PSI 25-50 Range for Optimal Hypnotic State for General Anesthesia

A Clinical Perspective

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Background

Greater than 25 years experience in research, design and development of Neurophysiology products/devices.

Research

- Sedation monitoring in the OR
- Head and spinal cord injury assessment
- Infant and neonatal neurological assessments through the use of EEG and Evoked Potentials
- EPs for pain assessment in burn victims
- QEEG for monitoring depth of anesthesia in general surgical patients with acupuncture anesthesia

Development

Development and successful launches of more than 10 neurophysiological OR monitoring and diagnostic devices (EEG, EPs, brain mapping, QEEG). Involved in identifying, evaluating and recommending EEG variables for the PSA 4000 algorithm.

- Key developer of the Hydrodot Neuromonitoring system and its accessories for neurodiagnostic labs and use in NASA space program
- Assisted in development of initial brain function monitoring system (Equinox)
- Originator of the idea to develop a level of sedation monitor using EEG: PSA 4000/SEDLine

Clinical

Develops and implements clinical study protocols for Hospira Sedation

Education

B.A. Psychology, graduate work in Physiological/neurophysiology

This Clinical Perspective is underwritten by Hospira. H. Rick Ortega, III's comments were taken from an interview conducted by representatives of Hospira.

The information contained in this article may not be typical of all hospitals.

Accurate monitoring of levels of sedation across today's diverse range of patient populations is piquing the interest of clinical specialists. Assessing and maintaining optimal patient drug titration throughout the surgical phases can be a challenge, in particular with certain patient subtypes (geriatric, bariatric, beta blocked and cardiac patients) as identified by the American Society of Anesthesia (ASA)[1]. Brain function monitoring used as an adjunct offers additional information to traditional armamentaria of physiological parameters to assess and optimize the level of sedation/anesthesia. Maintaining the optimal level of sedation/anesthesia through the use of brain function monitoring has been shown to improve traditional clinical endpoints (decrease recovery and emergence times).[2] Because each brain function monitor is not created equally, it is notable for the clinician to ask and understand how the quantitative level of consciousness ranges for each monitor was derived.

The Patient State Index™ (PSI) is a quantitative EEG index for assessing the level of consciousness during sedation and general anesthesia. The PSI values range from 0 (suppression of EEG) to 100 (fully awake and alert). For the PSA 4000® and SEDLine™ devices, a PSI in the range of 25–50 indicates an optimal hypnotic state for general anesthesia. The following information contains a discussion of the development of this optimal PSI range for the maintenance phase in general surgical procedures as applied to the PSA 4000 and SEDLine devices.

Prior to initiation of the PSA 4000 Monitor Multicenter Prospective Randomized Clinical study,[2] which was used to demonstrate the safety and efficacy of the monitor, there was much consideration regarding assigning the ideal PSI range for monitoring anesthesia maintenance during general surgery. The PSI range of 25 to 50 was selected for the following reasons:

1. Lower value (25): Based on clinician input, burst suppression (PSI range 0 to12) was integrated into the PSI value in addition to displaying it as a separate trend. The technical knowledge of how burst suppression is included in the PSI value led to setting of the lower range value (25) of the PSI scale to ensure that patients did not receive doses of anesthesia required to achieve sustained burst suppression.
2. Upper value (50): Data gathered from precursor studies (retrospective[3,4] and volunteer studies[5,6,7]) allowed for development of receiver operator curves (ROC) and comparisons of PSI to sedation scales. These data were analyzed and a higher range value (50) was selected to reduce the probability that an asleep patient would be classified as awake.

The results of the PSA 4000 Prospective Randomized study that validate the safety and efficacy of guiding anesthetic administration in the range of 25–50 PSI in general surgical patients were reported by Drover et al.[2] The efficacy results demonstrated that maintaining the PSI value in the specified range will lead to a statistically significant decrease in the average verbal command response time and a decrease in average propofol infusion rates. The safety results of this study demonstrated no change in likelihood or severity of safety episodes (somatic, hemodynamic, serious injury or death). It should be noted that none of the subjects in the control or treatment groups of this study reported any incident of recall.

