A comparison of the ability of the EEGo and BIS monitors to assess emergence following neurosurgery

Comparaison de la capacité des moniteurs EEGo et BIS pour évaluer le réveil après une neurochirurgie

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Abstract

Purpose Deep anesthesia during microvascular decompression (MVD) for trigeminal neuralgia and cerebral aneurysm clipping may delay emergence. A new electroencephalographic (EEG) monitor, the EEGo, processes a raw EEG signal using time-delay analysis to display a reproducible signal transition from deep anesthesia through the excitement state to the awake state. We hypothesized that the EEGo monitor would be superior to the bispectral (BIS) monitor, not only in aiding emergence but also in detecting sudden changes in levels of hypnosis. **Methods** Twenty-one patients undergoing neurosurgery were studied (16 MVD, 5 cerebral aneurysm clipping). Each patient had both EEGo and BIS monitoring with only one monitor available for viewing by the anesthesiologist. The anesthetic was titrated based on the available monitor, and the time to emergence was measured. Intraoperative detection of arousal and the timing of burst suppression during propofol administration were also examined.

Results In the MVD patients, there was no statistical difference in wake-up times between the EEGo and BIS groups. Additionally, there were no episodes of intraoperative awareness and no differences in patient satisfaction. Compared to EEGo waveform output, a decrease in BIS output was delayed in four patients receiving propofol for burst suppression during cerebral aneurysm clipping, indicating enhanced hypnosis. One case of intraoperative arousal, which occurred at a BIS reading of 43 arbitrary BIS units, was detected earlier with the EEGo.

Conclusions While the EEGo was faster than the BIS at indicating planned changes in levels of hypnosis throughout propofol administration prior to temporary clipping during aneurysm surgery, the EEGo was not superior to the BIS monitor in facilitating a more rapid emergence following neurosurgery.

Résumé

Objectif L'anesthésie profonde durant une décompression microvasculaire (DMV) dans le cadre d'une névralgie du nerf trijumeau et de claspement d'un anévrisme cérébral peut retarder le réveil. Un nouveau moniteur électroencéphalographique, l'EEGo, traite un signal EEG brut à l'aide d'une analyse temporisée pour afficher une transition de signal reproductible de l'anesthésie profonde via l'état d'excitation jusqu'à l'état de veille. Nous avons émis l'hypothèse que le moniteur EEGo serait plus précis que le moniteur bispectral (BIS), non-seulement pour aider au réveil mais aussi pour dépister des changements soudains du niveau d'hypnose.

Méthode Vingt-et-un patients subissant une neurochirurgie ont été analysés (16 DMV, 5 claspements d'anévrisme cérébral). Chaque patient a bénéficié d'un

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monitorage avec EEGo et BIS, mais un seul moniteur était à la disposition de l'anesthésiologiste pour visualisation. L'agent anesthésique a été titré en se basant sur le moniteur disponible, et le temps jusqu'au réveil a été mesuré. Le dépistage d'éveil peropératoire et le délai de tracé plat (« burst suppression ») pendant l'administration de propofol ont également été évalués.

Résultats *Chez les patients DMV, le temps de réveil n'était pas significativement différent entre les groupes EEGo et BIS. De plus, aucun épisode de conscience peropératoire ni aucune différence dans la satisfaction des patients n'ont été observés. Comparativement au tracé de l'EEGo, une diminution du tracé BIS a été retardée chez quatre patients recevant du propofol pour un tracé plat pendant un clampage d'anévrisme cérébral, indiquant une hypnose améliorée. Un cas de réveil peropératoire, survenu à un résultat BIS de 43 unités BIS arbitraires, a été dépisté plus tôt grâce à l'EEGo.*

Conclusion *Bien que l'EEGo ait indiqué plus rapidement les changements planifiés des niveaux de l'hypnose durant l'administration de propofol avant le clampage temporaire pendant les chirurgies de l'anévrisme, l'EEGo n'était pas supérieur au moniteur BIS pour favoriser un réveil plus rapide après une neurochirurgie.*

An important goal of neuroanesthesia is a prompt, controlled emergence following a neurosurgical procedure. There are neurosurgical cases where emergence may be delayed, especially after periods of deep anesthesia, for example, (1) cerebral protection induced by propofol or barbiturate administration to an isoelectric electroencephalogram (EEG) during temporary clipping of feeding vessels of cerebral aneurysms and (2) microvascular decompression (MVD) for trigeminal neuralgia. Deep anesthesia is standard for the latter procedure where motor-evoked potentials are assessed to prevent cranial nerve injury.

