IEEE Access
Multidisciplinary | Rapid Review | Open Access Journal

Received February 28, 2022, accepted April 1, 2022, date of publication April 6, 2022, date of current version April 18, 2022.

Digital Object Identifier 10.1109/ACCESS.2022.3165199

Complexity Analysis of EEG in Patients With Social Anxiety Disorder Using Fuzzy Entropy and Machine Learning Techniques

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This work involved human subjects or animals in its research. Approval of all ethical and experimental procedures and protocols was granted by the Medical Research Ethics Committee of the Royal College of Medicine Perak, Kuala Lumpur University, under Approval No. UniKLRCMP/MREC/2019/065, and performed in line with the Helsinki Declaration.

ABSTRACT The diagnosis of social anxiety disorder (SAD) is of great consequence not only due to its impacts on the individual and society but also the expenditures to the national health systems. There is yet a deficiency of objective neurophysiological information to assist the present clinical SAD diagnosis. The main objective of this study is to analyze the electroencephalogram (EEG) complexity of 88 SAD subjects, subdivided into 4 balanced groups (22 severe, 22 moderate, 22 mild, and 22 healthy controls (HCs) using Fuzzy Entropy measure (FE) and machine learning algorithms. In addition, this study aimed at designing a computer-aided diagnosis system to identify the severity of SAD (severe, moderate, mild, and HC) in different EEG frequency bands (delta, theta, alpha, and beta). The experimental results showed that among the HC and the three considered levels of SAD, SAD patients in fast-waves exhibited significantly less FE values in resting-state compared with HCs ($p \leq 0.05$). The EEG complexity analysis showed a discriminatory neuronal activity over the frontoparietal and occipital regions between SAD patients and HCs. Additionally, the FE values measured in the resting-state were positively correlated with Social Interaction Anxiety Scale (SIAS) scores in fast-waves (beta and alpha), indicating that the regional FE measures are putative biomarkers in assessing the clinical symptoms of SAD. Also, the classification results demonstrated that the proposed method outperformed the state of the art methods with an accuracy of 86.93 %, sensitivity of 92.46%, and specificity of 95.32% with the Naive Bayes (NB) classifier. This study emphasizes the viability of quantitative FE measures and the specific combinations involving the chosen classifiers could be considered as an alternative biomarker for future clinical SAD recognition.

INDEX TERMS Social anxiety disorder (SAD), fuzzy entropy, machine learning classification, naive bayes (NB), electroencephalography (EEG), neurofeedback.

I. INTRODUCTION

Social anxiety disorder (SAD) is a common mental disorder caused by an overwhelming fear of negative evaluation by others in social situations. SAD is an intense persistent fear with a current lifetime prevalence between 18% and 36 % [1]. SAD has been associated with a general trepidation and avoidance of social situations [2]. In particular, SAD correlates with negative conditions and behaviors, such as substances abuse, insomnia disorder, depression, mood disorder, and even suicidal behavior [3], [4]. Generally, SAD is found to affect physical and psychological behaviors of individuals [5]. Thus, early detection and recognition of SAD is a crucial element in different domains such as characterizing the level of individuals' mental and physical states, recognizing the emotional states, and quantifying

The associate editor coordinating the review of this manuscript and approving it for publication was Md. Kafiul Islam.

stress levels in social situations. To strengthen research in SAD recognition and provide effective therapy for individuals with SAD, researchers and clinicians attempted to have effective evaluation instruments for characterizing the disorder in terms of its diagnostic basis. Different biomarkers including electrocardiogram (ECG), physiological alterations between sequential heartbeats, electrodermal response, and neuro-electrophysiological signals have been used in literature to assess the severity of SAD [6]–[8].

Functional neuroimaging studies have been reported to provide quantitative information about brain activity and mental states of patients with SAD [9]. Among these techniques, Electroencephalography (EEG) is the most commonly non-invasive technique used to measure the electric field potentials generated by various neural activities of the brain. EEG sensors are mounted on a specific region of the scalp to capture the synchronized activities (electric potentials) generated by thousands of neurons. With the help of a high temporal resolution in the scale of milliseconds, EEG has emerged as an important mechanism for investigating the instant changing patterns of brain activity and is applied in the clinical evaluation of mental health conditions. EEG technique has shown its potential in detecting different emotions, stress, depression, and different brain disorders [10]–[12].

Recent research in neuroscience has proven that SAD affects the neural activities within the human brain, [19]. An extensive review of the major frequently deliberated EEG biomarkers related to SAD is summarized in this recent article [20]. EEG reveals potential patterns to identify alterations in brain oscillations as an outcome of SAD. There are many justifications for this; the first being that SAD is a cortical-based mental illness [21] and, thus, alterations to the neuroelectrical activities resulted from SAD can be reflected on EEGs. Therefore, the utilization of signal processing methods to extract neural features from EEG may assist in the identification of the brain changes that are associated with SAD state. In fact, several EEG features found to be aberrant in SAD patients, where a transfer of the power spectrum to smaller oscillations, a reduction of connectivity in cortical areas, and abnormal synchrony have been observed [22]. Despite these results, there is a need for applying new feature extraction methods for further study of SAD using EEG. In particular, entropy algorithms estimating complexity in EEG signals could be beneficial to capture distinctive alterations in brain activity caused by SAD states.

EEG Entropy is a nonlinear indicator that represents the severity of the disorder, allowing it to be applied for the investigation of brain dysfunctions [23]. Fuzzy Entropy (FE) is a new index of time series regularity developed for the identification of surface electrophysiological signals (EEG and EMG). Fuzzy Entropy is extremely sensitive to data irregularity and is insensitive to data noises [24]. Fuzzy Entropy measures, extracted from EEG signals, are used for the automatic diagnosis of abnormality of the EEG signals [25]. It has been found that FE–based methods were superior to the sample entropy-based measures in the classification of brain seizures [26]. Fuzzy Entropy also has been applied in different prospects of mental illness and neuroscience application such as seizure detection [26], person authentication [25], schizophrenia [27], Alzheimer's disease [28], and depression evaluation [29]. The FE-based method is believed to preclude the limitations of the previous entropy algorithms and produce steady results for various parameters and robust anti-noise (noise reduction) ability.

