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Unveiling Neurophysiological Markers of Consciousness Levels through EEG Exploration

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Abstract

The concept of consciousness levels typically refers to various aspects and tiers related to an individual's cognition, perception, thinking, and awareness. Although neurophysiological markers have not yet been definitively identified to distinguish between these nuanced levels, this paper introduces a robust marker, the Approximate Entropy (ApEn), which quantifies the complexity of EEG signals to differentiate states of altered consciousness. Utilizing ApEn, we analyze EEG data from the frontal lobe—a region closely associated with consciousness—in states indicative of severely altered conditions, specifically anesthesia, coma, and brain death. To enhance the precision of consciousness level assessment, we employ a Support Vector Machine (SVM) model, which classifies the states based on EEG complexity measures. This approach not only provides valuable insights into the neural correlations associated with changes in these critical states but also underscores the potential of combining quantitative EEG analysis with machine learning techniques to advance our understanding of consciousness. The findings demonstrate that EEG complexity, when analyzed using ApEn coupled with SVM classification, offers a novel and effective method for assessing and distinguishing between degrees of consciousness. This approach promises significant implications for clinical diagnostics and patient monitoring.

Keywords: EEG, Approximate Entropy, Consciousness Levels

I. Introduction

In the interdisciplinary quest to understand consciousness, scholars from philosophy, neuroscience, and psychology face an enduring challenge: defining the true essence of consciousness. This quest delves into the complex interplay between an individual's subjective awareness and their interactions with the internal and external worlds. Despite significant advancements in science and philosophy, consciousness remains a profound mystery, characterized by more than mere physiological responses to stimuli. It involves a deep, introspective experience, encompassing thoughts, feelings, and perceptions that are notoriously difficult to quantify or fully comprehend.

Recent neuroscientific breakthroughs have shed light on the potential mechanisms underlying consciousness, particularly emphasizing the role of gamma wave oscillations(Singer, 2007). These high-frequency neural oscillations are believed to be key in integrating disparate sensory information from across the brain into a coherent, unified experience. This integration is crucial for the seamless perception of reality, addressing the so-called 'binding problem' that has puzzled scientists for decades. EEG-based consciousness assessment has gained attention, with numerous studies focusing on evaluating consciousness levels using EEG signals (Jennett & Plum, 1972; Laureys et al., 2010; Schiff, 2010).

One of the pivotal insights in recent studies of consciousness is the recognition that subjective experiences, such as dreaming, can occur in states traditionally viewed as unconscious, such as during non-rapid eye movement (NREM) sleep or under anesthesia(Darracq et al., 2018; Mashour & Hudetz, 2018). This observation fundamentally challenges the long-held belief that unresponsiveness is synonymous with unconsciousness(Sanders et al., 2012). The clinical implications of this revelation are profound, especially in the context of anesthesia, where the phenomenon of intraoperative awareness, though rare, presents a significant risk of psychological trauma to patients. This risk, coupled with an incidence rate of approximately 0.2 % for post-traumatic stress disorder (PTSD) following such events(W. Liu et al., 1991; Sebel et al., 2004; van Oud-Alblas et al., 2008), highlights an urgent need for advancements in monitoring technologies capable of more accurately detecting and assessing consciousness levels. The complexity of accurately assessing altered states of consciousness is particularly crucial in diagnosing coma and brain death. These assessments are vital in cases of compromised neurological function. Current methods for determining brain death can be time-consuming and carry inherent risks ("A Definition of Irreversible Coma: Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death", 1968; Cao & Chen, 2008; Cui et al., 2017; Marks & Zisfein, 1990; Scott et al., 2013; Szurhaj et al., 2015). Moreover, the reliance on subjective assessment tools, such as the Glasgow Coma Scale (GCS) (Teasdale & Jennett, 1974), underscores the urgent need for objective and reliable markers that can provide more precise measures of consciousness. Developing such markers could revolutionize approaches to monitoring and managing patients in critical care settings, thereby enhancing outcomes and ethical considerations in patient treatment.