The bispectral index (BIS) monitor can aid emergence in outpatient procedures with respect to both time-to-wakening and length-of-stay in the recovery room.¹ However, the manner in which the BIS directs emergence is not highlighted, and a specific BIS number to indicate emergence is not suggested. A correlation between patient arousal and eye opening appeared poor during emergence, with the BIS output usually lower than pre-induction values.² On occasion, the BIS reading may be artifactually low during emergence. In these circumstances, it has been suggested that the raw EEG be observed to aid emergence.³ In addition, the BIS may correlate poorly with end-tidal desflurane ($E_T\text{Des}$) and the awake state.⁴ Thus, while the BIS can aid management of the depth of anesthesia during maintenance, it may not be ideally suited to direct a facilitated emergence.

Using the EEG to both monitor emergence and aid its progress makes sense. A monitor that could predict emergence with greater precision would be valuable. New EEG monitoring, engineered to potentially provide this information, is now available in the form of the EEGo,⁵ which processes the standard EEG signal through three-dimensional time-delay plots.⁶ With this monitor, a cascade of characteristic waveforms occurs from burst suppression to the awake state (Fig. 1a–c). These identifiable changes resemble phase transitions and occur rapidly from one state to the next.^{7,8} An analogy is the phase transition that occurs when water changes to ice and vice versa. Monitoring these transitions suggests a means to guide depth of hypnosis, which could potentially shorten emergence at end-procedure.

This study was designed to compare the ability of the BIS monitor with that of the EEGo monitor in facilitating prompt emergence from anesthesia, where EEG monitoring is done in specific neurosurgical procedures. We hypothesized that the EEGo would be superior to the BIS monitor, both in assessing depth of hypnosis during these procedures where deep levels of anesthesia are standard and in facilitating a more prompt emergence following these neurosurgical procedures.

Methods

The study was approved by the Biomedical Research Ethics Board at the University of Manitoba and registered at ClinicalTrials.gov with identifier NCT00443807. All adult patients undergoing neurosurgery where intraoperative EEG monitoring is the standard of care at our institution were approached in the Pre-Anesthetic Clinic. Exclusion criteria included patient refusal, a history of asthma requiring routine use of bronchodilators (due to the use of desflurane as the volatile agent), pregnancy, non-elective aneurysm clipping, and the presence of underlying neurological disorders. Patients who agreed to participate provided signed informed consent. Each patient received midazolam 1 milligram for pre-operative anxiolysis prior to placement of a 20-gauge radial artery cannula. All patients had a BIS monitor sensor strip applied, as per manufacturer's directions, to the contralateral hemisphere from the planned surgery. Standard monitors were applied. Patients were pre-oxygenated and anesthesia induced with remifentanyl $1 \mu\text{g} \cdot \text{kg}^{-1} \text{ iv}$, propofol $1.5\text{--}2.5 \text{ mg} \cdot \text{kg}^{-1} \text{ iv}$, lidocaine $1.5 \text{ mg} \cdot \text{kg}^{-1} \text{ iv}$, and rocuronium $0.6 \text{ mg} \cdot \text{kg}^{-1} \text{ iv}$. A 7- or 8-mm ID endotracheal tube was inserted by direct laryngoscopy. Post-induction, routine intraoperative monitoring (IOM) was established by the neurophysiologist. Needle electrodes were placed frontally and occipitally with a reference electrode over theinion using the international 10–20 system for bipolar recording of the

Fig. 1 Three characteristic images depicting depth of sedation with the electroencephalogram (EEGo) monitor. These are time-delay plots called attractors. Each figure shows the attractor in two views with the raw EEG signal at the bottom. **a** *Periodic attractor*: demonstrates an adequate depth of hypnosis. **b** *Toroidal attractor*: this doughnut-shaped attractor is the characteristic pre-emergent form seen prior to awakening. **c** *Chaotic attractor*: seen with an awake patient. The vertical bars (each in triplicate) individually highlight the time-delay

