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Identification of Salient Brain Regions for Anxiety Disorders Using Nonlinear EEG Feature Analysis

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Abstract. In this paper, we present a novel approach for identifying salient brain regions and interpreting the ability of nonlinear EEG features to discriminate between anxiety disorders and healthy controls. The proposed method involves the integration of advanced EEG preprocessing and artefact correction, nonlinear feature extraction using conditional permutation entropy, and interpretable machine learning to identify relevant electrodes. The extracted nonlinear features show statistically significant differences between classes, demonstrating high discriminative ability. The discriminative ability was confirmed with T-tests (p = 1.05e-10) and Mann-Whitney U tests (p = 2.65e-11), demonstrating robust statistical significance. Classification results support these findings and guide the identification of relevant electrodes, enhancing the interpretability of the discriminative features. This approach highlights potential brain regions critical for anxiety disorder diagnosis, paving the way for more targeted interventions and improved clinical outcomes.

Keywords. Anxiety disorders, EEG, conditional permutation entropy, nonlinear feature, discriminative ability

1. Introduction

Anxiety disorders (AD) are among the most prevalent mental health conditions globally, affecting approximately 301 million people worldwide [1]. These disorders significantly impair cognitive, social, and daily functioning, and they also increase the risk of developing comorbid conditions such as depression, substance use disorders, and suicidal behaviours [2]. The increasing prevalence of AD is exacerbated by modern stressors such as the COVID-19 pandemic, climate change, and geopolitical tensions, underscoring the urgent need for effective diagnostic and treatment strategies.

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As the central organ for emotional processing, the brain exhibits heightened activity in specific regions in individuals with AD. Electroencephalography (EEG) is a non-invasive, cost-effective method for monitoring brain activity and early detection and management of mental health disorders. Traditional EEG analysis methods often rely on linear features or simple time-frequency analysis, which may not fully capture the complex dynamics of brain activity. Recent advancements have focused on nonlinear dynamics, which provide a richer representation of brain function. For example, Bosl et al. [3] demonstrated that nonlinear features from repeated EEG assessments could serve as early biomarkers for AD before the onset of behavioural symptoms.

Nonlinear dynamic analysis of EEG signals involves transitioning scalar time-domain signals into vector representations in phase space, offering deeper insights into brain activity changes. This approach can uncover intricate patterns of brain activity that linear methods might miss [4]. However, the complexity of nonlinear dynamics presents challenges in understanding and interpreting the relationship between EEG signal complexity and behaviour. This is where interpretability technologies come into play, aiding clinical decision-making by providing clear, actionable insights [5 - 7].

This study aims to address these challenges by proposing a novel approach that leverages advanced EEG preprocessing, innovative nonlinear feature extraction using Conditional Permutation Entropy (CPE), and machine learning algorithms. Our goal is to identify salient brain regions associated with AD and interpret the discriminative ability of these nonlinear EEG features, thereby enhancing the diagnostic potential of EEG and contributing to more targeted and effective interventions for AD.

2. Methods

The proposed approach consists of four main steps: (1) advanced preprocessing, (2) innovative nonlinear feature extraction, (3) classification using state-of-the-art machine learning algorithms, and (4) identification of relevant electrodes and interpretation of discriminative ability using SHapley Additive exPlanations (SHAP).

2.1. Dataset and data preprocessing

For this study, we leveraged the dataset [8], which comprises a full brain 128-electrodes EEG records of 53 subjects collected in a resting state and labelled into two categories based on their diagnoses: 24 outpatients with depression and anxiety disorder (class MDD) and 29 healthy controls (class HC).

Preprocessing steps involve (1) power frequency noise removal using a 50-Hz notch filter and elimination of high-band noise caused by muscle constructions using a Finite Impulse Response (FIR) filter with a Blackman window; (2) advanced artefact correction using the combination of Independent Component Analysis (ICA) and automatic artefact removal algorithms to further clean the EEG signals. ICA demonstrated good performance in removing eye movement artefacts from EEG data, preserving the underlying neural signals [9]. After ICA, further refinement was achieved using the Artefact Subspace Reconstruction (ASR) algorithm, which dynamically identifies and corrects segments of data with artefacts. ASR has been shown to robustly correct various artefacts, including those caused by muscle contractions and electrical noise, without compromising the integrity of the neural signals [10]. To validate the effectiveness of the artefact correction process, we compared the raw and cleaned EEG signals. Further

validation was performed using quantitative metrics such as signal-to-noise ratio (SNR) and qualitative assessments by expert reviewers. By utilising advanced artefact correction and noise removal techniques, this study ensures higher signal quality, leading to more accurate feature extraction and classification.

