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A comparison of the SNAP II™ and BIS XP™ indices during sevoflurane and nitrous oxide anaesthesia at 1 and 1.5 MAC and at awakening

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Background. Monitoring level of consciousness during anaesthesia, with the ability to predict the intentional or unintentional return to consciousness, is desirable. The purpose of this study was to compare two processed electroencephalographic depth of anaesthesia monitors (SNAP II™ and BIS XP™) during sevoflurane and sevoflurane/nitrous oxide anaesthesia.

Methods. In total, 42 subjects received an interscalene block, followed by general anaesthesia with sevoflurane or sevoflurane/nitrous oxide. The indices were recorded at baseline, at 1.5 and 1.0 minimum alveolar concentration (MAC) equivalents, and during emergence.

Results. The SNAP and BIS indices decreased from baseline at 1.5 and 1.0 MAC equivalents, but there was no difference within groups between subjects who received nitrous oxide and those who did not. The SNAP index returned to baseline by 1 min before awakening and was higher than baseline at eye opening, but the BIS index remained below baseline at awakening. There was a bias of −1 (95% CI: −3 to 1) between the SNAP and BIS at baseline; this increased to 21 (95% CI: 19–23) during maintenance of anaesthesia and was 6 (95% CI: 4–8) at awakening.

Conclusions. The SNAP index tracks loss of consciousness and emergence from sevoflurane and sevoflurane/nitrous oxide anaesthesia. There is significant bias between the SNAP and BIS indices and therefore, the indices are not interchangeable. The SNAP index returns to baseline before awakening, whereas the BIS index remains below baseline at awakening, suggesting that the SNAP index may be more sensitive to unintentional awareness.

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Monitoring the level of consciousness during general anaesthesia is desirable for several reasons. It would prevent oversedation and associated undesirable haemodynamic effects, delayed awakening and possibly increased risk of death.[1] Undersedation during general anaesthesia may contribute to intraoperative awareness. Several monitoring modalities, including processed EEG signals, have been investigated to assess the level of consciousness during anaesthesia. A relatively new device on the market is the SNAP II™ (Everest Biomedical Instruments, Chesterfield, MO, USA). The SNAP II™ index is derived from an algorithm based on low-frequency (0.1–18 Hz) and high-frequency (80–420 Hz) EEG frequency analysis. There is increasing evidence that the high-frequency component of the EEG provides useful information regarding the state of consciousness.[2 3] We and others have demonstrated that the SNAP™ device (version 1) appeared to be a useful indicator of loss of consciousness.[4–6] At the time this study was initiated, device performance had not been assessed for maintenance inhalational anaesthesia or during emergence from anaesthesia.

We hypothesized that there would be a correlation between the SNAP II™ index and depth of sevoflurane or sevoflurane/nitrous oxide anaesthesia at 1.0 and 1.5 minimum alveolar concentration (MAC) equivalent, and at awakening. The primary aim of this study was to determine

the SNAP II™ index at 1.0 and 1.5 MAC equivalent sevoflurane and sevoflurane/nitrous oxide anaesthesia and during emergence, and to compare this value with the bispectral (BIS XP™ Aspect Medical Systems, Newton, MA, USA) index value. The secondary aim of the study was to evaluate the pharmacodynamic relationship between the indices and end-tidal sevoflurane concentration from the time of discontinuation of anaesthesia until awakening.

Methods

The study was approved by the Northwestern University Institutional Review Board. Patients, aged 18–55 yr, ASA I or II, undergoing orthopaedic surgery of the shoulder under combined interscalene block-general anaesthesia were eligible for participation. Exclusion criteria included a history of drug or alcohol abuse, Mallampati class 3 or 4 airway, chronic sedation or hypnotic drug use, or a contraindication to laryngeal mask airway (LMA)† use or sevoflurane anaesthesia.

Written informed consent was obtained. Subjects were premedicated with midazolam 2–4 mg. An interscalene block was performed with bupivacaine (5 mg ml^{-1}, total volume 35–40 ml) and epinephrine (3.3 $\mu g\ ml^{-1}$) by a member of the regional anaesthesia team. No other i.v. drugs, including vasoactive agents, were administered during the study period. Subjects were transported to the operating room, standard monitors were applied, and the blocked arm was tested for completeness of anaesthesia, defined as the inability to move the shoulder and sensory anaesthesia from dermatomes C4 to C7. Subjects were excluded from the study if the block was not complete.