(8–10 samples at $1200 \text{ samples} \cdot \text{s}^{-1}$). The distance between the vertical bars indicates the composite graphical display of the two images displayed above the raw EEG signal. In this situation a small dot is seen in the centre of the rotating box irrespective of orientation with isoelectricity. A video link from the original paper describing the EEGo can be accessed at: http://download.lww.com/wolterskluwer_vitalstream_com/pt/anes/v105n5p927.mov

raw EEG. Appropriate impedance characteristics were obtained, and acceptable signals were confirmed with the neurophysiologist. The analog EEG signal was processed by a Neurotrac EEG Analyzer, and the output signal was digitized by a DAQ Module USB1420 and cabled to a free-standing laptop computer with EEGo software.

Both the BIS Vista® and the EEGo signals were continuously measured for each patient. To aid management, the clinician was given access to only one of the monitors, as randomly allocated by a third party with a coin toss to either EEGo (heads) or BIS (tails). Continuous data acquisition of blood pressure, heart rate, end-tidal CO_2 , BIS, and $\text{E}_\text{T}\text{Des}$ displayed on a Philips Intellivue MP70™ monitor were secured by a second computer running Trendface Solo™ software.

Anesthesia was maintained with desflurane between 0.5 and 1.5 MAC (to maintain mean arterial pressure in the range of 70–100 mmHg—usual dose 1.0 MAC), remifentanyl $0.05\text{--}0.1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, and propofol up to $50 \mu\text{g}^{-1} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (during the period of dissection of

vessels about the brainstem with MVD surgery). Incremental doses of propofol (usually 50–100 mg) were administered just prior to temporary clipping of feeding vessels during cerebral aneurysm surgery. Mean arterial pressure was supported at 90–100 mmHg with phenylephrine infusion ($0.1\text{--}0.5 \mu\text{g}^{-1} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) during the period of temporary clipping. Recording of the EEGo and BIS signals were continuously obtained during this period of deep hypnosis. Dexamethasone 6 mg *iv* and granisetron 1 mg *iv* were administered within 1 hr of emergence for anti-emetic prophylaxis. Morphine $0.1 \text{ mg} \cdot \text{kg}^{-1} \text{ iv}$ was provided during scalp closure for post-operative analgesia.

With scalp closure, the depth of anesthesia was lightened to facilitate emergence. In the BIS group, the patient was lightened to 60 ABU. In the EEGo group, the patient was lightened to near-toroidal attractor (Fig. 1b). Ventilation parameters were adjusted to an end-tidal CO_2 of 40–45 mmHg.

Desflurane was discontinued immediately prior to removal of the Mayfield clamp, while a remifentanyl

infusion of $0.03 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ continued until the clamp was removed. Fresh gas flows were then increased to $8 \text{ L} \cdot \text{min}^{-1}$ to encourage wash-out of desflurane. Once the patient made respiratory efforts, the ventilation was changed from pressure control to pressure support. The time was noted from when the desflurane was discontinued to when the patient was able to follow commands. The patient was deemed awake once her/his eyes opened to command. Following tracheal extubation, the patient was asked person, place, and date at 15-sec intervals until best answer. The duration of time until the patient became oriented was recorded.

An assessment of quality of emergence, smooth (1), single cough (2), multiple coughs (3), along with an overall impression on a scale of 1–10, was offered by the neurosurgeon. The neurosurgery resident determined a Glasgow Coma Score (GCS) when the patient was admitted to the postanesthesia care unit (PACU). Time until discharge was determined. Twenty-four hours following surgery, a survey of patient satisfaction⁹ and a query regarding awareness¹⁰ were completed by an anesthesiologist blinded to the mode of EEG monitoring.