Thus for, to the author's best knowledge, this is the first analysis that addresses the issue of estimating the EEG signal complexity in patients with SAD. In this study, the main objective is to investigate whether FE of brain signals is detectable across SAD patients (severe, average, mild, and HC) in a big set of clinical-EEG data at different frequencies (delta, theta, alpha, and beta). It is hypothesized that FE measures could recognize differences between the complexity of EEG signals from three SAD groups and HCs, and that these differences could be used to help in the classification of EEG signals. The quality of the classification has been assessed using five types of machine learning classifiers K-nearest neighbour (KNN), linear discriminant analysis (LDA), naive bayes classifier (NBC), decision tree (DT), and support vector machine (SVM). The central contributions of this research are:

- We quantified the severity of SAD using FE algorithm, which increases the prediction accuracy compared with the existing features.
- We presented a multi-class classification model of SAD based on the cortical complexity of EEG signals in resting-state.

The remaining parts of the paper are structured as follows. Section II presents entropic measure types for uncertainty quantification of EEG complexity. The III describes the data pre-processing procedure that is applied to raw EEG data, along with an explanation of the mechanism behind the computation of the FE matrices that assists the measurement of the complexity of EEG signals. The methodology for the extraction of features is also presented in this section. Section IV explains the proposed features extraction methods, statistical analysis along with classification models. The experimental discussion are presented in Section V, and the final conclusion is presented in Section VI.

II. ENTROPY MEASURES FOR UNCERTAINTY QUANTIFICATION OF EEG COMPLEXITY

The quantification of brain complexity of perceived time-series EEG data allows for a better comprehension of the characteristics of neural networks organization. The entropic uncertainty is one of the most efficient metrics to estimate the complexity of brain signals. Various entropic measures have been utilized and investigated in biomedical EEG signals, as reported in [30], including Shannon entropy [31], Tsallis entropy [32], Sample entropy [33], Permutation entropy [34], Approximate entropy [35], and Transfer entropy [36]. All of these algorithms have been utilized to different levels in the estimation of cognitive mental conditions and sleep disorders

TABLE 1. A comparison of different entropy measures for EEG complexity quantification.

Ref	Measure entropy	Definition	Advantages	Limitations
[13]	Multiscale entropy	It relies on the quantification of the sample entropy and coarse-grained time series that represent the system dynamics on different scales	It is independent of the sequence length and the model. Moreover, it can be applied to relatively short, noisy data sets.	There are no guidelines to determine the optimum values for sample length m and a tolerance window r, which makes the system highly sensitive to the noise.
[14]	Permutation entropy	It is a quantity used to encode how consecutive time series entries relate to one another in terms of position and value.	Permutation entropy is an appropriate complexity measure for chaotic time series	The amplitude information is discarded. Moreover, the performance under noisy conditions remains to be improved.
[15]	Sample entropy	It is the negative natural logarithm of the conditional probability that two sequences similar for m points remain similar at the next point	Statistically robust and it does not count self-matches.	High influence of the arbitrary constants sample length N and tolerance window r
[16]	Approximate entropy	It is utilized to measure patterns in time series and uncover the regularities by extracting the noises from the original EEG data.	Reliable characterization of the entropy of finite, short, and noisy biomedical signals	It depends heavily on the recorded length. It shows inconsistency when different input parameter values
[17]	Transfer entropy	Cross-correlation measures are utilized to obtain the asynchrony, information flow between the time series, respectively.	Robust method for studying brain directed connectivity	it is believed to be preferable applied when there are huge data sets and no time for pre-processing and fine-tuning of parameters.
[18]	Fuzzy entropy	It is a relative degree of uncertainty. It has been applied to estimate the fuzziness in a fuzzy set of EEG signals.	It is Insensitive to noise but sensitive to signal complexity. It does not count self-matches and can be applied to short or large sample points	dependent on the values of the input parameters, sample length (N), width and gradient (n, r), and sequences length (m)

using EEG data [26]. In comparison with other entropy measures, FE is more applicable in biomedical signals for its high quality in fast computation and simple conceptualization. Furthermore, it is not specific to a certain type of signal but is viable to different types of signals (e.g., deterministic, chaotic, stochastic, stationary, or nonstationary). Therefore, we do believe that the application of FE approach is capable to overcome the limitations associated with the other entropic measures. A comparative review is presented in table 1 to discuss different types of entropy measures that have been actively applied in EEG signal analysis.

Machine learning-based classification methods advance and enhance the decision-making processes in different domains of mental health care, including prognosis, disease monitoring, and diagnostic testing. Nevertheless, FE is believed to be applied for better feature extraction with different classifiers [37]. The feature selection based on FE is found to minimize noise and thus elevate the classification accuracy [38]. Several studies have achieved high classification accuracy by using FE features as input using different classifiers [39].

III. MATERIALS AND METHODS

A. CLINICAL ASSESSMENT

Social interaction anxiety scale (SIAS) assesses the approximated panic of social interaction according to the Social Phobia-Circumscribed DSM-III-R definitions [40]. It has been found to reveal high inner uniformity levels and precision for testing-retests analysis. SIAS has the ability to segregate between different types of anxiety such as social phobia, agoraphobia, and simple samples of phobia [41]. Moreover, the SIAS scale is observed to be precise, effective, adequate, and easily scored for clinical and research needs [42].The respondents were segregated into four groups: HC (SAIS score $<$ 20), mild (SIAS score $<$ 40), moderate (SIAS score $<$ 60), and severe (SIAS score $\geq$ 60). The selected participants have been interviewed by clinical specialized psychiatrist, and were diagnosed with SAD using the DSM-IV-based Composite International Diagnostic Interview [43]. Table 2 represents the demographic data and participants' characteristics.