This research aims to advance our understanding of consciousness through the application of the Approximate Entropy (ApEn)(Pincus, 1991; Shi et al., 2010) algorithm in analyzing EEG data from states indicative of altered consciousness, such as under anesthesia, during coma, and at the point of brain death. By identifying distinct EEG patterns that correlate with varying levels of consciousness, the research seeks to uncover novel neurophysiological markers. These markers have the potential not only to enhance our theoretical understanding of consciousness but also to foster the development of advanced diagnostic and monitoring tools, thereby improving patient care in various medical contexts.

II. MATERIALS AND METHODS

a. Data recording

In the exploration of consciousness levels across different states, this study utilized EEG recordings from a cohort of 57 patients, comprising 34 cases of coma and 23 cases of near-brain death. The EEG data for these patients, ranging in age from 17 to 85 years, were collected with the consent of their families. The recordings were obtained during preliminary EEG examinations conducted from June 2004 to March 2006 at a hospital in Shanghai(Cao, 2006). Given the specific nature of the patients' conditions, the EEG examinations employed a method of recording that involved placing high-purity electrodes on the forehead. For these recordings, a portable EEG machine equipped with the NEUROSCAN ESI-64 system was used. Seven electrodes were positioned on the patients' foreheads: six exploratory electrodes (Fp1, Fp2, F3, F4, F7, F8) and one ground electrode (GND), with two additional electrodes (A1, A2) placed at the earlobes to serve as reference electrodes. The EEG recordings were captured at a sampling rate of 1000Hz, with electrode impedances maintained below $8k\Omega$.

The anesthesia data were sourced from an open dataset provided by National Taiwan University Hospital (NTUH)(Q. Liu et al., 2018), Written informed consent was secured from all participants. Patients undergoing routine surgeries under general anesthesia (GA) were recruited, excluding those undergoing high-risk surgeries related to the brain, heart, lungs, etc. Individuals with habits of alcoholism or smoking, or those with diseases that could affect data recording, were excluded. A total of 24 patients , Age (yr): 44.5 ± 12.9, Height (cm): 164.2 ± 7.1, Weight (kg): 63.4 ± 14.8, BMI (kg/m^2): 23.4 ± 4.2, Gender: 14 females / 10 males) qualified for inclusion. According to the anesthesia records, surgeries lasted an average of 126.4 ± 72.9 minutes. Before EEG recording, conductive paste was applied to improve contact between the forehead skin and the EEG BIS™ Quatro Sensor, lowering impedance to below $5k\Omega$. The EEG sensor was connected to the MP60 machine using a standard factory connection cable. Raw continuous EEG waveform data were acquired at a sampling rate of 128 Hz. Recordings commenced 5 minutes prior to induction when the patient was fully awake and concluded upon the patient's response to auditory or physical stimuli.

b. Data Preprocessing

In the data preprocessing section, the approach was meticulously designed to ensure the integrity and reliability of EEG data across various consciousness states. Initially,a 50Hz notch filter was employed for both the coma and brain death data as well as the sleep data to attenuate electrical noise from the power supply. In contrast, the anesthesia data were treated with a 60Hz notch filter, tailored to the specific electrical grid frequency of the recording environment. These filtering steps are essential for reducing noise artifacts from medical devices and patient movements. This distinction in filtering strategies is essential due to the different power line frequencies encountered in the recording environments.

The next phase involved employing advanced signal processing techniques to further clean the EEG data. The use of the cleanline EEGLAB plugin, based on the multi-taper decomposition method from the Chronux toolbox, facilitated the efficient removal of line noise components with minimal impact on the underlying neural signals(Bigdely-Shamlo et al., 2015). This step is crucial for maintaining the fidelity of the neural signals in subsequent analyses.

Considering the significant influence of sampling rate on data analysis(Cohen, 2014), especially for metrics such as ApEn, the study standardized the sampling rate across all datasets to 1000Hz. To achieve this standardization, data initially recorded at lower sampling rates were resampled using the 'resample' function from Python's 'scipy' library. This process involved interpolating the data to enhance the sampling frequency, thereby ensuring uniformity across the recordings and enhancing the resolution of EEG signals for complexity analysis.

c. ApEn Calculation Method

ApEn is a statistical measure used to quantify the regularity and unpredictability in time-series data. It is particularly useful in analyzing the complexity of physiological signals such as EEG. The calculation of ApEn involves selecting two parameters, m and r, where m represents the length of sequences to be compared, and r is the tolerance for determining similarity between these sequences.