Statistical analysis

With on-line EEG processing to aid emergence at end-anesthesia, we hypothesized that the EEGo could decrease emergence from 10 to 5 min from last stitch to awake. With an α -value of 0.05, a $1 - \beta$ of 0.80, a standard deviation of 5 and 2.5 min, respectively, and an allocation ratio of 1, we required ten patients per EEG monitoring strategy to have sufficient power to demonstrate this difference with a two-sided statistical test. Between-group comparisons of continuous data were made using Student's unpaired *t*-test, $P \leq 0.05$ considered significant. Using Student's paired *t*-test, $P \leq 0.05$ considered significant, within-group comparisons of the time course of deepening hypnosis were observed following propofol administration, as correlated from the raw EEG isoelectricity to both processed EEG monitors prior to temporary clipping of feeding vessels. Comparisons of ordinal data were made using the Mann–Whitney *U*-test, $P \leq 0.05$ considered

significant. Interval differences are reported with confidence intervals (CI) of $\pm 95\%$.

Results

Of 23 patients who were screened, one did not meet eligibility requirements as he was receiving multiple antipsychotic medications. One patient refused to participate. All 21 recruited patients completed the protocol, for which data collection took place between October 10, 2007 and April 1, 2008. Five patients underwent cerebral aneurysm clipping, while 16 had MVD for trigeminal neuralgia. The two surgical groups behaved very differently on emergence. For this reason, the aneurysm patients were not compared with the MVD patients to assess emergence criteria. Demographics and emergence time data for the five cerebral aneurysm patients are shown in Table 1. There was no difference in demographic characteristics between groups for the 16 MVD patients (Table 2).

EEGo and BIS monitoring of burst suppression during cerebral aneurysm surgery

Four of the five patients undergoing elective aneurysm clipping had complete recordings with both EEG monitoring modalities during burst suppression with propofol administration prior to placing temporary vessel clips. The time delay to onset of isoelectricity, as identified by the raw EEG between the two processed EEG monitors, is shown in Table 3. A representative time course comparing the two EEG monitors for the period of burst suppression is shown in Fig. 2.

EEGo and BIS monitoring of patients undergoing MVD surgery

Depicted in Fig. 3 is the anesthetic course of one patient who demonstrated arousal during MVD surgery. There were no differences between the BIS and EEGo groups in terms of the time to wake-up, time until orientation, total time to orientation, and time spent in the PACU (Table 4).

Table 1 Demographic data and emergence times for patients undergoing cerebral aneurysm clipping

Patient	Group	Demographics					Times (hr:min)		
		ASA	Age	Sex	Ht	Wt	Wakeup	Oriented	PACU
3	EEGo	2	69	M	177	87	00:11	00:15	04:46
8	BIS	3	75	F	157	49	00:31	01:25	08:00
10	EEGo	2	50	F	162	82	00:11	00:13	02:40
18	EEGo	2	63	F	165	87	00:06	>6 hr	05:30
20	BIS	2	56	F	160	77	00:05	00:41	03:00

ASA American Society of Anesthesiologists; PACU postanesthesia care unit

Table 2 Demographics for patients undergoing MVD surgery

	BIS group (<i>n</i> = 8)	EEGo group (<i>n</i> = 8)	95% CI	<i>P</i> -value
Female sex (<i>n</i>)	6	6		
Age (yr)	49.9 (19.1)	59.6 (11.0)	(−26.4, 7.0)	0.23
Height (cm)	166.5 (12.3)	161.4 (7.0)	(−5.6, 15.8)	0.33
Weight (kg)	68.4 (18.9)	72.8 (14.7)	(−22.6, 13.8)	0.61
ASA physical status				
I, II	6	6		
III, IV	2	2		
Mean (SD)				
Data analyzed by unpaired <i>t</i> -test				
No significant differences (<i>P</i> < 0.05) between the two groups were found				

ASA American Society of Anesthesiologists; *BIS* bispectral index; *EEGo* electroencephalographic(o)

Table 3 Assessment of burst suppression comparing BIS to EEGo monitors

Patient	Propofol dose	Time (min:sec)			95% CI	<i>P</i> -value
		EEGo	BIS	Difference BIS − EEGo		
3	100 mg	5:50	7:07	1:17		
8	50 mg	4:14	5:57	1:43		
10	50 mg	1:30	4:02	2:32		
18	100 mg	0:48	1:21	0:33		
Mean		3:06	4:36	1:31	(0:12, 2:50)	0.035
SD		2:20	2:30	0:48		
EEGo data = Time to burst suppression						
BIS = Time to ABU <30						
Data analyzed by paired <i>t</i> -test						

For abbreviations, please refer to the legend of Table 2

For patients undergoing MVD, there was no difference in the initial GCS (median value 15, in both groups) in the PACU, the surgeon's overall impression of emergence (median value 2, in both groups), or emergence quality (median value 8/10, in both groups). There was no difference in the total number of patients requiring narcotics in the recovery room. There was no difference between the two groups in terms of overall patient drowsiness, pain, nausea, cognition, satisfaction with emergence, satisfaction with pain management, nausea/vomiting, and assessment of anesthesia care at 24 hr post-surgery. Additionally, none of the patients reported evidence of intraoperative awareness at 24 hr post-surgery.