Standard SNAP II™ (version 2.0) and BIS XP™ (version 3.3, A2000 with XP upgrade 186-0125) monitors with respective SNAP and BIS electrode montages were applied to the subject's forehead in accordance with the manufacturers' specifications and connected to their respective monitors. The specific side (left or right) of placement depended upon forehead size and surgical position, and the electrodes did not overlap. The side for each montage was noted. BIS impedance checking was disabled in order to prevent the current output from interfering with acquisition of the SNAP signal. Baseline data were acquired for several minutes. SNAP and BIS data were collected by an anaesthesia research nurse with no responsibilities for the administration of anaesthesia, but who was aware of the subject's group assignment. General anaesthesia was administered by an anaesthetist investigator independent of the SNAP and BIS values. The anaesthetist was blinded to the SNAP index. Preparation for the surgical procedure and the surgical procedure proceeded after the induction of general anaesthesia.

Subjects with complete regional anaesthesia were randomized by a computer-generated random assignment to receive either sevoflurane alone or sevoflurane with 50% nitrous oxide. Group assignments were contained in a sealed opaque envelope that was opened after complete regional anaesthesia was obtained. After preoxygenation with 100% oxygen delivered through a face mask connected to the anaesthesia machine via a circle system, general anaesthesia was induced with sevoflurane in either 50% oxygen/air, or 50% oxygen/nitrous oxide until the subject had attained sufficient depth of anaesthesia to insert an LMA. Inspired sevoflurane concentration was adjusted to attain an end-tidal sevoflurane concentration of 1.5 MAC determined using the MAC readout on the calibrated infrared analyser (Capnomac Ultima, Datex-Engstrom, Helsinki, Finland) and maintained at this concentration for 15 min. Subjects were allowed to breathe spontaneously. At the end of the 15 min period the BIS and SNAP values displayed on the monitors were recorded, as well as the end-tidal sevoflurane and nitrous oxide concentrations, end-tidal CO_2 concentration, blood pressure and heart rate. The sevoflurane concentration was then decreased to 1.0 MAC equivalent and held at this concentration for 15 min. The above values were again recorded. The recording periods were completed before surgery involving the bone. For the remainder of the surgical procedure the sevoflurane and nitrous oxide concentrations were adjusted to the clinical needs of the subject.

When it was time to awaken the patient, the inhaled anaesthetic agents were discontinued and 100% oxygen administered. During awakening, SNAP and BIS index values and the expired sevoflurane and/or nitrous oxide concentrations were recorded every minute until the subject opened his/her eyes to command. Every 30 s the subject was addressed by name and asked to open his/her eyes. At awakening, the SNAP and BIS index values, vital signs and the sevoflurane and nitrous oxide concentrations were recorded. The study ended when the subject was awake and responding to verbal commands.

The sample size of the study was calculated by assuming two groups with five repeated measures in each subject. This design achieves 80% power to test the within subject factor (MAC equivalent) difference in the SNAP indices using a Geisser-Greenhouse corrected *F*-test at the 5% significance level with an actual effect SD of 0.8 (an effect size of 0.65). A total of 40 subjects (20 per group) were needed.

SNAP and BIS values, end-tidal sevoflurane and nitrous oxide concentrations, end-tidal CO_2 concentration, blood pressure and heart rate were compared (before induction, at 1.5 and 1.0 MAC equivalents, at discontinuation of anaesthesia, 1 min before awakening, and at awakening) between groups, using a doubly multivariate repeated measures ANOVA. Side of montage placement was a covariate for the SNAP and BIS values. Within group subject comparisons to baseline values were made for both the SNAP and BIS indices. *Post hoc* analysis was performed using Student *t*-tests with Bonferroni correction for multiple comparisons. Bland–Altman analysis of the SNAP and BIS indices was applied at each measurement interval. The relationship

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Table 1 End-tidal sevoflurane or sevoflurane/nitrous oxide concentrations. Values are given as mean (SD).*Nitrous oxide concentration was not recorded at eye opening

	Sevoflurane	Sevoflurane/N_2O
1.5 MAC (%)	3.2 (0.2)	2.1 (0.2)/46.5 (3.6)
1.0 MAC (%)	2.1 (0.2)	1.1 (0.2)/47.0 (3.1)
Discontinuation of anaesthesia (%)	1.7 (0.4)	1.0 (0.2)/42.8 (11.1)
Eye opening (%)	0.3 (0.2)	0.2 (0.1)*

between end-tidal sevoflurane concentration and the indices, measured at 1 min intervals from discontinuation of anaesthesia to eye opening regression was examined by fitting these values to a Hill equation. $P<0.05$ was required to reject the null hypothesis.