B. PARTICIPANTS

Eighty-eight participants were selected from 417 registered respondents (35 females and 54 males; 18–24 years old (mean (M) = 22.32, standard deviation (SD) = 1.48) (M = 23.30, SD = 1.73)). All participants have reported that they are mentally healthy, right handed, have normal vision or corrected to normal vision, and had no history of neurological, psychotropic medication, or surgical disabilities. A single sheet including all study details and a waiver of written informed consent was provided to all chosen participants with an honorarium to compensate them for their time and cooperation. It should be noted that this procedure is coordinated with the Helsinki Declaration [44]. The procedure for this study has been closely reviewed, endorsed, and approved by the Medical Science Ethics Committee of the Royal College of Medicine of Perak, Kuala Lumpur University) with code number (UniKLRCMP/MREC/2019/065).

C. EEG RECORDING

The EEG data were recorded during a three-minute baseline term using a referential 32-channel shielded cap (ANT Neuro, Enschede, Netherlands). Thirty electrodes (FP1, FP2, FPz,

TABLE 2. Demographic data and group characteristics.

Group	Number of participants		Total	Age		SIAS score	
	Female	Male		Female	Male	Female	Male
Severe	12	10	22	22.13 ± 2.78	23.11 ± 1.02	67.53 ± 6.21	66.81 ± 5.32
Moderate	7	15	22	21.98 ± 3.11	22.21 ± 1.25	55.7 3± 7.81	54.41 ± 6.61
Mild	12	10	22	22.61 ± 2.32	21.71 ±2 .31	38.32 ± 512	37.71 ± 5.81
Control	8	14	22	21.76 ± 1.73	23.62 ± 1.65	14.71 ± 6.74	16.61 ± 7.34

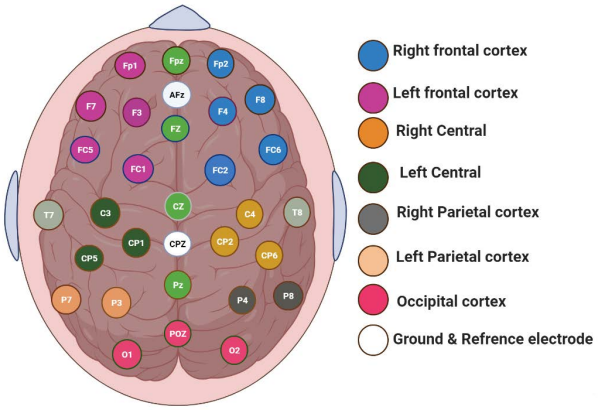

FIGURE 1. Topographical placement of 32 regions of interest (electrodes) using the extended international system 10-20, indicating the distribution of the electrodes on the cortical scalp. Note. LF, Left Frontal; RF, Right Frontal; LC, Left Central; RC, Right Central; LP, Left Parietal; RP, Right Parietal, O, Occipital.

F7, F8, F3, F4, FC5, FC1, FC2, FC6, Fz, Cz, T8, P7, P8, C3, C4, C3, CP2, CP4, CP1, CP6, CP5, P3, P4, PZ, O1, O2, and POz) were mounted to the cerebral cortex with a constant spatial arrangement according to the international 10–20 system, referenced to CPz and grounded at AFz. The impedance of all electrodes was maintained below 10 kΩ using a conductive gel. During the EEG data acquisition, all participants were asked to close their eyes, calm down, let their minds wander freely to obtain as many artifact-free EEG data as possible.

D. EEG PREPROCESSING AND FUZZY ENTROPY IMPLEMENTATION

The obtained EEG signals were pre-processed offline using EEGLAB toolbox and custom script developed in our previous studies [45]–[47]. To eliminate the high-frequency electrocortical artifacts, signal noise, and low-frequency deflections, we applied a band-pass filter to acquire the superlative segments between the frequency range of 0.4 and 50 Hz. Artifacts such as eye motions, breathing, power interference, and cardiac movements were visually inspected and automatically discarded using Spatial filters based on artifact detection and correction and brain signal topographies provided by EEGLAB toolbox [48]. The data then downsampled to 256 Hz from the original sample recorded rate of 2048 Hz. The clean EEG data were then segmented into short data epochs (3-seconds) for further complexity analysis. Based on the previous literature, we considered 7 asymmetrical distributed regions of interest (ROI) as shown in Fig. 1, and the averaged EEG data within each region was considered for FE analyses: left frontal (FP1, F3, F7, FC3, and FC5), right frontal (FP2, F4, F6, FC4, and FC6), left central (C3, CP1, and CP5), right central (C4, CP2, and CP6), left parietal (P5, P7), and right parietal (P6, P8), and occipital (O1, POz, O2).The EEG complexity of the resting state over 30 electrodes was computed and analyzed by the FE algorithm.

FE is an improved algorithm based on SE for overcoming the drawbacks of it [49]. Fuzzy Entropy offered better noise resistance using the fuzzy membership function. It uses the Gaussian function to measure the similarity of two vectors instead of the Heaviside function. The FE not only takes the advantages of SE but also has less dependence on the length of time series and possesses better robustness to the signal's noise. It is more suitable than the SE as a measure of time series complexity. The calculation algorithms of AE, SE, and FE are clearly defined in [46]. Additionally, for the FE index gradient n, we set $n = 2$ and $t = 1$ after applying several iterations. Fuzzy Entropy can be computed using the following equations: For a time series of $N4$ length, the algorithm is expressed as [u(1), u(2),, u(N)].

