Monitoring the effect of fentanyl on the Stress Activity (SA) index during general anaesthesia using EEG and Heart Rate Variability.

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Introduction: The surface electroencephalogram (EEG) is a non-invasive tool that allows for real-time assessment of brain electrical activity. Brain activity (BA) is derived from the EEG signal, allowing for the observation of the patient's neurological state, while stress activity (SA) is defined by parameters from both the EEG and heart rate variability (HRV), as the combination of these can reveal changes in brain function and the body's autonomic response that may not be evident if monitored in isolation. Variations in these indices may reflect the effects of anesthesia, the impact of the surgical procedure, and recovery in the post-anesthesia care unit (PACU).

Method: This analysis included data from 13 patients who participated in a randomized controlled trial ("Recovery of Ventilation after General Anesthesia for Robotic-Assisted Laparoscopic Nephrectomy or Prostatectomy: The Effect of Oxygen Supplementation"; Institutional Review Board, #63878) at Stanford Health Care, and were scheduled for surgery under general anesthesia. Surface EEG was recorded with the CoreSys One monitor (CoreSys Health, Barcelona, Spain) at five key points during the perioperative process: before anesthesia (awake), at the onset of anesthesia, at the end of the surgery, upon admission to the PACU, and at discharge from the PACU. From these data, two indices were calculated: BA and SA. The BA index assessed general neuronal activity, while the SA index measured the stress response. The values of both indices were recorded and **analyzed at each phase** to identify significant changes. Additionally, the exact time of the first dose of fentanyl administered during the surgery was recorded to evaluate its potential impact on SA.

The first dose of fentanyl administered during the surgery was identified, and the SA index was analyzed in a 5-minute interval before and 5 minutes after administration to **determine significant changes in SA following fentanyl administration**. The Jarque-Bera test was conducted to check if the data followed a normal distribution; if so, a Student's t-test was used, otherwise, the Wilcoxon test was applied **to evaluate significant differences between SA before and after fentanyl administration.** For the SA and BA indices, the Kruskal-Wallis statistical test was employed to identify significant differences **among the 5 perioperative states** and to assess the effects of anesthesia on brain activity and stress. Finally, to analyze the data related to BA, SA, and fentanyl administration, medians were calculated and results were presented in boxplots, determining the interquartile range to evaluate data dispersion.

Results: The results show that the data before and after the administration of fentanyl follow a normal distribution, according to the Jarque-Bera test. Therefore, a Student's t-test for dependent samples was performed, yielding a p-value <0.0001, which indicates a significant difference in SA before and after fentanyl administration. Additionally, the Kruskal-Wallis test revealed significant differences in the BA and SA index ($p < 0.0001$) among the five perioperative states.

Figure 1 shows the median of brain activity (BA) at different stages: while the patient was awake, at the onset of anesthesia, at the end of surgery, upon admission to the PACU, and at discharge from the PACU. During the awake state, BA was 95. At the onset of anesthesia, there was a significant decrease, reaching a minimum of 45, due to the effects of anesthetic agents that reduce neuronal activity. As the surgery progressed, BA increased slightly to 61, which could indicate a gradual decrease in the anesthetic effect or preparation for recovery. Upon admission to the PACU, brain activity recovered considerably to 93, approaching normal levels. Finally, at discharge from the PACU, BA stabilized at 89, indicating that brain function began to normalize as the effects of anesthesia wore off [1].

Figure 2 shows that SA decrease markedly at the onset of anesthesia (58) and reach their lowest point at the end of surgery (42), reflecting the suppression of the stress response by anesthesia. However, upon arrival at PACU, SA returns to maximum levels (99), remaining high at discharge from PACU, which could be due to factors such as postoperative pain, discomfort, or anxiety related to recovery [2]. Figure 3 shows that the median of stress activity (SA) was 98 five minutes before the administration of the first dose of fentanyl (100 mcg) and decreased to 63.5 five minutes after. This reduction indicates that fentanyl, by acting on opioid receptors in the brain and spinal cord, has been effective in relieving pain and providing sedation. Fentanyl not only reduces pain perception but also modulates the body's response to surgical stress, resulting in a decrease in SA and a calmer and more stable patient response during surgery. This pattern highlights the effectiveness of fentanyl in improving the overall patient condition and emphasizes the importance of continued monitoring of stress activity and other parameters to ensure that the surgery is effective and safe [3].