2.2. Feature Extraction

Unlike traditional methods that often rely on linear features or simple time-frequency analysis, in this study, we use advanced nonlinear dynamics and CPE, which provide a more nuanced understanding of brain activity. This approach captures complex patterns that are not detectable with linear methods. The presentation of EEG nonlinear dynamics involves: (1) Defining the time delay (τ) and embedding dimension (m) for the vector; (2) Determining the ordinal pattern of each embedding vector based on its element values; (3) Repeating the ordinal pattern determination for all embedding vectors of the EEG signal; (4) Constructing the EEG latent space network, where nodes represent unique ordinal patterns and edges connect nodes based on the embedding time delay parameter. CPE was used to calculate the complexity of the constructed EEG latent space network. This technique has demonstrated high discriminative ability in previous research [11] and was employed to extract information about EEG nonlinear dynamics. To validate the feature's ability to discriminate anxiety disorders, T-tests and Mann-Whitney U tests assess the CPE differences between the two EEG classes.

2.3. Classification and Identification of Relevant Electrodes using SHAP

A set of machine learning algorithms is used to classify extracted features and to get the input information for interpretation. For this study, classification was conducted using the MLP, Logistic regression, SVM, and RF algorithms. The final step involves SHAP technique to identify relevant electrodes and explain the model's results based on the discriminative ability of the features.

3. Results and Discussion

EEG preprocessing was performed using a 50-Hz notch filter and FIR filter with a Blackman window. Optimal time delay (τ = 6) and embedding dimension (m = 5) were achieved using methods [12-15] and tools from NeuroKit2 [16]. Boxplot diagrams (Fig. 1) illustrate the CPE variance for the two classes, showing lower values for the HC class, and indicating the discriminative ability of CPE. In addition, statistical analysis using T-tests and Mann-Whitney U tests revealed significant differences between the two classes, with p-values less than 0.05, also indicating the discriminative ability of CPE (Table 1).

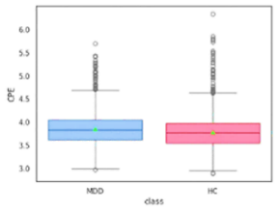

Figure 1. CPE variance for the two classes.

Table 1. CPE statistical analysis

Test	Statistics	p-value
T-tests	6.471	1.05e-10
Mann-Whitney U Tests	5181899.0	2.65e-11

Classification results showed that MLP and Logistic Regression achieved the highest accuracy of 72%, outperforming SVM (63%) and RF (54%).

The SHAP analysis identified electrodes 25, 54, 69, 73, and 81 as the most discriminative, indicating salient brain regions involved in AD. These regions correspond with known neurophysiological mechanisms where frontal and temporal areas are implicated in emotional processing and regulation (Fig. 2).

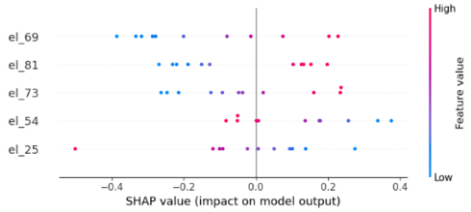

Figure 2. Five electrodes with the highest discriminative ability.

To further analyse salient brain regions, a mapping of five electrode connectivity based on Pearson coefficients between EEG electrodes is performed, as shown in Fig.3.

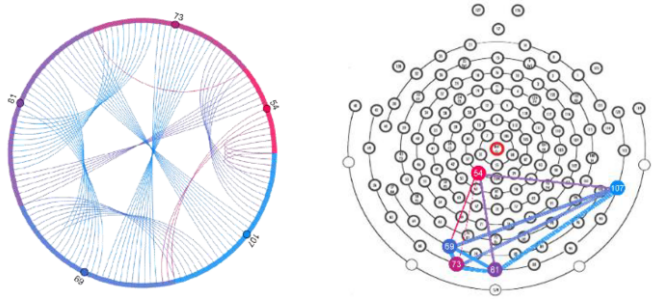

Figure 3. Connectivity of five EEG electrodes with the highest discriminative ability between two classes.

Compared to traditional EEG analysis, this approach offers several advantages. While linear methods are limited in their ability to capture complex brain dynamics, the use of nonlinear features provides a more detailed and nuanced understanding of brain activity. Additionally, the integration of advanced artefact correction techniques, such as ICA and ASR, ensures higher signal quality, leading to more accurate feature extraction and classification. This comprehensive approach not only enhances the reliability of the findings but also sets a new standard for future EEG studies in mental health research.

4. Conclusions

This study presents a novel approach to identifying salient brain regions and interpreting the discriminative ability of EEG nonlinear features in detecting anxiety disorders. Using CPE as a measure of EEG complexity, we found significant differences between the MDD and HC classes. The classification results, particularly from MLP and Logistic Regression models, demonstrated the potential of CPE in discriminating these classes.

The SHAP analysis identified electrodes with high discriminative ability, suggesting regions of the brain that may be crucial in AD diagnostics. The identification of specific brain regions associated with AD has significant clinical implications. It opens up new avenues for targeted interventions and personalized treatment plans. For instance, neurofeedback and brain stimulation techniques could be tailored to modulate activity in these identified regions, potentially offering more effective therapeutic outcomes. Future research will focus on validating these findings with larger datasets and exploring the clinical implications of these salient brain regions.

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