Carry out phase space reconstruction of the original time series and define the dimension $m(m \leqq N-2)$ of phase space. After reconstruction, as shown in formula 1,

$$X_i^m = [u(1, u(i+1), \ldots, u(i+m-1-1))] \tag{1}$$

$i = 1, 2, \ldots, N - m + 1$, $U_0(i)$ is the average, and the formula is shown in formula 2

$$U_0(i) = \frac{1}{m} \sum_{j=0}^{m-1} u(1+j) \tag{2}$$

The distance d_{ij}^m is recognized as the maximum difference between the corresponding elements of vector X_i^m and vector X_j^m, that is,

$$\begin{aligned} d[X_i^m, X_j^m] = max_{p=12,.,m}([u(i+p-1) \\ - u_0(i)] - [u(j+p-1) - u_0(j)]) \\ (i, j = 1, 2, ., N - m + 1, j \neq i) \end{aligned} \tag{3}$$

The similarity between vector X_i^m and vector X_j^m is defined by the fuzzy membership function $(d_{ij}{}^m, n, r)$ as shown in

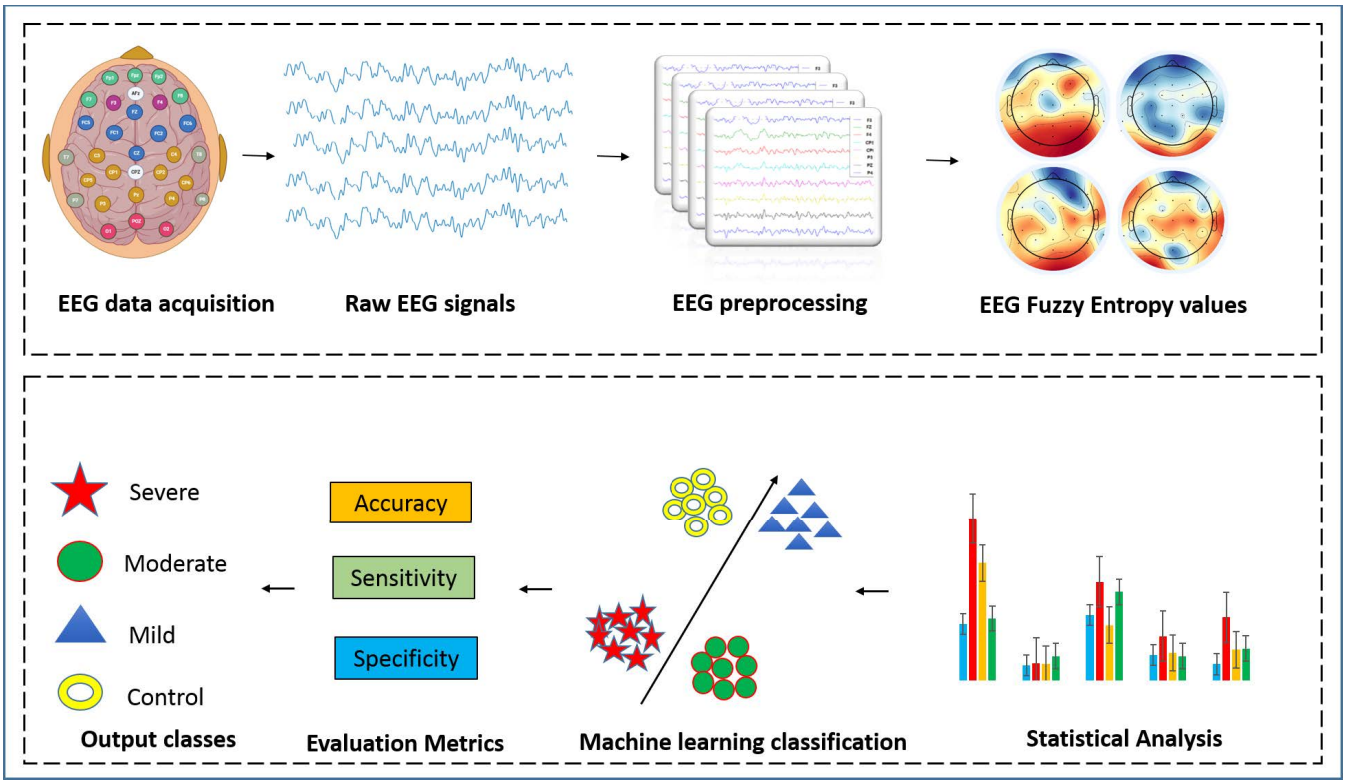

FIGURE 2. Block diagram for the EEG data analysis module to identify the parameters of FE values and perform classification methods..

formula 5:

$$(D_{ij^m}) = u(d_{ij^m}, n, r) = \exp\left(\frac{-(d_{ij^m})^n}{r}\right) \tag{4}$$

$u(d_{ij^m}, n, r)$ are are exponential functions; n and r are the gradient and the width, respectively, of the exponential functions.

$\phi^m(n, r)$ is shown in formula 6:

$$(\phi^m(n, r)) = \frac{1}{N-m}\sum_{i=1}^{N-m}\left(\left(\frac{1}{N-m-1}\right)\sum_{j=1, j\neq i}^{N-m} D_{ij}^m\right) \tag{5}$$

By including dimension $m+1$, the $\phi^m(n, r)$ function is obtained:

$$(\phi^{m+1}(n, r)) = \frac{1}{N-m}\sum_{i=1}^{N-m}\left(\left(\frac{1}{N-m-1}\right)\sum_{j=1, j\neq i}^{N-m} D_{ij}^m + 1\right) \tag{6}$$

The Fuzzy Entropy is

$$FE(m, n, r) = \lim_{N\to\infty} \ln(\phi^m(n, r) - \ln(\phi^{m+1}(n, r) \tag{7}$$

However, the length of the time series N is limited in the actual operation, and the FE is estimated as follows:

$$FE(m, r, N) = \ln(\phi^m(n, r) - \ln(\phi^{m+1}(n, r) \tag{8}$$

Fuzzy Entropy values were computed from 30 different nodes in the brain (captured by 30 electrodes). The output Fuzzy values rely substantially on the selection of the input parameters such as (length of data and tolerance value). To restrain non-stationary disruption, we epoched the data into approximately stationary nonoverlapping short time-series segments. We selected segment lengths of 3s to achieve a balance between the stationarity and the FE parameters. For our analysis, we found that shorter epochs (1–2 s) negatively influenced the performance of machine learning classification and FE algorithms. Thus, each 3-sec (256 samples/second) segment gives one FE matrix,which collectively yields M matrices of FE over the 30 channels for 1 subject in this study. Specifically, the FE measurement calculation will result in a balanced matrix of 30 (channels) × 20 (epochs) × 88 (subjects)). The overall process of the EEG analysis is elucidated in Fig. 2.

