Best Practice & Research Clinical Anaesthesiology
Vol. 20, No. 1, pp. 121–128, 2006
doi:10.1016/j.bpa.2005.07.008
available online at http://www.sciencedirect.com

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Patient state index

David Drover* MD

Assistant Professor of Anaesthesia

Department of Anesthesia, H3580, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305-5640, USA

H.R. (Rick) Ortega[1] BA

Manager

Technology and Clinical Development Physiometrix Inc., Five Billerica Park, 101 Billerica Ave., N. Billerica, MA 01862, USA

The patient state index (PSI) is a clinically validated measure of the effect of anaesthesia and sedation. The PSI is calculated via a proprietary algorithm by a high-resolution 4-channel electroencephalograph (EEG) monitor after advanced artifact rejection. The PSI has been designed specifically for intra-operative and intensive care use to monitor patient sedation and drug effect. The algorithm relies on EEG power, frequency and phase information from anterior–posterior relationships of the brain as well as coherence between bilateral brain regions. The EEG monitor, initially called the PSA4000®, is also the SEDLine® monitor, the newest generation of the device. The SEDLine® system provides the clinician the option of storing and downloading patient data for future use as well as monitoring bilateral brain function and symmetry with a density spectral array (DSA) display.

Key words: Patient state index; PSI; EEG; electroencephalography.

INTRODUCTION

The patient state index (PSI) (Physiometrix Inc., North Billerica, MA, USA) is a processed parameter of a 4-channel electroencephalograph (EEG). The EEG effect of various medications including those used for anaesthesia has been well documented. Predictable changes in brain electrical activity displayed by the raw EEG has been shown for loss of consciousness from anaesthesia medications as well as for the onset of any sleep states.

* Corresponding author. Tel.: +1–650–725–0364; fax: +1–650–725–8544.
E-mail addresses: ddrover@stanford.edu (D. Drover), rortega@physiometrix.com (H.R. Ortega).
[1] Tel.: +1 800 474 9746x298; fax: +1 978 670 2817.

Historically, the indicators of depth of anaesthesia have encompassed both autonomic and somatic responses. Autonomic signs commonly used by the clinician to guide anaesthetic dosing include heart rate and blood pressure changes, diaphoresis and lacrimation. Somatic signs are movement, whether purposeful or reflex in nature. It has been shown that many of the autonomic and somatic events are poor indicators of anaesthetic depth. The unreliability of these items commonly comes from their blockage by many medications used by the patient pre-operatively or by the anaesthesiologist intra-operatively. Many anti-hypertensive medications prevent heart rate and blood pressure responses to inadequate anaesthesia and many anaesthetic drugs impair diaphoresis and lacrimation. The use of muscle relaxant drugs can totally impair any somatic movement responses of the patient.

The goal of general anaesthesia is to produce amnesia, sedation, analgesia and frequently immobility. The majority of anaesthetic medications (with the exclusion of muscle relaxants) affect the electrical activity of the brain. Considering the inherent limitations of autonomic signs and the influence of most anaesthetic drugs on the EEG, a monitor that measures anaesthetic effect would have clear utility in clinical practice.

THEORY BEHIND PSI DEVELOPMENT

The electrical activity of the brain can be measured with simple surface electrodes placed on the scalp. The EEG activity recorded from any point on the surface relates to the complex EEG signals generated by millions of pyramidal cells of the cerebral cortex. The electrical signal in the simplest form can be broken down into amplitude, frequency and phase of the waveform. The brain's electrical activity, as characterized by the EEG, is precisely regulated by a complex neuroanatomical/neurochemical system. Computer-based quantitative analysis (QEEG) has established that the electroencephalogram's power spectrum has a stable (over the age span), state dependent frequency composition and that this EEG frequency information can be characterized on a regional basis.[1,2]

An alert patient's quantitative descriptors of the power spectrum, as the power in a particular frequency band over a specific region of the scalp, will correspond closely to normative data. An individual's state dependent QEEG is extremely stable and reproducible if there has been no change in the state of the subject. However, the administration of any substance that acts upon the brain will produce a disturbance in the chemical equilibrium of the brain, causing characteristic changes in the QEEG both within and between regions. Certain invariable changes in the QEEG are highly correlated with administration of particular anaesthetic agents.