Results

Forty-four subjects were enrolled and included in the study. Sevoflurane was administered to 22 subjects and sevoflurane–nitrous oxide to 22 subjects. The data from 42 subjects were analysed; two subjects in the sevoflurane–nitrous oxide group had incomplete data because of technical malfunction early in the study protocol. Thirty-three of the subjects were male and the mean (range) age was 41 (18–55) yr. The mean (SD) heights and weights of the subjects were 176 (10) cm and 82 (13) kg, respectively. No subject received supplemental vasoactive medications.

There was no difference between groups in end-tidal CO_2 concentration, blood pressure and heart rate at baseline or other recorded intervals. Within each group baseline values were different than values recorded during maintenance and discontinuation of anaesthesia. End-tidal sevoflurane concentrations after the 15 min equilibration periods at 1.5 and 1.0 MAC equivalents, discontinuation of anaesthesia and at awakening are shown in Table 1.

The SNAP index decreased from baseline at 1.5 and 1.0 MAC equivalents and at discontinuation of anaesthesia. Mean index values had returned to baseline values 1 min before awakening and were higher than the baseline values at awakening for both sevoflurane and sevoflurane/nitrous oxide (Figs 1 and 2). Similarly, the BIS index decreased from baseline at 1.5 and 1.0 MAC equivalents and at discontinuation of anaesthesia for both sevoflurane and sevoflurane/nitrous oxide. In contrast to the SNAP index, the BIS values at 1 min before awakening and at awakening were lower than the baseline values. There was no significant difference within groups between either indices at 1.5 and 1.0 MAC equivalents. There were no differences in the SNAP values, or the BIS values, between the sevoflurane and sevoflurane–nitrous oxide groups at any time point. The side of montage placement did not affect SNAP or BIS index.

Bland–Altman analysis demonstrated a bias between the SNAP II™ and BIS XP™ of −1 (95% CI: −3 to 1) before the induction of anaesthesia, that rose to 21 (95% CI: 19–23)

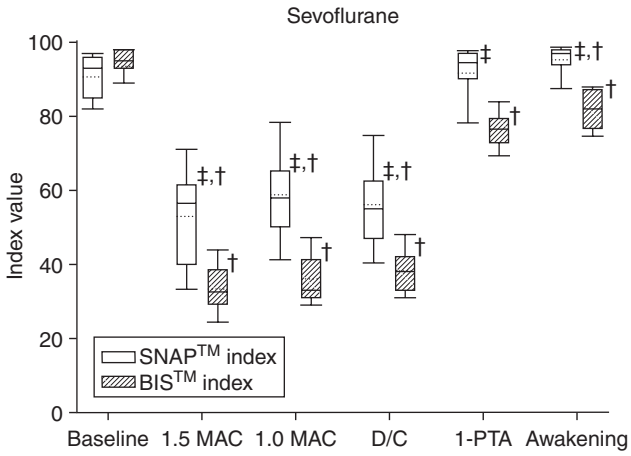

Fig 1 SNAP and BIS indices at different time intervals in subjects receiving sevoflurane. MAC, minimum alveolar concentration equivalent; D/C, discontinuation of anaesthesia; 1-PTA, 1 min before awakening; awakening, eye opening in response to verbal request. †$P<0.05$ compared with baseline, ‡$P<0.05$ compared with BIS.