E. CLASSIFICATION PERFORMANCE

This section explains classification methodology applied to characterize SAD groups from a healthy group. To identify the complexity of EEG signals in four different classes of SAD, we applied five classifiers namely, KNN, linear discriminant analysis (LDA), naive bayes classifier (NBC), decision tree (DT), and SVM. The tuning parameters for these classifiers can be found in our previous studies [50], [51]. These classifiers are picked due to their high ability and effectiveness in the classification performance in the field of neuroscience as they can execute both linear and

non-linear classification. In all the classification models, we have applied 10 fold cross validation to evaluate the classification precision of different SAD states and to minimize the variation of a random segmentation of the dataset. The EEG dataset of 80% of the participants is applied for training classifiers, and the remaining EEG data of 20% of the participants are utilized as testing data. The mean classification accuracies and standard deviations corresponding to the proposed methods of EEG analysis at the four frequency bands in four classes of SAD are respectively computed. To present an enhanced instinctive performance and understandable method to calculate the prediction quality and building an effective machine learning model, the following three different parameters are used to examine performance quality:

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN} \times 100 \quad (9)$$

$$Sensitivity = \frac{TP}{TP + FN} \times 100 \quad (10)$$

$$Specificity = \frac{TN}{TN + FP} \times 100 \quad (11)$$

The specificity is estimated as a true negative (TN) rate and calculates the probability of a test to correctly preclude the disease (not identify the disease) when the disease is absent. The sensitivity is also called a true positive (TP) rate calculates the probability of a test to identify the disease when the disease is present. In our analysis, sensitivity is the probability of a false positive (FP) diagnosis of SAD, while specificity represents the ability of a false negative (FN) diagnosis. Accuracy is estimated as the number of all correct diagnoses divided by the sum number of the datasets.

F. STATISTICAL ANALYSIS

The distribution of the FE measurements was assessed with the univariate ANOVA test, and the statistical findings are reported by F value and significant values (P). All the statistical findings were presented as the mean ± standard deviation. The analysis of mean variances in our study included two independent variables (Group: severe, moderate, mild, and control) * (Regions; FP1, FP2, CP3, O1 ...) * and one dependent variable (FE values)); therefore, a one-way Univariate ANOVA and Tukey's HSD post-hoc test for different comparisons ($p < 0.05$) was performed to evaluate the main differences between the self-similarity of time series data of SAD groups. The effect size of the magnitude of mean differences between the SAD groups is represented by Cohen's d values (η^2). The SPSS software (version 25.0.0.0, IBM Corp., Armonk, NY) was used for all the statistical analyses.

IV. RESULT

A. CLINICAL ASSESSMENT RESULT

In this study, clinical assessments of the SAD patients and HCs were conducted based on a clinically relevant scale which is SIAS. According to the SIAS scores, there are 22 severe subjects (M = 22.52 years, SD = 2.48), 22 moderate subjects (M = 23.01, SD = 1.25), 22 mild subjects (M = 22.94, SD = 2.74), and 22 HCs (M = 23.11 years, SD = 1.93). Age did not exhibit any significant differences between the groups, F (1, 87) = 3.457, p = 062, $\eta^2 = 0.089$. No significant differences were found in gender ratio and age between SAD patients and HCs, F (1, 87) = 1.271, p = 0.8, $\eta^2 = 0.032$. As predicted, patients with SAD reported higher symptom severity indicated by SIAS (severe 67.75 ± 14.34; moderate 48.12 ± 12.51; mild 31.82 ± 15.21) compared with (HC 11.03 ± 9.22), (all p's < 0.05). A significant difference between the SAD groups in SIAS scores was found, F (1, 87) = 7.67, p = 0.001, $\eta^2 = 0.361$. Table 5 summarizes The Statistical analyses over the 7 regions of interest in patients with SAD and control subjects.

TABLE 3. The mean values of FE and the related test results in four SAD groups in alpha frequency band.

Frequency	Group	Mean	± SD	F	P value	η^2
LF	severe	0.478	0.078	0.125	0.94	0.03
	Moderate	0.457	0.075			
	Mild	0.448	0.077			
	Control	0.471	0.075			
RF	severe	0.423	0.124	0.011	0.998	0.002
	Moderate	0.406	0.183			
	Mild	0.408	0.190			
	Control	0.417	0.203			
LC	severe	0.567	0.047	17.53	0.001*	0.934
	Moderate	0.854	0.042			
	Mild	0.843	0.054			
	Control	0.658	0.074			
RC	severe	0.778	0.190	0.012	0.298	0.004
	Moderate	0.774	0.184			
	Mild	0.756	0.207			
	Control	0.784	0.178			
LP	severe	0.524	0.007	3.769	0.116	0.739
	Moderate	0.54	0.006			
	Mild	0.55	0.020			
	Control	0.562	0.002			
RP	severe	0.786	0.070	0.083	0.966	0.059
	Moderate	0.80	0.072			
	Mild	0.813	0.054			
	Control	0.781	0.068			
O	severe	0.650	0.032	14.63	0.002*	0.971
	Moderate	0.628	0.025			
	Mild	0.385	0.097			
	Control	0.774	0.070			