Since the execution of the PSA 4000 Prospective Randomized study, the PSI technology has evolved from an initial algorithm that used a fronto-posterior set of electrodes (PSArray) to an algorithm that uses a pre-frontal, frontal set of electrodes (PSArray^2 and SEDTrace®). The behavior of the PSI derived from the original PSArray® electrode set has been shown to be equivalent to the PSI derived from the new PSArray^2 / SEDTrace electrode set.[8]

The following paragraphs summarize the Drover study and additional studies that validated using a 25-50 PSI range. The studies were conducted to support the equivalence and the clinical utility of the PSArray and PSArray^2 / SEDTrace.

RETROSPECTIVE STUDY — ROC ANALYSES[3,4]

The objective of the retrospective study was to gather electrophysiological data on patients undergoing surgery with a variety of anesthetic agents, administered using conventional anesthetic approaches. To determine the descriptors of processed EEG that could be used with self-norming techniques to monitor anesthetic depth, data were collected from 19 electrode sites as defined by the International

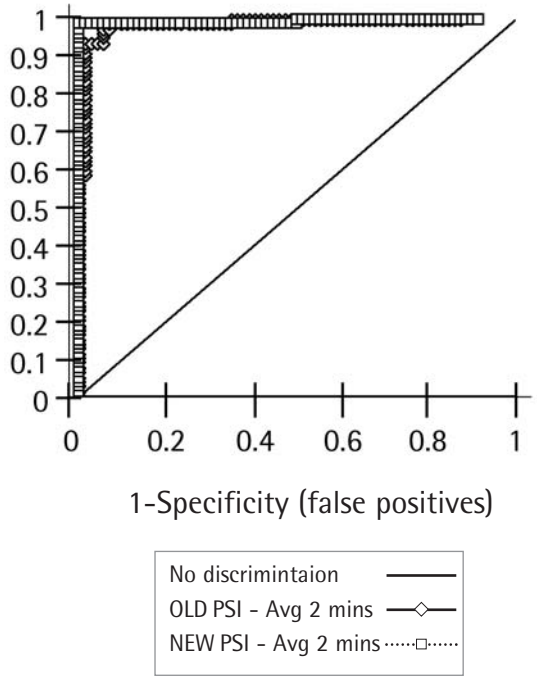
10-20 System for Electrode Placement using Spectrum 32 EEG Acquisition Systems (Cadwell Laboratories, Kennewick, Wash.). The analyzed EEG data from this study were used to develop the algorithm underlying the PSI.

In addition, these data were used to generate ROC curves for comparing the ability of the algorithm to correctly classify patients as "awake" or "asleep." The results of this analysis indicated that the PSArray PSI value was effective at differentiating between the "awake" and "asleep" states. The area under the curve and 95% Confidence Interval for the PSI were calculated to be 0.941 (0.916–0.966). This is clinically significant as it exceeds standard criteria for clinically significant sensitivity and specificity (minimum area under curve of 0.80 taken from Thomas G. Tape, M.D., *Interpreting Diagnostic Tests,* University of Nebraska Medical Center[9]).

Additional ROC analyses have been conducted for the PSI based on retrospective analysis using EEG collected from PSArray^2 / SEDTrace® electrode sites in the retrospective study. This new data set, derived from the SEDTrace electrodes, also yielded clinically significant results, 0.869 (0.829–0.909).

Analysis was also conducted using an additional data set (CP-08-001 Hypnos Data Study).[8] The area under the curve and Confidence Interval for the PSArray PSI and PSArray^2 / SEDTrace PSI were calculated to be 0.995 (0.988–1.000) and 0.987 (0.972–1.000), respectively. Note that the Confidence Interval for the PSArray^2 / SEDTrace PSI is contained within the Confidence Interval for the PSArray PSI. See Figure 1, which compares the two ROC curves for the two electrode sets.