Given a time series $\{u(i)\}_{i=1}^{N}$, the ApEn for embedding dimension m and tolerance r is defined as:

$$\mathrm{ApEn}(m, r, N) = \Phi^m(r) - \Phi^{m+1}(r) \tag{1}$$

where

$$\Phi^m(r) = \frac{1}{N - m + 1} \sum_{i=1}^{N-m+1} \ln C_i^m(r) \tag{2}$$

and $C_i^m(r)$ is the fraction of m-length sequences that are similar to the m-length sequence starting at point i, within a tolerance of r. Similarity is defined based on the maximum absolute difference between corresponding elements of the sequences being less than r.

The choice of parameters m and r is crucial, as they influence the sensitivity and specificity of ApEn in detecting regularity within the time series. Typically, m is chosen to be 2 or 3, and r is a small percentage of the standard deviation of the time series. This measure effectively quantifies the predictability of subsequent samples in a time series, with lower values indicating greater regularity.

III. EXPERIMENT

a. Comparative Analysis of EEG Complexity Across Consciousness States

In this comprehensive analysis, we investigated the complexity of EEG signals across four distinct states of consciousness: sleep, anesthesia, coma, and brain death. Utilizing the ApEn as a measure of signal complexity, we calculated ApEn values for 200-second data segments randomly selected from each state. The median ApEn values were determined for the broader datasets to gain insights into the general complexity trends associated with each state.

The results, summarized in Figure 1, reveal a gradation of complexity across the states examined. Brain death exhibited the highest median complexity (ApEn = 1.15), suggesting a higher degree of signal unpredictability or complexity than traditionally anticipated. This was followed by coma (ApEn = 0.56), indicating a moderate level of complexity. Anesthesia showed the lowest level of complexity (ApEn = 0.19), illustrating significant reduction in neural activity compared to more active states.

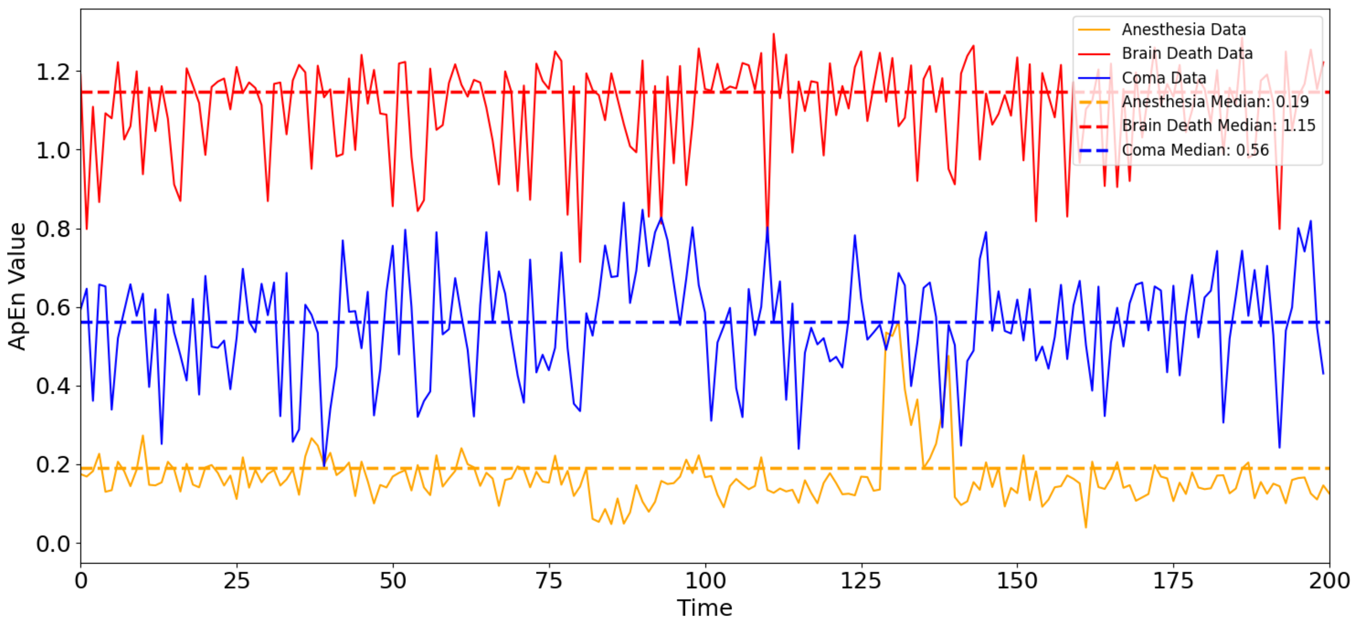

Figure 1. Comparison of ApEn across states of consciousness.

