## #13\_Validation of the NAS index in TIVA

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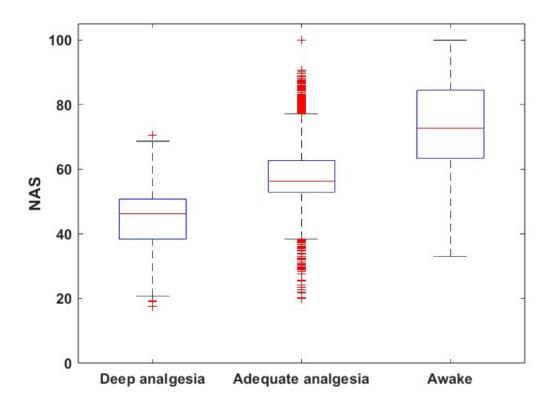
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**Introduction**: The autonomic nervous system (ANS) modulates cardiovascular responses to nociception during anesthesia and analgesia. Heart rate variability (HRV) analysis provides a non-invasive way to track these dynamics. The CoreSafe One (CoreSafe, Barcelona, Spain) is a chestworn device that acquires electrocardiogram (ECG) signals for real-time HRV feature extraction. This study expands on previous work by increasing the dataset and retraining an Adaptive Neuro-Fuzzy Inference System (ANFIS) to develop the Neuro-Autonomic State (NAS) index, an ECG-based indicator of nociception likelihood for continuous intraoperative monitoring.

Methods: After approval from the local ethics committee, data was collected from 29 surgical patients undergoing general anesthesia with propofol and remifentanil; the ECG signals were recorded from a single chest placement throughout surgery. Raw ECG data were preprocessed to remove noise and artifacts, detect R-peaks, and compute HRV metrics. Four normalized HRV features (heart rate (HR), root mean square of successive differences (RMSSD), percentage of successive intervals differing by more than 50 ms (PNN50), and the low-frequency to high-frequency power ratio (LF/HF)) were extracted in two-minute windows, updated every 6 seconds. An ANFIS model was trained using three Gaussian membership functions per input, a linear output function, and 500 training epochs. The target output was an index of analgesia based on EEG signals. In contrast, the ANFIS model was trained exclusively on ECG-derived HRV features from the CoreSafe One and given a scale from 1 to 100.

**Results**: The ANFIS model demonstrated a moderate correlation with the target index from the EEG-based reference device ( $R^2 = 0.5047$ ; smoothed  $R^2 = 0.6205$ ), with an average absolute error of 37.28 and RMSE of 39.10. As shown in Figure 1, NAS values were lowest during deep analgesia, intermediate during adequate analgesia, and highest when patients were awake. This separation between conditions supports the potential of NAS to discriminate autonomic states associated with different levels of nociception.

**Conclusion**: The proposed ANFIS-based NAS index shows potential for estimating nociception using only ECG-derived HRV features, providing a non-invasive and portable alternative to EEG-based monitoring. Although performance is moderate, the improved correlation after smoothing suggests that temporal averaging can enhance reliability.



**Figure 1.** Distribution of NAS values across different surgical states (Deep analgesia, Adequate analgesia, Awake).

## References

- 1. Papaioannou, V. E., et al. "Heart Rate Variability as a Diagnostic Tool in Critical Care." BioMedical Engineering OnLine, vol. 12, 2013, article 95. doi.org/10.1186/1475-925X-12-95.
- 2. Jensen, E. W., Manjarres, M. A., Jospin, M., & Doufas, A. G. (2024, October). Monitoring the effect of fentanyl on the Stress Activity (SA) index during general anaesthesia using EEG and heart rate variability. Presented at the International Society for Anaesthetic Pharmacology Annual Meeting.
- 3. Broucqsault-Dédrie, C., De Jonckheere, J., Jeanne, M., & Nseir, S. Measurement of heart rate variability to assess pain in sedated critically ill patients: A prospective observational study. PLoS ONE, 11(1), 2016. https://doi.org/10.1371/journal.pone.0147720
- 4. Forte, G., Troisi, G., Pazzaglia, M., De Pascalis, V., & Casagrande, M. (2022). Heart rate variability and pain: A systematic review. Brain Sciences, 12(2), 153. https://doi.org/10.3390/brainsci12020153

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