correlation of *r*=0.83 was used: Narcotrend index=6.6+45.3/(1+exp(−(BIS−29.8)/2.4))$^{0.6}$; *r*=0.83.

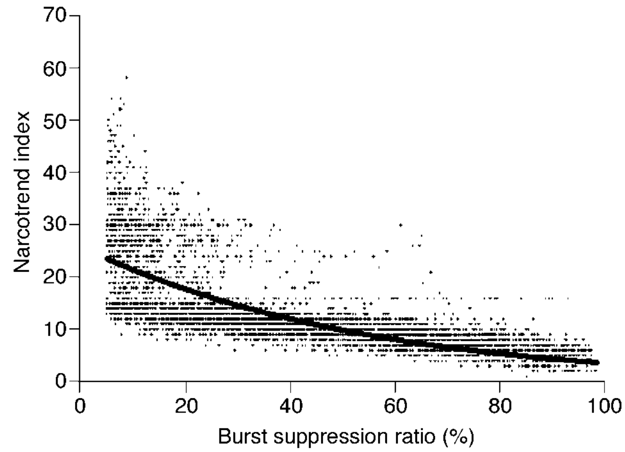

Fig 4 Relationship between the suppression ratio as calculated by the A-2000 BIS monitor and the Narcotrend index. Every dot represents the parameter values of one epoch with a suppression ratio >5%. The relationship is best described by a sigmoid model: Narcotrend index=265/(1+exp(−(BSR+108)/−49)); *r*=0.73.

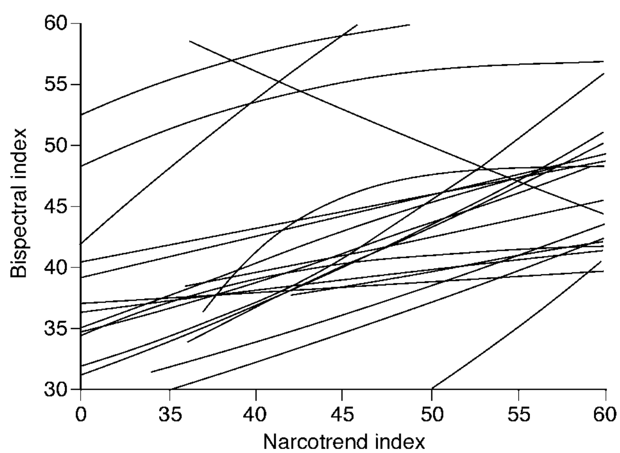

Fig 3 Individual correlation curves between BIS and Narcotrend index for BIS and Narcotrend index values between 60 and 30 (*r*=0.43±0.20; range 0.73–0.11).

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 colleagues[19] 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,[20] 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.[18] Especially this last dynamic approach for the detection of artefacts, relying on comparison with the EEG parameter values of surrounding epochs, seems theoretically favourable,[21] 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,[22] 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[23] with an older version of the Narcotrend software before the introduction of the Narcotrend index, Narcotrend stage C_1 was proposed as equivalent to a BIS of 60 and Narcotrend stage D_0 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.[18] According to the results of our present study, Narcotrend stage C_1 can be translated into Narcotrend index values from 70 to 74, corresponding to median BIS values from 59 to 64. Narcotrend stage D_0 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.[24] An increasing anaesthetic 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[25] and near or at the beginning of burst suppression.[12] 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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