Fig.2 illustrates the distribution of ApEn values across three distinct states of altered consciousness, presented in box plot format to delineate the variability and central tendencies within each group. The box plots reveal the interquartile range (IQR) and highlight the 25th percentile (Q1), the median, and the 75th percentile (Q3) for each state, providing a quantifiable depiction of EEG signal complexity.

Anesthesia: The median ApEn value has been observed at 0.22, with the interquartile range extending from Q1 at 0.15 to Q3 at 0.27. This variation indicates a broader spread of EEG complexity than previously recorded, reflecting a nuanced pattern of neural activity characteristic of the anesthetized state, which may suggest variability in anesthetic depth or patient-specific responses to anesthesia. Brain Death: The data exhibit a median ApEn value of 1.15, consistent with an IQR from Q1 at 1.05 to Q3 at 1.19. These values are notably higher than traditionally expected in states devoid of consciousness, suggesting that while brain death is clinically defined by the cessation of neural activity, the recorded high ApEn values likely result from EEG artifacts or inherent noise rather than conscious neural processes. This finding highlights the complexities of interpreting EEG data in the context of brain death and underscores the necessity for rigorous analytical methodologies. Coma: Exhibiting a median ApEn value of 0.56 with an IQR from 0.48 to 0.65, the coma state presents a moderate yet substantive range of signal complexity. This indicates the presence of varying degrees of neural activity, which may correlate with differing levels of consciousness within the coma spectrum, potentially offering valuable insights into patient status and prognosis.

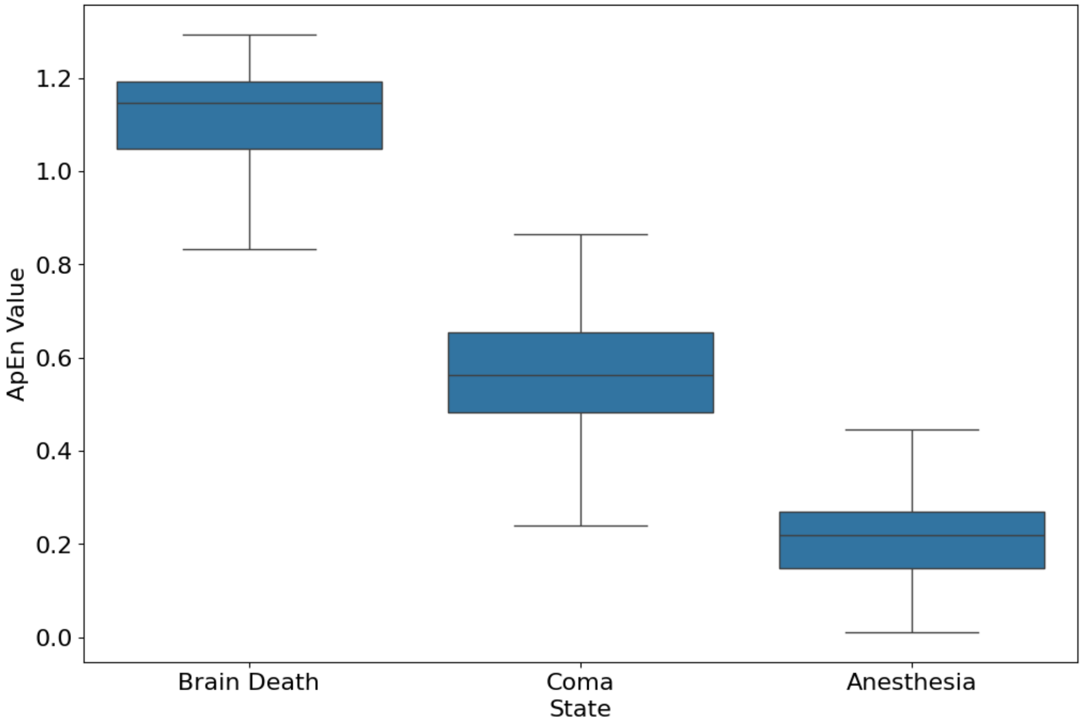

Figure 2. ApEn distribution of each state of consciousness.