Loss of consciousness is associated with an increase in beta (12.5–25 Hz) frequencies in the frontal areas of the brain. A similar parallel anteriorization of power occurs in delta, theta, and alpha bands. A loss of consciousness is associated with a global decrease in gamma frequencies (>25 Hz) that is distinct from loss of electromyographic (EMG) activity, which can produce interference in the same gamma frequency band.

Coherence of the EEG signal describes the order and relation between particular areas of the brain, which may thereby establish an association between these brain regions. The anteriorization of power at loss of consciousness is accompanied by a loss of coherence of cerebral hemispheres, more so in the posterior areas of the brain. This lack of coherence is consistent during various stages of anaesthesia. The largest

difference seen during loss of consciousness is a posterior–anterior change but a significant alteration also occurs in hemispheric relationships. Pre-frontal and frontal regions of each hemisphere become more closely coupled, while uncoupling occurs in the anterior and posterior regions on each hemisphere, as well as in homologous regions between the two hemispheres. These same changes noted at loss of consciousness are reversed during return of consciousness.[3] Also, these same reversal changes have been found to be independent of anaesthetic type with respect to volatile agents as well as nitrous/narcotic anaesthesia.[2,4] John and Prichep have proposed a neurobiologic theory of the action of anaesthetics and how anaesthetics suppress awareness.[5] This further supports the theory that a measurable QEEG algorithm should be able to indicate anaesthetic dose effect and the likelihood of amnesia independent of anaesthetic type. Prichep and John[2] employed QEEG variable resolution electromagnetic tomography imaging technology to localize the source of the power in the brain that was involved with loss and return of consciousness during different surgical stages across anaesthetic regimens. These findings support the theory that a complex neuroanatomical system is responsible for the regulation of the frequency composition of EEG signals. It also suggests that common QEEG features correlate with depth of consciousness, and that a monitor based on QEEG would be a valid basis for monitoring levels of sedation.

PATIENT STATE INDEX (PSI) DEVELOPMENT

The patient state index (PSI) uses a proprietary algorithm that incorporates a combination of quantitative EEG parameters that have been described as being sensitive to changes during anaesthesia but insensitive to different anaesthetic regimens. The PSI is the result of a complex computation that combines weighted quantitative EEG parameters reflecting many dimensions of brain electrical activity such as: (1) changes in power in various EEG frequency bands; (2) changes in symmetry and synchronization between critical brain regions; and (3) the inhibition/activation of regions of the frontal cortex. The next generation monitor is SEDLine® (Figure 1) which has increased capabilities including a density spectral array (DSA) display.

If a single EEG electrode is used, the information obtained will produce a global picture of the activity of the brain based on that one point of reference. Alternatively,

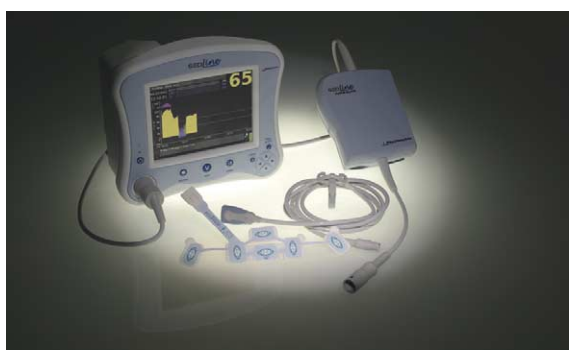

Figure 1. Picture of the SEDLine® EEG instrument that is capable of calculation of PSI, display of DSA, storage and download of patient data.