Discussion

This study comparing the EEGo monitor to the BIS monitor in assessing emergence following neurosurgery is the first formal comparison of the EEGo monitor to an existing monitor. Based on a 50% decrease in emergence time with the EEGo monitor, we initially hypothesized that we would require 20 patients to show a statistically significant

difference between the two groups. Our study was underpowered to show a difference between processed EEG monitors due to a smaller than anticipated difference in emergence time between groups. The 95% CI of −3.7 to 5.3 min indicating the difference between mean wake-up times closely approximated the presumed clinically important difference of 5 min that we set *a priori*. We excluded the five patients undergoing cerebral aneurysm clipping from our formal comparisons of emergence times. After performing a number of these cases, we discovered that the two surgery groups were not comparable. Compared to those patients undergoing MVD, the aneurysm patients tended to take longer to wake-up and become oriented. At the time this study was designed, there were a larger number of elective cerebral aneurysm surgeries being performed in our institution. Increasingly, more and more of these patients are having their aneurysms coiled in the radiology suite rather than clipped via surgical intervention. This has resulted in a higher proportion of surgical interventions involving more technically complicated aneurysms. These cases may have longer temporary clamp times, longer overall procedure times, and higher total doses of anesthesia. This may have been a contributing

Fig. 2 A time chart representing the period of cerebral protection for a patient undergoing elective cerebral aneurysm clipping with burst suppression following propofol administration prior to temporary clipping of the feeding vessel. Bispectral index (BIS) Vista® monitor data taken from downloaded information from a BIS-ready Philips MP70 monitor to Trendface Solo™ software, representing second by

second BIS readings in arbitrary BIS units (ABU). Electroencephalogram (EEGo) data can be interpreted based on right-sided y-axis as follows: 3 (Periodic attractor) patient is deeply sedated; 4 (Point attractor) periods of isoelectric EEG with burst suppression (see Fig. 1 for further description). The raw EEG horizontal line represents the length of time that burst suppression was noted by this modality

Fig. 3 Time course of an arousal state in a 66-year old female admitted for increasing trigeminal neuralgia (distribution in all three divisions of cranial nerve V). She was receiving carbamazepine. The patient also had a history of hypertension managed with hydrochlorothiazide. At approximately 1 hr and 45 min after induction of anesthesia, the neurosurgeon commented that the patient coughed with incision of the dura. The bispectral index (BIS) output was 43 arbitrary BIS units (ABU). A series of coughs followed, causing bulging of the cerebellum through the dural opening. The patient was immediately deepened by increasing the desflurane concentration, by administering

100 mg of propofol and, subsequently, by administering a further 100 mg of propofol. Hemodynamics (mean arterial pressure; MAP in mmHg), end-tidal desflurane (E_T Des; % vapour output), BIS Vista® output in ABU, and anesthetic stage based on EEGo output are shown. Note that the EEGo shows evidence of arousal sooner (change from Stage 3 to Stage 2 depth of sedation) than with the BIS monitor. The patient coughed at 13:19 (noted by the asterisk) with incision of the dura. Following propofol administration to deepen the level of sedation, the EEGo indicated an isoelectric EEG (Stage 2 to Stage 4 depth of sedation) earlier than seen with the BIS Vista®

factor to the noticeable differences between the MVD and the cerebral aneurysm patients in terms of emergence times, time to orientation, and time in the PACU.