These distributions underscore the distinct neural dynamics characterizing each state. The interpretation of high variability and complexity in brain death necessitates caution, recognizing that these measurements are likely reflective of signal properties rather than conscious neural processes. Meanwhile, the observed level of complexity in anesthesia corresponds to the expected neural activity patterns, effectively illustrating the broad spectrum of consciousness and unconsciousness as reflected in EEG complexity measures.

In the detailed exploration of EEG signal complexity, illustrated in Fig.3, we delve into the intricacies of consciousness through the lens of ApEn, analyzing 15 distinct segments from three states of altered consciousness: anesthesia, coma, and brain death. This granular analysis reveals a rich tapestry of neural activity and complexity across and within these states. By examining these specific segments, we get a deeper understanding of the neurophysiological variations that distinguish each state, offering valuable insights into their respective neural dynamics.

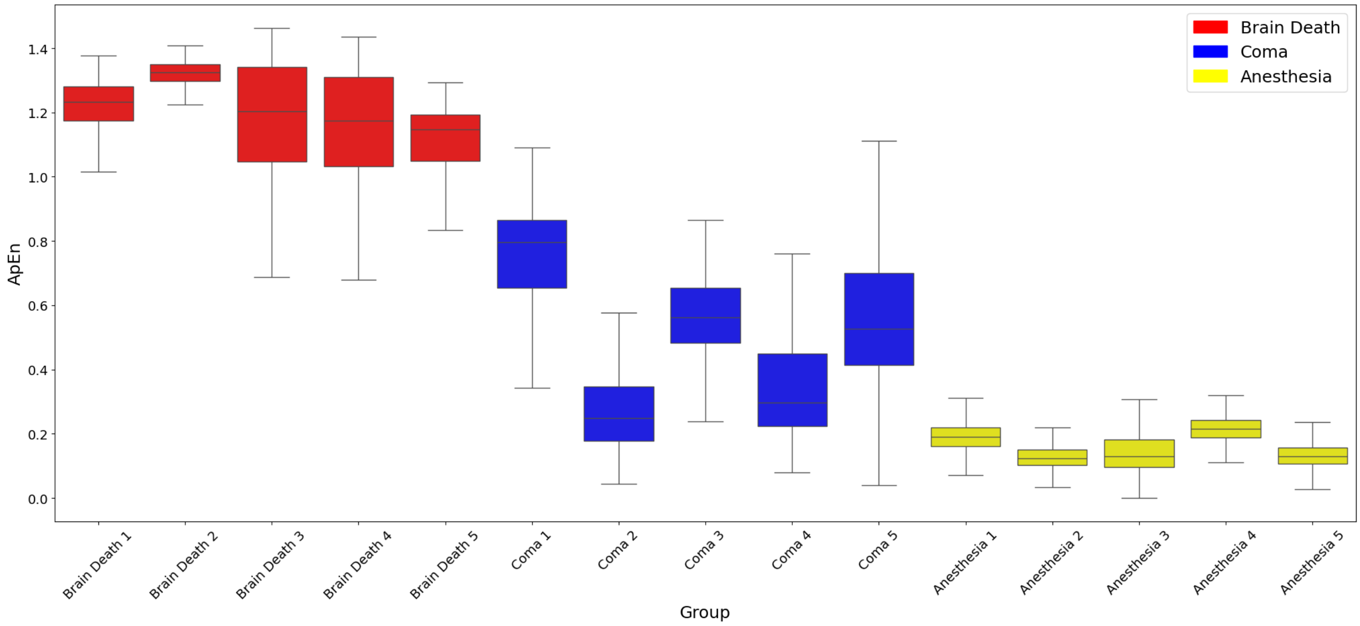

Figure 3. Distribution of ApEn Values Across Consciousness States: Brain Death, Coma, and Anesthesia.