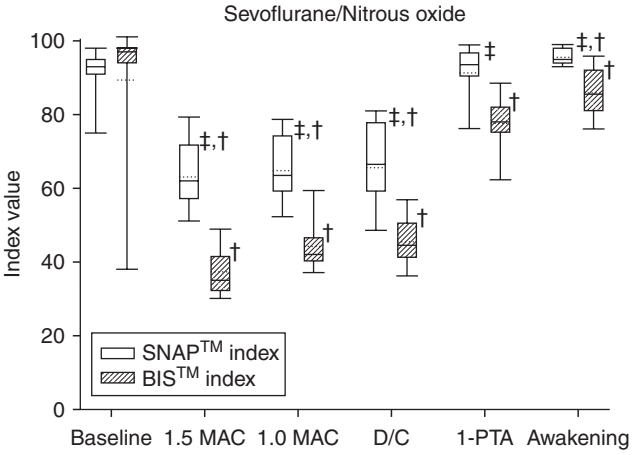

Fig 2 SNAP and BIS indices at different time intervals in subjects receiving sevoflurane with nitrous oxide. MAC, minimum alveolar concentration equivalent; D/C, discontinuation of anaesthesia; 1-PTA, 1 min before awakening; awakening, eye opening in response to verbal request. †$P<0.05$ compared with baseline, ‡ $P<0.05$ compared with BIS.

during the maintenance phase of anaesthesia. During emergence from general anaesthesia the SNAP II™ values were consistently higher than the BIS XP™ values and remained so at eye opening. At awakening the bias was 6 (95% CI: 4–8).

There was a significant relationship between the indices and the end-tidal sevoflurane concentrations during emergence of anaesthesia (Fig. 3). In the sevoflurane group the estimated EC_{50} and Hillslope for the SNAP II™ (r^2=0.45) were 0.64 (0.04) and 6.1 (2.3), and for the BIS XP™ (r^2=0.59) the values were 0.61 (0.04) and 4.4 (1.2), respectively. The combination of sevoflurane and nitrous oxide shifted the EC_{50} to 0.42 (0.06) for the SNAP II™ (r^2=0.36) and to 0.31 (0.04) for the BIS XP™ (r^2=0.41). The

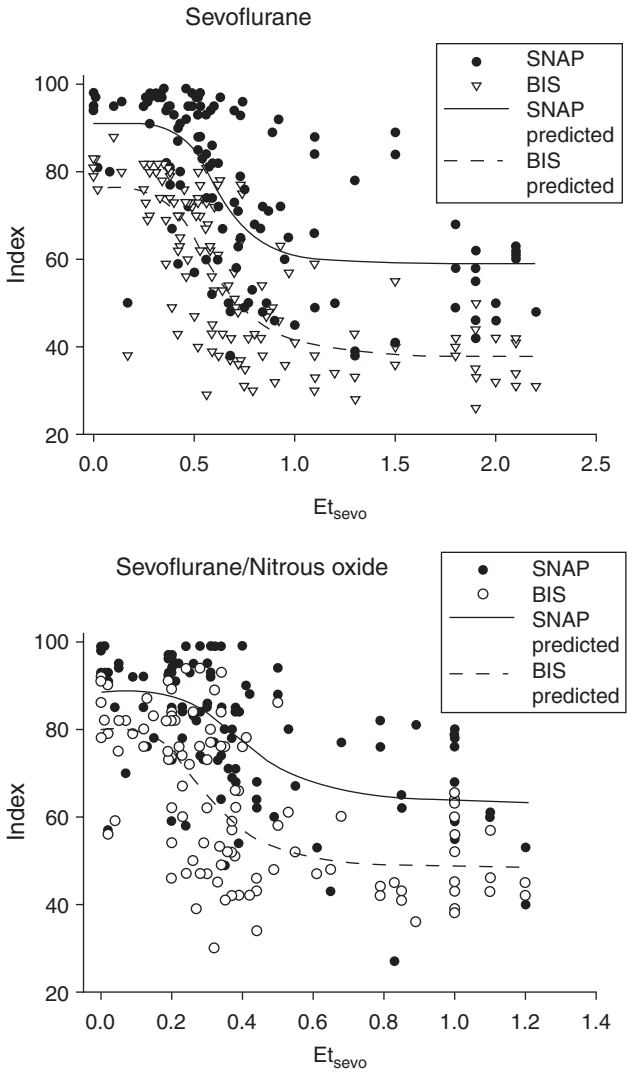

Fig 3 Scattergram of SNAP and BIS values *vs* end-tidal (Et) sevoflurane concentrations recorded every minute from the time of discontinuation of anaesthesia until eye opening in response to verbal request. Line plots are predicted index values *vs* end-tidal sevoflurane concentration determined by fitting these data to a Hill equation. The equation was $E=E_{min}+(E_{max}-E_{min})/[(1+(E'_{sevo}/EC_{50})^{\gamma}]$, where E was the index value, E_{max} and E_{min} the highest and lowest index values respectively, E'_{sevo} the end-tidal sevoflurane concentration, EC_{50} the end-tidal sevoflurane concentration associated with a half maximal effect and γ is the Hillslope.