B. FUZZY ENTROPY RESULTS

Figure 2 shows the topographical representation of the normalized FE complexity values across the scalp in all the frequency bands for all SAD groups. The obtained results showed that the complexity level varies across all SAD groups. The severe and moderate SAD group showed the highest complexity at the occipital, left central (fronto-parietal), and right parietal region in delta and theta bands. In addition, in the beta frequency band, the LF and RF regions and LC showed the highest complexity compared to other regions. Meanwhile, the mild group has shown deficit activity in the frontal cortex in delta and theta frequency bands, HC group has shown greater EEG complexity at the parietal side in delta and alpha bands. Likewise, the HC group showed different complexity levels within each of

the frequency bands. In delta band, the complexity level is relatively small within the occipital, temporal, central and parietal regions compared to the other different groups. Statistically, We did not find any significant differences between the 7 brain regions in delta, theta, and beta. By iterated computations analysis of variance (ANOVA), we found a major significant difference between the SAD groups in alpha frequency band over the Left central and occipital regions $F(1, 2) = 17.55$, $p = 0.001$, $\eta^2 = 0.934$. and $F(1, 2) = 14.632$, $p = 0.002$, $\eta^2 = 0.971$, respectively. Table 3, showed the statistical analysis between the selected 7 brain regions between SAD groups in alpha frequency band. Contrarily, HC subjects have shown the highest values of complexity (FE), (0.660 ± 0.198), (0.629 ± 0.271), (0.727 ± 0.253), and (0.840 ± 0.303) for beta, alpha, theta, and delta, respectively. We did not find any significant differences between the FE values of SAD groups in the LF, RF, RC, LP, and RP regions in alpha band, $F(1, 5) = 0.125$, $p = 0.94$, $\eta^2 = 0.03$; $F(1, 5) = 0.011$, $p = 0.998$, $\eta^2 = 0.002$, $F(1, 2) = 0.116$, $p = 0.116$, $\eta^2 = 0.004$, $F(1, 2) = 3.76$, $p = 0.116$, $\eta^2 = 0.059$, $F(1, 2) = 0.083$, $p = 0.966$, $\eta^2 = 0.236$, respectively.

C. RELATIONSHIP BETWEEN SYMPTOM SEVERITY SCORES AND FUZZY ENTROPY VALUES

We investigated the correlation analysis between the self-report SIAS scores and the normalized averaged FE measures of all participants in the four SAD states for all the frequency bands. In beta band, all participants in all SAD groups have shown strongly significant positive correlation, $r(1, 21) = 0.67$, $p < 0.001$; $r(1, 21) = 0.39$, $p < 0.07$; $r(1, 21) = 0.71$, $p < 0.002$, $r(1, 21) = 0.62$; $p < 0.002$, for HC, mild, moderate, and severe, respectively. All correlations in delta have shown less correlation between SIAS and FE values in most of the SAD conditions, $r(1,21) = 0.39$, $p < 0.07$; $r(1,21) = -0.19$, $p < 0.43$; $r(1, 21) = 0.05$, $p < 0.81$, $r(1, 21) = 0.06$; $p < 0.77$, for HC, mild, moderate, and severe, respectively. A complete compression of correlation is shown in Fig 4. There was no significant correlation found between the SIAS scores and the normalized theta FE values in all SAD groups except for the mild group, $r(1, 21) = 0.62$, $p < 0.002$.

D. CLASSIFICATION PERFORMANCE RESULT

Machine learning is used to advance computer-aided diagnostic methods for clinical implementations and examine the pathophysiological mechanisms of diseases. We assessed the performance of the proposed FE feature extraction method using five different classifiers KNN, LDA, NBC, DT, and SVM. The mean classification accuracies, sensitivities, and specificities with the $\pm$ SD through different SAD classes in all frequency bands are summarized in Table 4. The classification performance in identifying these classes with NB and LDA classifier at the beta band are (accuracy 87.10 %, sensitivity 95.34 %, and specificity 96.20 %), (accuracy 85.91%, sensitivity 94.23 %, and specificity 95.43 %), respectively. From table 4, we obtain the following significant points:

- For all types of classifiers, the classification accuracies correlated with fast frequency rhythms (beta and alpha) are higher than the ones in the slow frequency waves (delta and theta) in all classifiers using FE values.
- For the applied features (FE), NB outperforms the other classifiers in our analysis methods. Therefore, we restricted our discussion to the findings acquired by NB classifier.

V. DISCUSSION

This paper is a modest contribution to the ongoing discussions on the influence of SAD on electrocortical brain complexity. In this study, we proposed to utilize the EEG complexity measured by FE to classify the severity of SAD in resting-state. In our analysis, we found that SAD patients have shown less irregularity of brain fluctuations compared to the HCs. In addition, our analysis has shown positive correlations between the severity symptom scores and EEG complexity in fast-frequency bands (alpha and beta), but less correlation in slow-frequency bands(delta and theta). Furthermore, using the complexity of EEG signals (FE) as features, we achieved the highest classification accuracy in high-frequency bands as shown in Table 4. To the best of our knowledge, this is the first study to use FE features to categorize the SAD severity using machine learning methods.

A. FUZZY ENTROPY ESTIMATION

In this paper, the FE values were quantified in four frequency bands to measure brain signals complexity. In general, the complexity of EEG signals of SAD patients is smaller than those of HCs in resting-state. These results are consistent with the previous studies that found severe SAD individuals exhibited relatively less cortical activity during resting-state EEG [57]. The EEG signals of patients with SAD were more regular, and thus, have smaller FE compared to the EEG signals of HCs. It also has been found that patients with depression and schizophrenia showed significantly different FE values from HCs [58]. Conventionally, the enhancement in FE values demonstrates that, a group of neurons involved in the information processing of SAD states. The increment in the functional complexity is associated with an enhancement in the number of synchronously active regions reflecting the system's degree of freedom. Compared with the SAD, the brain activity of HCs is found to be more vigorous and aroused, the possibility of generating new patterns of EEG signals is higher, and the irregularity of EEG is also higher [59]. Moreover, HCs have shown greater EEG complexity in occipital and left central lobes.While the increment of central lob (covered by C3, CP1, and CP5) EEG activity in resting-state may indicate the maintenance of self-focused awareness [60]. The increment of occipital complexity may reflect some of the features of attention, such as vigilance, expectations, and the state of emotional transformation [61].