In anesthesia, ApEn values illustrate a substantial spread, with minimum values nearing zero, suggesting profound neural suppression in some instances, while maximum values reaching up to 0.57 indicate less suppressed neural activities in other cases. This variability is captured by the median ApEn values, which range from 0.123 to 0.215 across different segments, suggesting that anesthesia's effect on neural activity is highly patient-specific and variable. The standard deviations in these segments, such as 0.058 in one and 0.074 in another, further highlight the inconsistency in neural responses to anesthesia, potentially influenced by the type of anesthesia, patient physiology, and procedural contexts.

As for brain death, where one might expect minimal to no EEG activity, the analysis unexpectedly shows high ApEn values across all segments, with medians consistently above 1.1 and reaching as high as 1.33. These elevated values suggest a high degree of complexity and variability, which are more likely due to EEG artifacts or electrical noise rather than true neural activity. This scenario underscores the critical need for meticulous data handling and interpretation when using EEG to confirm brain death, as traditional assumptions of absent neural activity are challenged by the presence of high entropy values.

Coma states shown a broad spectrum of ApEn values, reflecting the diverse clinical manifestations of coma. ApEn values range dramatically from as low as 0.04, indicative of very deep coma with minimal detectable brain activity, to as high as 1.33, which may suggest partial consciousness or less severe impairment. The median values in these segments, such as 0.797 in one and 0.249 in another, along with their respective standard deviations, highlight the significant variability within coma patients. This range not only illustrates the varied degrees of brain injury but also points to the potential for recovery, emphasizing the dynamic and individual nature of coma as a state of altered consciousness. This detailed exploration of ApEn across these states not only highlights the individual differences and complexities within each state but also illustrates the broader spectrum of neural dynamics under clinical conditions.

Fig.4 presents a consolidated analysis of ApEn across altered states of consciousness, specifically focusing on anesthesia, brain death, and coma, encompassing the entire dataset for each state. Through a comprehensive analysis of ApEn across an extensive dataset, our study elucidates the diverse complexities of neural activities associated with these states of altered consciousness. Rigorous data filtration techniques have been employed to remove noise artifacts, enabling a precise quantification of EEG complexities that distinctively categorize each state.

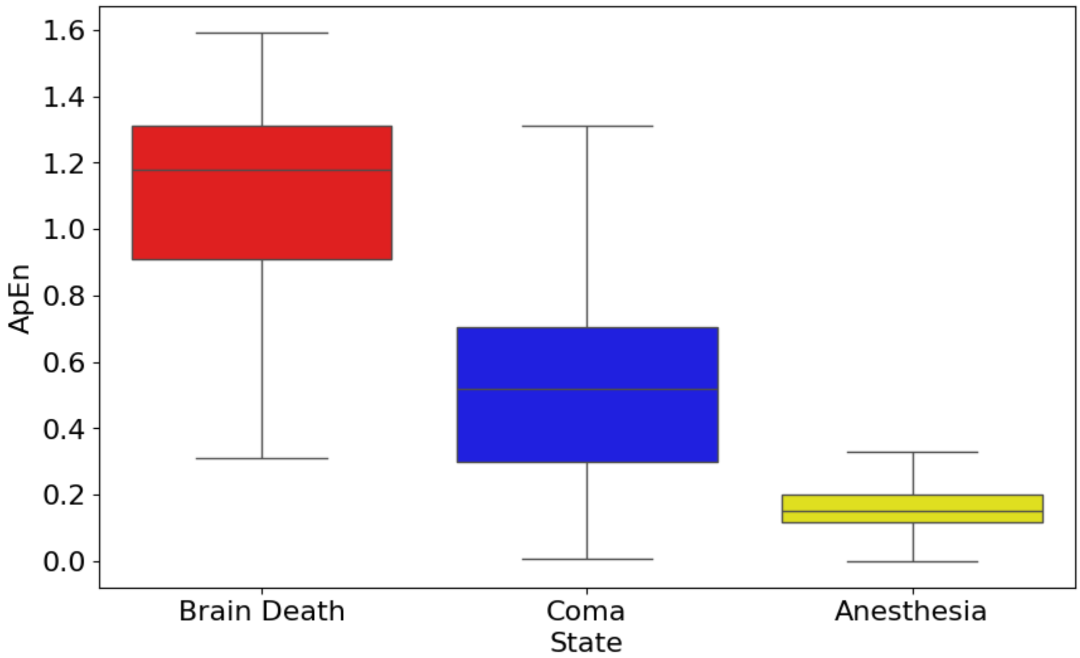

Figure 4. Consolidated Analysis of Approximate Entropy Across Consciousness States.