Hillslope for the combination was 4.2 (2.3) for the SNAP II^{TM} and 3.7 (1.5) for the BIS XP^{TM} (Fig. 3).

Discussion

Traditionally, level of consciousness or depth of general anaesthesia has been monitored indirectly using clinical indicators such as blood pressure, heart rate, or even patient movement. Defining 'depth of anaesthesia' has proved difficult because adequate 'anaesthesia' has many components, including analgesia, hypnosis and non-responsiveness to surgical stimuli.[7] Therefore, monitoring level of consciousness or depth of anaesthesia with one physiological parameter has proved elusive. In the past year the Joint Commission on the Accreditation for Hospitals, an influential American non-governmental hospital accrediting organization, issued an alert about intraoperative awareness (Joint Commission on the Accreditation of Healthcare Organizations. Preventing, and managing the impact of, anaesthesia awareness. Sentinel Event Alert, Issue 32, October 6, 2004. Available from http://www.jcaho.org/about+us/news+letters/sentinel+event+alert/sea_32.htm). In the alert the organization cited the high incidence of mental distress that may occur after such an event, and outlined methods that may help decrease the likelihood of intraoperative awareness, including processed EEG monitoring. The ASA issued practice guidelines in October 2005 that support the role of processed EEG monitoring in preventing intraoperative awareness in some patients (American Society of Anesthesiologists. Practice advisory for intraoperative awareness and brain function monitoring. October 25, 2005. Available from http://www.asahq.org/publicationsAndServices/practiceparam.htm#brain). The guidelines emphasize that the general clinical applicability of these monitors in preventing intraoperative awareness has not been established, but based on anaesthetic and patient characteristics, anaesthetists may wish to consider intraoperative processed EEG monitoring, particularly for patients at high risk for intraoperative awareness.

The SNAP II is a relative newcomer among level of consciousness monitoring devices. The SNAP index, a dimensionless number from 0 to 100 (with 100 representing the awake state), is derived from an algorithm based on low- and high-frequency EEG components. Similar to other monitors of depth of anaesthesia, the low frequency component of the SNAP index is determined by spectral analysis of EEG signals in the α, β, θ and δ frequency ranges. Spectral frequencies from 18 to 80 Hz are not utilized because of their low correlation to consciousness,[2,3] and owing to EMG interference in this frequency range. The SNAP algorithm, however, incorporates high (80–420 Hz) frequency EEG components. These components may be sensitive to vigilance states and anaesthetics.[3] Anaesthetic agents may directly or indirectly influence these fast potentials and therefore analysis of this component of the EEG may contribute to the ability to differentiate between the awake and anaesthetized state.[8]

The SNAP I^{TM} has been compared with the BIS XP^{TM} device during propofol–remifentanil[5] and balanced (propofol, fentanyl, sevoflurane, nitrous oxide)[6] anaesthesia. Our study compared the devices at specified levels of sevoflurane and sevoflurane/nitrous oxide anaesthesia using the SNAP II^{TM} device. The index values generated by both the SNAP and BIS monitors decreased from the awake values with increasing concentrations of sevoflurane and sevoflurane combined with nitrous oxide. While our data do suggest a dose-dependent change in these indices

during emergence, neither index demonstrated a significant change when the equilibrium end-tidal concentration of sevoflurane was decreased from 1.5 to 1.0 MAC equivalents. The lack of dose–response at clinical depths of anaesthesia is similar to that observed by others using the BIS monitor during sevoflurane anaesthesia.[9–11] In a study of patients undergoing abdominal surgery with epidural/sevoflurane anaesthesia, sevoflurane decreased BIS index values in a dose-dependent manner until reaching a plateau at approximately 1 MAC.[9]

The lack of a dose–response pattern at clinical anaesthesia sevoflurane concentrations may reflect the relatively deeper plane of anaesthesia during this study compared with the usual clinical environment where the operative site is not blocked,[12] or may reflect the relative lack of sensitivity of these devices to the actual depth of anaesthesia once loss of consciousness has occurred. The monotonic relationship between depth of anaesthesia and the BIS index may be altered with the appearance of a burst suppression pattern in the EEG as sevoflurane concentration increases and the BIS index value is adjusted for the burst suppression ratio. The BIS index tracks linearly from 30 down to 0 as burst suppression increases from 40 to 100%.[13] Thus, up to 40% burst suppression may have been detected by the BIS in patients with index values in the 30s. The SNAP II™ monitor also incorporates a burst suppression algorithm which automatically adjusts the level of the index based on the percentage of burst suppression pattern present in the EEG.