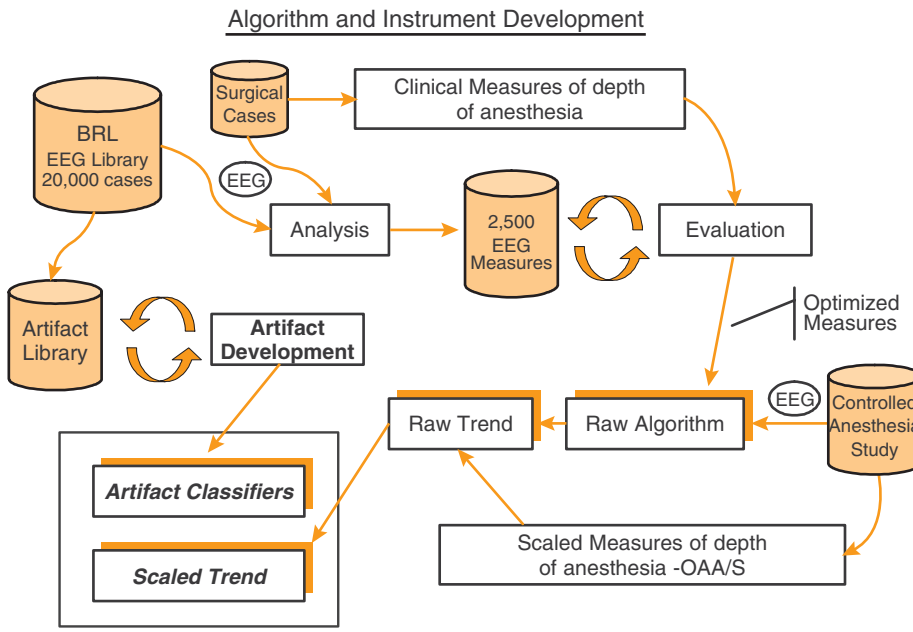

Figure 2. Schematic representation of the development of the PSI algorithm.

the instrument that calculates the PSI uses four distinct electrodes plus an additional reference and ground electrode. Integration of the information from four EEG electrodes has enabled the PSI algorithm to incorporate information from various brain regions to simultaneously reflect global and regional brain state changes. Referential and bipolar combinations of these four channels allow enhanced capabilities to detect subtle regional differences that cannot be captured in a single channel system. The final PSI algorithm was developed from quantitative EEG information collected from an existing patient database and clinical cases. The PSI value is calculated using statistical analysis to estimate likelihood that a patient is adequately anaesthetized. The PSI was then clinically validated in prospectively controlled studies.

A schematic representation of the PSI development process is provided in Figure 2.

DEVELOPMENT SCHEMATIC

An electrophysiological database of 20 000 patients developed by the Brain Research Laboratories (BRL) of New York University School of Medicine was initially used to identify potential quantitative EEG measures that were sensitive to brain state changes in normal, psychiatric, neurological and surgical patients. Statistical normative distributions for these QEEG measures were computed from these recordings. The BRL database also provided a library of the characteristics of artifact, non-EEG signals that were used to develop algorithms for automatic identification and real-time exclusion of artifact from subsequent data processing.

A surgical database of continuous EEG recordings from a large surgical population of patients undergoing general anaesthesia with a variety of agents, administered under

standard clinical practice, was acquired to add to the BRL database. In each case, quantitative EEG measures were extracted under defined states and conditions. These QEEG measures (approximately 2500 per session) included spectral and bi-spectral measures of power and coherence and were used to form a new level of consciousness database. The database identified a subset of candidate measures that changed in an invariant way with deepening levels of sedation and loss of consciousness and that reversed with return of consciousness. Candidate measures were used to form mathematical classifier functions estimating the most probable level of consciousness. The candidate classifier functions were evaluated retrospectively for correlates of depth of sedation, as defined by the attending anaesthesiologist. Figure 3 reveals the PSI relationship to surgical stages with different anaesthetic regimens. The data reveal a statistically significant difference ($p < 0.0001$) between mean PSI values at baseline compared to each surgical stage for all anaesthetics, total intravenous anaesthesia and nitrous/narcotic except at the spontaneous somatic events stage.