In our study, the EEG data analysis across brain death, coma, and anesthesia illustrates distinct ApEn patterns that reflect different levels of reduced brain activity. In brain death, the median ApEn value is notably high at 1.180 with a mean of 1.100, which is indicative of the highest level of disorganized electrical activity, typically associated with the absence of functional neural activity. This high entropy suggests an absence of coordinated brain processes, aligning with the clinical definition of brain death where neural activity is expected to cease. For coma patients, the ApEn values also show significant variability, with a median of 0.517 and a mean of 0.518, reflecting a range of brain activity levels. The higher values in this range indicate deeper levels of unconsciousness, where brain activity is more disorganized and random, pointing to severe impairments in neural functions. Lower values within this range may indicate a lighter coma state, with somewhat more organized neural activity, suggesting a potential for recovery. Contrastingly, anesthesia results in the lowest complexity levels among the three states, with a median ApEn of 0.151 and a mean of 0.161. These lower entropy values under anesthesia reflect a more controlled and reduced level of brain activity, managed medically to achieve a stable state of unconsciousness during surgical procedures.

This comparative analysis across the three states using ApEn effectively demonstrates how varying levels of entropy correlate with the degree of brain activity suppression. The high entropy in brain death and varying levels in coma provide insights into the extent of neural dysfunction, while the lower entropy in anesthesia underscores the controlled reduction of brain activity. This comprehensive visualization in Fig.4 underscores the efficacy of ApEn as a diagnostic tool to differentiate between states of altered consciousness and provides a statistical foundation for its use in clinical settings. Our collective data, analyzed across a broad range of ApEn values, not only reinforces the existing understanding of EEG complexities but also offers new insights into the gradations of consciousness. These insights could significantly impact therapeutic approaches and patient monitoring in clinical practice.

b. Results

Our study employed a Support Vector Machine (SVM)(Chang & Lin, 2011; Drucker et al., 1996) to classify EEG data into three distinct consciousness states based on ApEn: Unconsciousness, Potential Low Consciousness, and Potential Consciousness. This classification reflects clinical observations and EEG characteristics: Unconsciousness includes brain death, Potential Low Consciousness encompasses coma states, and Potential Consciousness is represented solely by anesthesia due to its EEG complexities.

This classification led the understanding that anesthesia, while indicative of reduced consciousness compared to full wakefulness, maintains functional brain processes that allow for relatively quick recovery to full consciousness. This contrasts with the more profound and uncertain states of coma or brain death, where neural activity is significantly suppressed or absent.

The SVM model demonstrated robust discriminative power, achieving an overall accuracy of 85%. The precision rates were high across the categories, with 88% for Unconsciousness, 86% for Potential Consciousness, and 80% for Low Consciousness. Recall rates were 70% for Unconsciousness, 99% for Potential Consciousness, and 66% for Low Consciousness, indicating that while the model is highly effective in identifying Potential Consciousness, it faces challenges distinguishing between Unconsciousness and Low Consciousness due to overlapping low-activity EEG patterns in these states.

These metrics reveal the model's effectiveness in accurately classifying EEG complexities within defined categories, enhancing our understanding of the nuanced differences in brain activity across various states of reduced consciousness. This comprehensive approach underscores the utility of ApEn as a quantitative tool for differentiating states of consciousness in clinical settings, offering valuable insights that could significantly impact therapeutic strategies and patient monitoring practices.