Conclusion: Monitoring of brain activity (BA) shows a significant decrease at the onset of anesthesia, followed by a recovery during the post-anesthesia care unit (PACU) phase. On the other hand, stress activity (SA) decreases significantly after the administration of the first dose of fentanyl. Statistical analyses confirm these observations, with significant differences in p-values (<0.05).

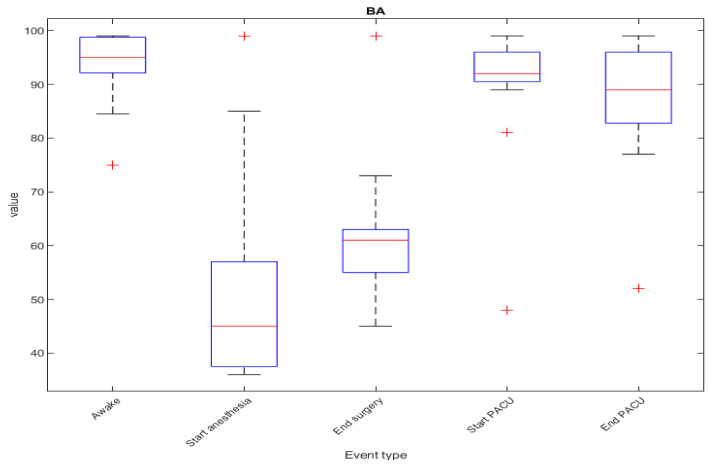

Figure 1. Brain Activity During the Perioperative Period

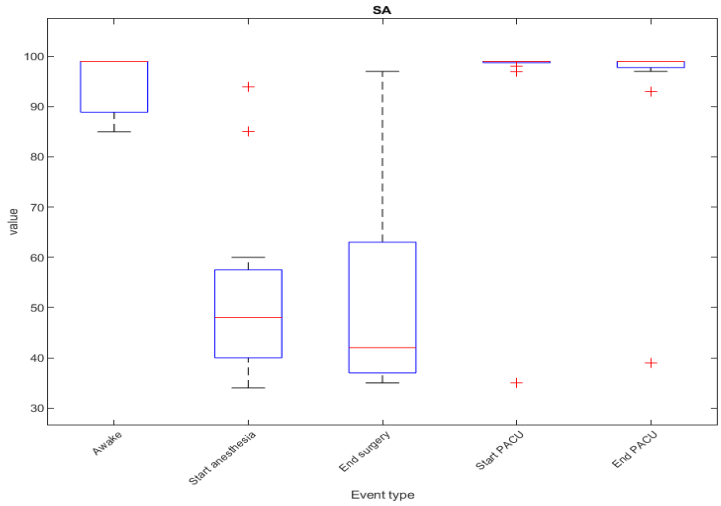

Figure 2. Stress Activity During the Perioperative Period

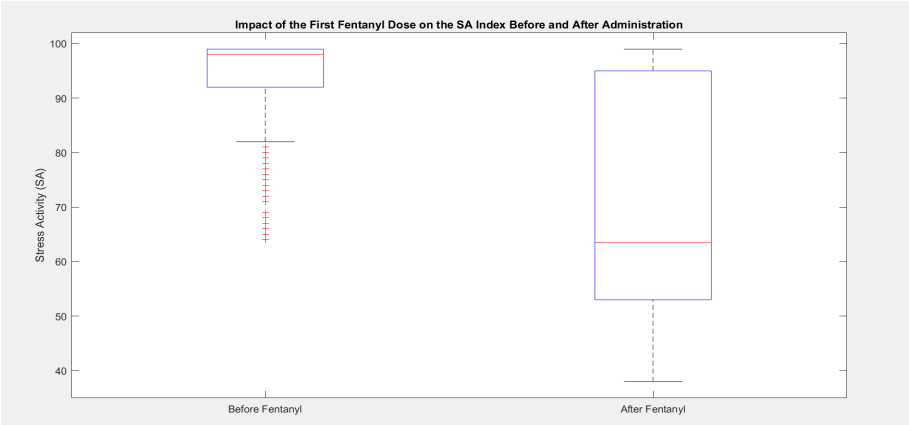

Figure 3. Effect of the First Dose of Fentanyl on Stress Activity During Surgery

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