From that we could confirm that the two hemispheres of the human brain are not identical. Comparative functional differences between the left and the right hemispheres of the

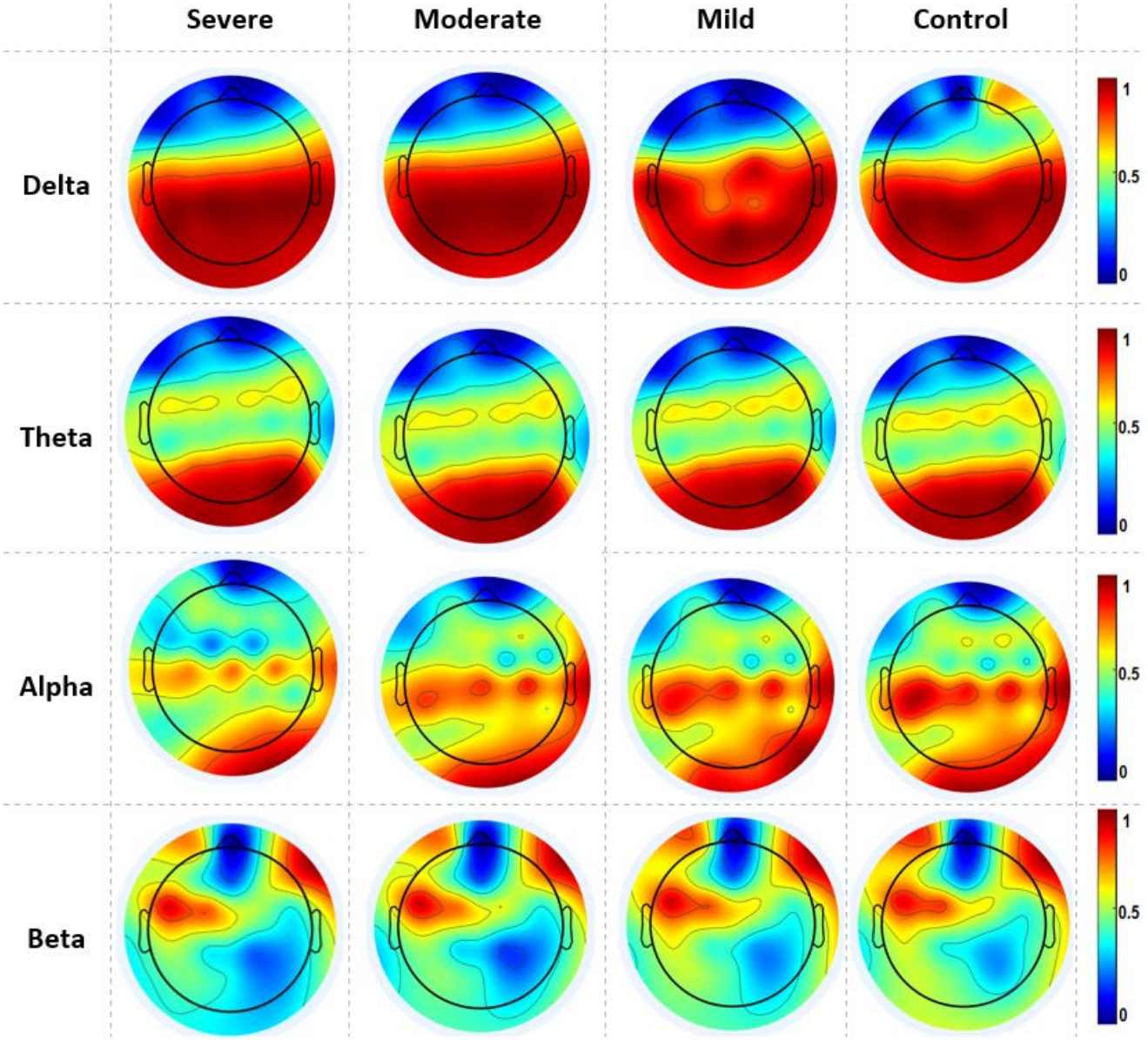

FIGURE 3. Topological maps of the normalized averaged Fuzzy Entropy for all three SAD groups and HCs in four different frequency bands in resting-state (eyes closed). The topographies maps have shown similar spatial distributions of the EEG complexity in delta, theta, and beta frequency bands across all ROIs. These topographies are prominently showing distinctive patterns in the alpha band at two regions only, LC (left frontal cortex) and O (occipital cortex). The red color indicates a higher complexity of the EEG signals, and the blue color indicates less complexity.

brain have been proven in several cognitive functions. The frontoparietal network is crucial for our potency to coordinate behavior in a immediate, accurate, and resilient goal-driven system [62]. Cognitive control is not accomplished by a singular brain area or singular brain network, but rather by various broadly non-overlapping brain networks, each involving of a comparatively major set of anatomically distributed neurons.

B. CORRELATION BETWEEN BRAIN COMPLEXITY AND CLINICAL ASSESSMENT

In this analysis, we found that normalized FE measures in the cortical activity exhibited positive correlations with SIAS scores in high-frequency bands as shown in Fig 4. Greater FE values and greater SIAS scores reveal a more serious mental disorder [45]. These results proved that the smaller complexity of EEG signals is correlated with the higher severe clinical syndromes in high frequency bands (beta). Similar to our result, previous researches have also demonstrated that the neurophysiological data and cognitive conditions of the brain can be investigated using EEG complexity measurements [63]. These findings suggested that EEG irregularity could be a valuable marker to reveal the neurophysiological states of the brain and clinical assessments. We did not find any significant correlations between the SIAS scores and normalized FE in the low-frequency band (delta) in all