FIGURE 1

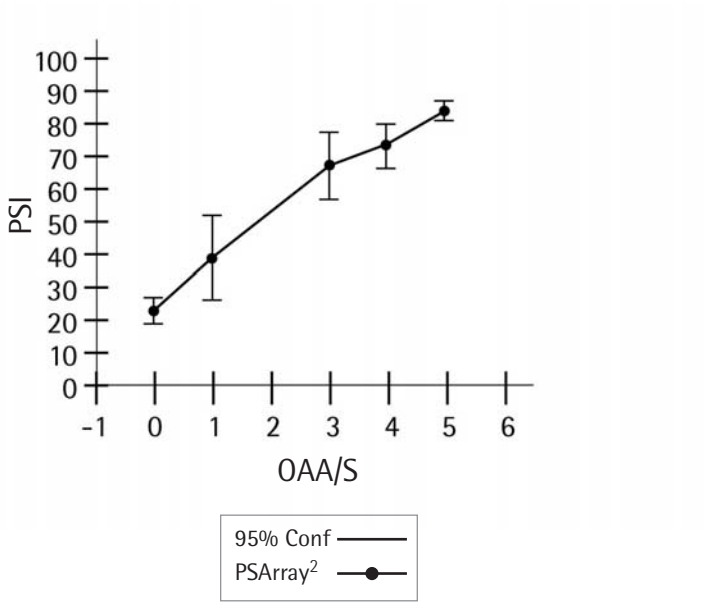


VOLUNTEER STUDY SUMMARY – OAA/S ASSESSMENTS[5,6,7]

A database was generated from 64 procedures on healthy volunteer subjects utilizing various anesthetics (Sevoflurane, propofol, Nitrous/narcotic, Methohexital and Etomidate). These anesthetics were administered incrementally (0.1 MAC/MEC steps to loss of consciousness and return of consciousness) and systematically decreased until return of consciousness was observed. During each step down and step up, a modified Observer's Assessment of Alertness Scale (OAA/S) score was assessed and EEG, EPs and BIS values were recorded. To better simulate surgical stimulation, an OAA/S of 1 was defined as no response to a Train of Four (ToF) stimulation, and an OAA/S of 0 was defined as no response to a 50 Hz titanic stimulation.

Figure 2 reveals the relationship of the PSArray^2 PSI to the OAA/S for the PSI based on EEG collected from PSArray^2 electrode sites. The plot presents the mean PSI and 95% Confidence Interval. It was noted that patients lost consciousness at a PSI value of approximately 60.

FIGURE 2



A repeated measures multivariate analysis of variance (MANOVA) was conducted, testing for the significance of the difference between the PSArray PSI and PSArray^2 / SEDTrace PSI across all arousal levels. The PSArray PSI and PSArray^2 / SEDTrace PSI were not significantly different from each other across the various arousal states ($p = 0.152$). In summary, this analysis supports the equivalence between PSArray PSI and PSArray^2 / SEDTrace PSI.

In addition to collecting PSI and OAA/S data, this study also tested incidence of recall following anesthesia. During step phased reduction in anesthetic agents, subjects were shown a picture at each level and a verbal response was elicited. In post-op recovery, each subject was asked to recall the pictures; none of the subjects had any recall.

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PROSPECTIVE STUDY – PSI COMPARISON[2]

This pivotal study (1998–2000) was a prospective, randomized, blinded evaluation of the PSA 4000® device as an adjunct to standard anesthetic care. The study was designed to assess the efficacy of the PSI algorithm as a pharmacodynamic measure of patient response to propofol.