A volunteer database was collected during 64 procedures in which various anaesthetics were administered incrementally (0.1 MAC steps to loss of consciousness and return of consciousness) to healthy volunteer subjects. QEEG and clinical measures extracted from this database were used to assist in the calibration of the PSI. Figure 4 reveals the relationship of the PSI to the Modified Observer's Assessment of Alertness Scale (OAA/S).

The PSI was then clinically validated in a prospectively controlled study using propofol, alfentanil and nitrous oxide.[6] In this study of 306 patients, the group that had their anaesthesia guided by the PSI received significantly less propofol and emerged from anaesthesia more quickly. These same patients had no increase in unwanted autonomic or somatic responses.

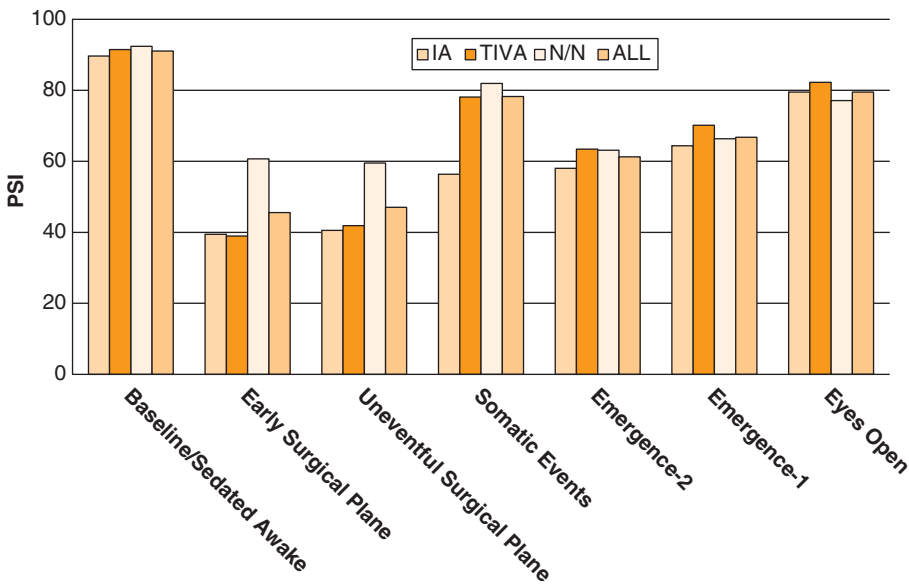

Figure 3. Mean PSI (PSArray2) Across Surgical Stages by Anesthesia Regimen. Retrospective Data Collection Study, N = 176, Physiometrix Data on File, 2002.

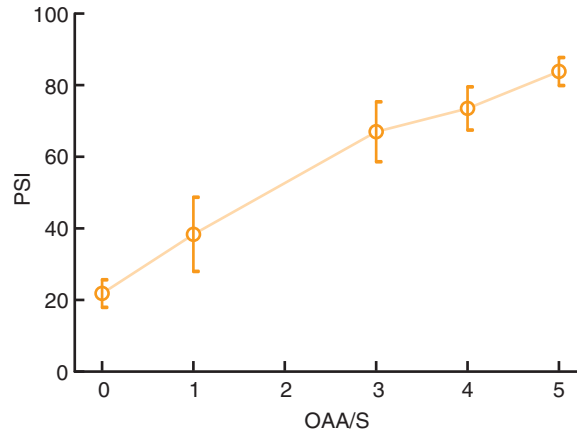

Figure 4. Relationship of the PSI to the Modified Observer's Assessment of Alertness Scale (OAA/S).