The effect of nitrous oxide on the index values derived from the EEG may depend on multiple factors, including plane of anaesthesia and concomitant drugs. This may explain why the observed effects of nitrous oxide alone or in combination with other anaesthetics on the BIS index have been inconsistent. Nakayama and colleagues[9] reported the sevoflurane concentration required to attain a BIS index value of 50 was lower in patients receiving sevoflurane plus nitrous oxide compared with sevoflurane alone. Conversely, increased BIS index values with the combination of nitrous oxide and isoflurane have been reported.[14] Finally, investigators found that nitrous oxide alone,[15] or nitrous oxide added to isoflurane,[16] or propofol[17] did not change BIS index values. We found that the addition of sevoflurane to 50% nitrous oxide in concentrations sufficient to achieve similar MAC equivalent to sevoflurane alone did not significantly change either the SNAP or BIS values. A limitation to this study was that it was underpowered to detect a small difference between indices with and without nitrous oxide. Although both SNAP and BIS index values were slightly higher with the sevoflurane/nitrous oxide combination, these values were still significantly lower than the awake values for both devices.

There was no difference in the awake baseline values of the SNAP and BIS indices. In contrast we observed a bias of 21 between BIS and SNAP values during sevoflurane anaesthesia at 1.0 and 1.5 MAC equivalents. This offset was similar to the difference that we previously observed (C.A. Wong, personal communication) and similar to the bias of 14 (95% CI: 13–41) observed by other investigators during sevoflurane/nitrous oxide anaesthesia. The authors of another study using propofol/reminfentanil anaesthesia did not specifically calculate bias; however, a review of their data suggests a bias of approximately 20. It is apparent that the two indices cannot be interchanged during maintenance of anaesthesia.

The SNAP index 1 min before awakening had returned to or exceeded the baseline awake value in 64% of the subjects, and in 90% of the subjects at awakening. The corresponding percentages for the BIS were 8% at both times. Therefore the SNAP II™ may have an advantage compared with the BIS in predicting imminent awakening when compared with the awake baseline values. The faster return to baseline found with the SNAP device may be a result of the inclusion of a high-frequency EEG component in the calculation of the index, as frequencies as high as 128 Hz have shown a high prediction probability for separation of 'awareness' and 'unresponsiveness'.[2,18] The observation of a higher baseline BIS value compared with recovery of consciousness value has been made by others.[5,6,19] The delayed return to baseline of the BIS index during emergence may reflect a lag in index calculation, poor correlation of the monitored frequencies with the transition to awareness, or a greater sensitivity to low concentrations of sevoflurane. Index discordance between loss and gain of consciousness has been found for other brain monitoring modalities.[20]

We did not determine the indices at loss of consciousness in this study. In a previous study we showed that the SNAP™ (version 1.1) monitor reliably predicted loss of consciousness, with a ED_{95} index value of 71 (95% CI: 63–74) after a bolus dose of propofol.[4] In this study, all subjects awakened with SNAP index values $\geqslant 84$. Additional limitations to this study may include the disabling of the BIS monitor continuous impedance checking function to prevent interference with the acquisition of the SNAP signal. This may have affected the optimal performance of the monitor. Baseline index values were obtained after midazolam was administered for placement of the interscalene block. This may have reduced the measured index value compared with an unsedated baseline.

In conclusion, processed EEG monitors for detecting unconsciousness and return to responsiveness have been recommended for preventing intraoperative awareness during general anaesthesia, especially in patients at high risk for operative recall. Our data suggest that the SNAP II™ index, which is derived from analysis of low (0–18 Hz) and high frequency (>80 Hz) EEG signals, may be a more sensitive indicator of return to responsiveness than the BIS XP™ index after sevoflurane anaesthesia when awake baseline index values are used to predict the awake state. Further studies involving high frequency EEG signal processing for detection of the transition between consciousness and unconsciousness, both intentional and unintentional, are warranted.

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