The 224 patient study (n = 112—Standard Practice Control group / n = 112—PSI group) evaluated the efficacy of the PSA 4000 with PSArray PSI as an adjunct to standard anesthetic care for monitoring the state of the brain in patients receiving intravenous propofol anesthesia during general surgery. Anesthetic was administered according to standard clinical practice (SP group) or as required to maintain the PSI in the range of 25 to 50 (TG group). EEG, PSI, hemodynamics and key surgical events were recorded.

Results of this study demonstrated that maintaining the PSI value in the range of 25 to 50 during the maintenance phase of general anesthesia led to statistically significant decreases in the average verbal command, emergence response and extubation times, as well as decreases in average propofol infusion rates. Clinical endpoints in this study indicated that patients were eligible for discharge from the OR sooner. Additionally, the results demonstrated no change in likelihood or severity of safety episodes (somatic, hemodynamic, serious injury or death).

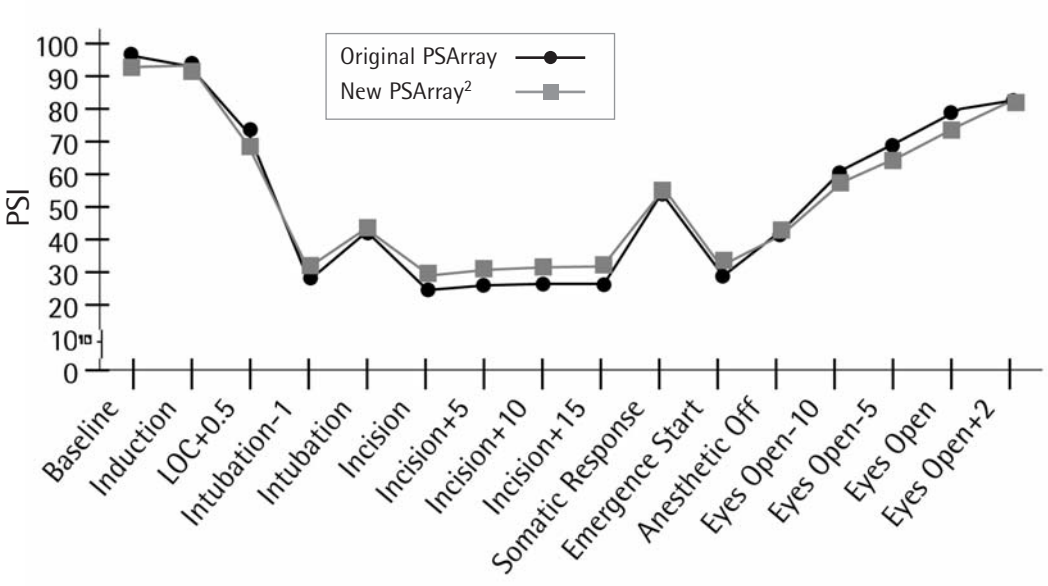
PSARRAY AND PSARRAY[2] DATA COLLECTION STUDY[8]

This study collected EEG data simultaneously from the PSArray and PSArray[2] EEG electrodes sites from 103 adult patients undergoing general anesthesia during routine surgical procedures. The anesthetic regimen was randomly distributed between propofol/nitrous, narcotic/alfentanil and any other regimen. EEG, PSI, vital signs and key surgical events were recorded.

The average PSI values during key surgical stages were calculated for the PSArray and for the PSArray[2] / SEDTrace® and compared. The calculated PSI values for the two array configurations are shown in Figure 3. Note that there are no clinically relevant differences at any of the surgical stages.

The data reviewed in Figure 3 provide the rationale for setting the 25 to 50 PSI range when the monitor is used for general anesthesia. In addition, these data demonstrate the equivalent performance of the PSI algorithms (PSArray and PSArray[2] / SEDTrace), justifying the use of the same 25 to 50 range for the PSA/SEDLine™ system.

FIGURE 3 — PSI AT VARIOUS ANESTHETIC ENDPOINTS



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