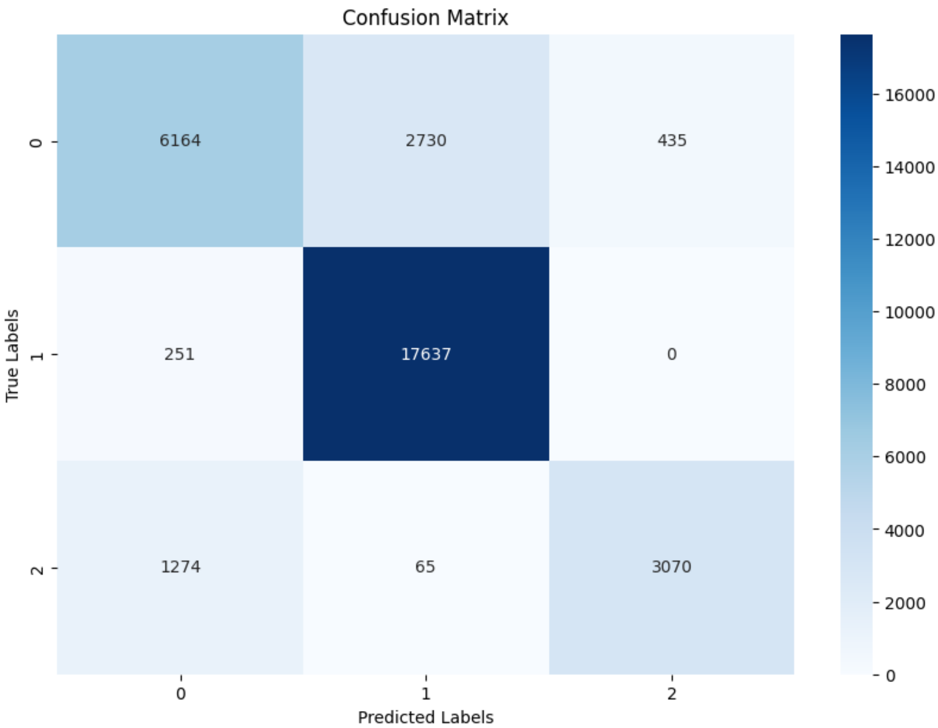

Figure 5. Confusion matrix of svm outputs.

The effectiveness of the model in classifying these states is detailed in the confusion matrix shown in Fig.5. This matrix illustrates the distribution of predictions against actual categories, clearly demonstrating the model's strengths in accurately recognizing and categorizing EEG patterns associated with different levels of consciousness. The high number of correct predictions, especially for Potential Consciousness, underscores the model's capability to effectively recognize and categorize EEG patterns. These results confirm the potential of ApEn as a reliable feature in EEG data for assessing states of consciousness, advocating for its continued development and integration into diagnostic tools in neurology and critical care. The method enriches our understanding of the EEG complexities associated with different states of consciousness and enhances clinical evaluations and interventions based on precise EEG data analyses.

IV. CONCLUSION

This study embarked on an ambitious quest to develop a quantitative indicator of consciousness levels, leveraging the complexity of EEG signals as measured by ApEn and employing machine learning techniques for classification. Through meticulous analysis, we classified EEG recordings into three categories—Low Consciousness, Potential Low Consciousness, and Unconsciousness—reflecting varying states of consciousness from Anesthesia to brain death.

Our findings reveal that ApEn, as a metric of EEG signal complexity, holds significant promise for differentiating between these states. The Support Vector Machine (SVM) model demonstrated a notable capacity to distinguish between the nuanced distinctions of consciousness states with a high degree of accuracy. Particularly, the model's proficiency in identifying the state of Unconsciousness underscores the potential of EEG complexity measures to capture the intricate neural dynamics persisting even in states traditionally perceived as devoid of consciousness.

These results contribute profoundly to the field of neuroscience, offering a novel approach to quantifying consciousness that transcends subjective clinical assessments. The proposed indicator has the potential not only to enhance clinical diagnostics and patient monitoring but also to illuminate the neural basis of consciousness and its gradations.

As we look ahead, several avenues emerge for extending this research. Further refinement of the classification model, integration of additional EEG features, and exploration of advanced machine learning algorithms could improve the sensitivity and specificity of the consciousness level indicator. Expanding the dataset, particularly with more granular distinctions within each consciousness state, will be crucial for enhancing the model's applicability and robustness.

Moreover, the ultimate validation of this indicator in clinical settings will determine its utility in real-world applications. The potential to inform treatment decisions, especially in critical care and neurological rehabilitation, offers a compelling case for continued investigation and development.

We concluded that this study represents a significant step toward a more objective and quantifiable understanding of consciousness levels. By bridging the gap between neurophysiological data and machine learning, we pave the way for groundbreaking advancements in neuroscience research and clinical practice. It should be noted that the dialogue between technology and biology promises not only to deepen our understanding of the human brain but also to enhance our capacity to care for it.

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Conflicts of Interest

The authors have no conflict of interest about anything in this article.

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