The following assertion about the BIS monitor is on the Aspect Medical Corporation website, <http://www.aspectmedical.com/assets/Documents/MonitoringConsciousness>

[Using the Bispectral Index During Anesthesia-Pocket Guide.pdf](#):

“A BIS value, while extremely responsive, is not instantaneously altered by changes in clinical status. When abrupt changes occur in hypnotic state—for example, during induction or rapid emergence—the BIS value may lag behind the observed clinical change by approximately 5

Table 4 Emergence times, PACU times for MVD groups

	BIS group	EEGo group	95% CI	<i>P</i> -value
Time to wake-up (min:sec)	9:03 (5:00)	8:14 (3:07)	(−3:39, 5:17)	0.70
Time oriented (min:sec)	3:23 (3:45)	3:17 (2:57)	(−3:31, 3:43)	0.95
Total Time to orientation (min:sec)	12:26 (7:18)	11:31 (3:02)	(−5:05, 6:55)	0.75
Time in PACU (hr:min)	2:29 (1:06)	2:16 (0:27)	(−0:40, 1:08)	0.59
Mean (SD)				
Data analyzed by unpaired <i>t</i> -test				
No significant differences ($P < 0.05$) between the two groups were found				

MVD microvascular decompression. For other abbreviations, please refer to the legend of Table 2

to 10 seconds.” While administering propofol to induce an isoelectric EEG with temporary clipping of feeding vessels during aneurysm surgery, our study suggests that the abrupt changes observed in the hypnotic state were displayed more slow, in the BIS monitor, by an average of nearly one order of magnitude. Despite continued burst suppression by raw EEG output, evidence of BIS output above 30 ABU was seen in all examples during the periods of temporary arterial occlusion. Kreuer *et al.*⁴ have demonstrated the inability of the BIS monitor to accurately trend deep levels of desflurane anesthesia.

The EEGo monitor has a processing delay of 50 msec prior to display of the time-delayed raw EEG signal.⁵ The twice delayed raw EEG signal allows characteristic plots of the signal to be displayed in a continuously rotating 3D box. In the four patients studied who had propofol administered for burst suppression, the EEGo indicated changing depth of sedation by a mean difference of 91 sec more quickly than seen with the BIS Vista® monitor (from 12 to 170 sec for the 95% CI; $P = 0.035$). When compared to the BIS monitor, the EEGo was more prompt in one incidence at indicating an episode of intraoperative arousal (Fig. 3).

The principal finding of this study indicated no difference between the EEGo and the BIS monitors in facilitating wake-up time, time until orientation, or time spent in the PACU. Additionally, there was no difference in patient satisfaction between the two groups. These results were contradictory to our initial hypothesis. We speculate that there may have been reluctance by the attending anesthesiologist to titrate the anesthetic to the light levels described in the protocol while the patient’s head was still in the Mayfield clamp. Additionally, the transition from periodic attractor (demonstrating an adequate depth of anesthesia; Fig. 1a) to toroidal attractor (demonstrating pre-emergence; Fig. 1b) to chaotic attractor (awake state; Fig. 1c) was very rapid. If vigilance in monitoring the EEGo monitor was not maintained, these rapid changes could have been missed. Rapidly eliminated agents, such as desflurane and remifentanyl, potentially

make differences in emergence times more difficult to demonstrate than would be the case with longer acting anesthetic agents.

The EEGo has limitations as currently configured. Assessing depth of sedation requires moment-by-moment attention to the graphical output to detect the attendant changes (Fig. 1a–c). Off-line data processing can demonstrate a change in fractal dimension, but is not currently available in real-time. Such a capability would permit trending similar to that seen with the BIS display. Another limitation is that a commercial EEGo monitor is not currently available. We are using beta software provided by the developers of the EEGo. Also, a learning curve to identify the characteristic rotational plots is required. A further limitation is that a sensor strip, as with the BIS, is not available at present (needle electrodes provide the best tracings). Despite the inability to demonstrate a difference in emergence times between the two EEG monitors in this study, the EEGo merits further study as a depth of hypnosis monitor. The EEGo may have merit to identify rapid changes in depth of hypnosis. Potential limitations of both processed EEG monitors are discussed. Some combination of the two processed EEG technologies may be potentially beneficial to aid intraoperative anesthetic management.

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Conflicts of interest Dr. Mutch has received software from the developers of the EEGo monitor. He has no financial interest in either processed EEG monitor in this paper. No other author has any financial relationship with the manufacturer of either monitor.

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