A follow-up investigation with a limited sample size has demonstrated similar results that add to the potential utility of the device. Twenty-three patients (ASA I&II, ages 19–41) undergoing outpatient laparoscopic gynecological surgery were administered anaesthesia titrated by routine clinical methods ($N=10$) and PSI alone ($N=13$), targeting PSIs between 38 and 50. Both groups received 0.05 mg/kg midazolam and 30 mg ketorolac as pre-medicants. Patients were induced with 1.75 mg/kg propofol, 0.75 mg/kg esmolol, 5 mg morphine and 0.1 mg/kg vecuronium. Anaesthesia was maintained with propofol infusions and 65%/35% N_2O/O_2. Muscle relaxants were reversed, propofol was discontinued and 5 mg morphine was administered as surgical trocars were removed. All patients were extubated within 5 minutes. Results from this limited study demonstrated a 32% propofol reduction when guiding anaesthetic depth using the PSI, as well as a 25% reduction in time to operating room discharge and a 19% reduction in time for PACU discharge eligibility.[7]

Additional investigations have supported the potential utility of the PSA4000® in assessing patient's level of sedation when used to monitor the anaesthetic sparing capability of dexmedetomidine (71% reduction of Desflurane)[8], monitoring the EEG effects of hypoglycemia during a resection of an insulinoma[9], and its potential use during a cardiac arrest.[10]

Two studies have compared the responsiveness of the PSI and BIS (Aspect Medical Systems, Natick, MA, USA) values during the perioperative period. Chen et al[11], reported comparative PSI (PSArray) and BIS (A2000) values during induction, maintenance and emergence periods. The receiver operator curve (ROC curve) for detection of consciousness indicated a better performance with the PSI (0.95 ± 0.04) than the BIS (0.79 ± 0.04) and the PSI values were less affected by the electrocautery unit during surgery (PSI 16% versus BIS 65%).

A follow-up study conducted by White et al[12], compared the latest versions (PSA Frontal Array and the BIS Xp Sensor) during the perioperative period. As reported in the initial comparison, a similar overall performance during induction, maintenance and emergence periods were found. In this report, the ROC curve between the two monitors revealed a similar performance (PSI 0.98 ± 0.05, BIS 0.97 ± 0.05) while the differences to electrocautery interference were slightly different than the previous report, with the PSI still being less susceptible to interference (PSI 31% versus BIS 73%).

Two other important differences were noted; the PSI displayed a better correlation with the end-tidal concentration of desflurane at the time of eye opening (PSI $r=0.57$, BIS $r=0.11$) and at the time of extubation (PSI $r=0.72$, BIS $r=0.33$).

The PSA4000® has also been investigated for its relationship of the PSI to level of sedation in the Intensive Care Unit. Schneider et. al.[13] reported in this study of 41 intubated and ventilated patients a high prediction probability (0.92 ± 0.037) of the relationship between Ramsay Sedation Scores (RSS) and PSI values. Ramsay et al[14] have also reported a strong relationship between PSI and RSS assessments in 30 CVICU patients (correlation coefficient of -0.98).

SUMMARY

The patient state index (PSI) is a clinically validated measure of the effect of anaesthesia and sedation. The PSI has been designed specifically for intra-operative and intensive care use to monitor patient sedation and drug effect. The algorithm relies on 4-channel EEG providing information on power, frequency and phase from anterior–posterior relationships of the brain as well as coherence between bilateral brain regions. The PSA4000® EEG monitor has become the SEDLine® system as the next generation of the PSI monitor. The SEDLine monitor uses advanced artifact rejection techniques to further reduce the sensitivity to sources of electrical interference, in particular, electrocautery. This newest generation of the monitor also stores up to 50 hours of raw and processed data. The addition of a dual, color density spectral array (DSA) provides the clinician with a concise spectral time history of EGG behavior permitting rapid assessment of frontal bilateral brain function.

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