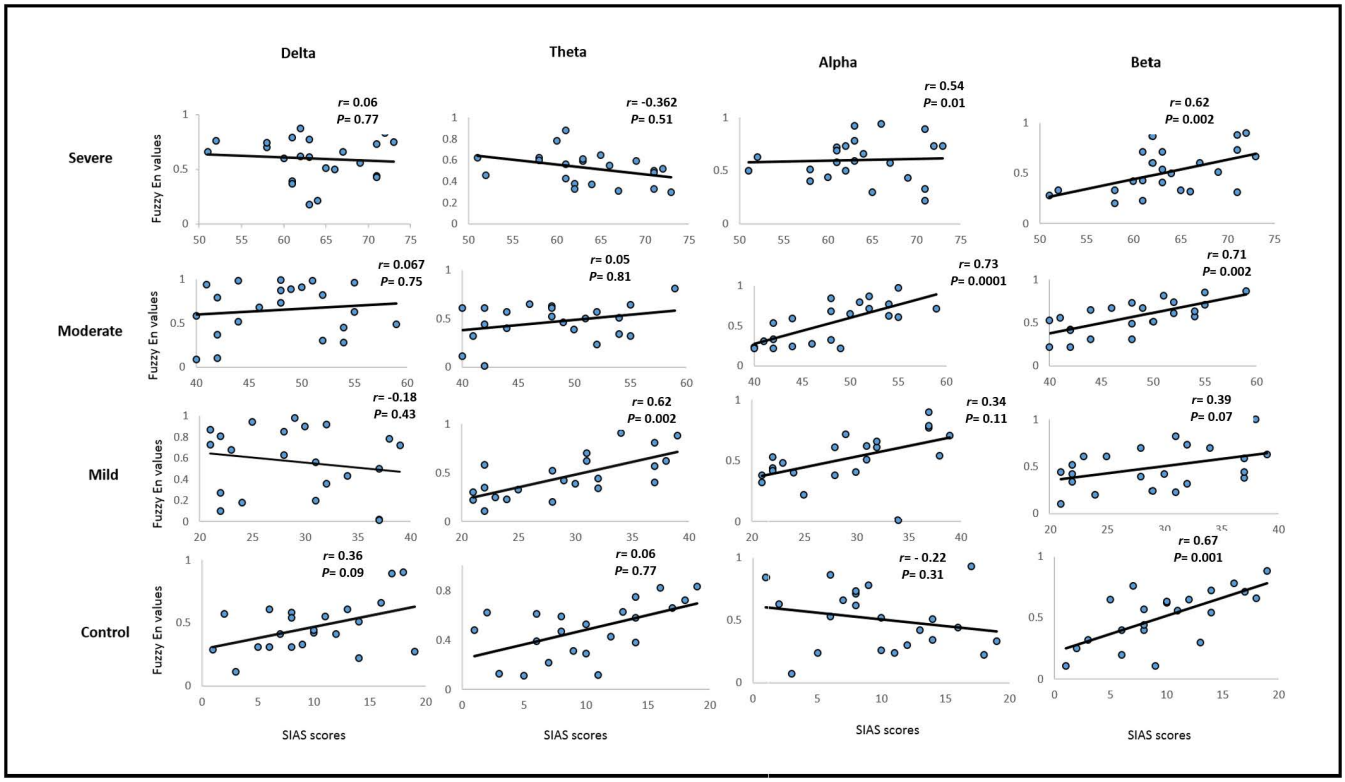

FIGURE 4. The correlation between SAD severity scores and the complexity of brain signals EEG (FE measures) in the four different frequency bands.

TABLE 4. The classification performance using FE features in different frequency bands with five different machine learning classifiers.

Machine.L Classifiers	Evaluation Metrics	Frequency bands			
		Delta (0.5-4 Hz)	Theta (4-8 Hz)	Alpha (8-12 Hz)	Beta (21-30 Hz)
KNN	Sensitivity (%)	83.49 ± 16.43	88.30 ± 10.87	79.67 ± 16.16	92.90 ± 8.93
	Specificity (%)	73.72 ± 20.74	82.06 ± 21.23	54.35 ± 28.71	86.54 ± 18.80
	Accuracy (%)	57.21 ± 9.74	67.38 ± 10.62	43.63 ± 8.20	76.64 ± 11.09
LDA	Sensitivity (%)	84.55 ± 20.21	85.49 ± 12.74	76.91 ± 18.31	97.08 ± 5.50
	Specificity (%)	83.40 ± 15.07	87.59 ± 11.53	94.44 ± 13.71	94.90 ± 6.50
	Accuracy (%)	63.35 ± 9.35	69.48 ± 11.30	53.29 ± 11.35	86.25 ± 12.09
NB	Sensitivity (%)	85.79 ± 13.83	86.60 ± 15.46	86.25 ± 18.94	92.46 ± 10.78
	Specificity (%)	88.68 ± 15.17	90.69 ± 13.07	88.25 ± 13.58	95.32 ± 6.34
	Accuracy (%)	70.62 ± 9.52	72.21 ± 9.90	78.61 ± 17.92	86.93 ± 10.35
DT	Sensitivity (%)	89.06 ± 12.91	86.83 ± 16.02	78.71 ± 17.48	91.97 ± 13.83
	Specificity (%)	82.78 ± 18.65	87.00 ± 11.28	78.72 ± 22.92	88.89 ± 12.80
	Accuracy (%)	66.42 ± 10.40	70.56 ± 11.12	58.06 ± 11.44	81.70 ± 11.05
SVM	Sensitivity (%)	81.04 ± 19.07	83.91 ± 14.19	77.32 ± 16.48	89.82 ± 14.07
	Specificity (%)	86.79 ± 14.88	89.31± 13.46	87.32 ± 16.98	93.12 ± 9.98
	Accuracy (%)	64.20 ± 9.81	72.10 ± 10.31	55.28 ± 8.87	82.72 ± 10.69

TABLE 5. Comparison of the proposed technique with recent machine learning techniques.

Ref	year	Features	subjects	classes	Classifier	ACC (%)	SEN (%)	SPE (%)
[52]	2020	Time series data	93	2	SVM	72.0	N/A	N/A
[53]	2013	Functional connections	40	2	SVM	82.5	85.0	80.0
[54]	2019	Raw EEG data	26	3	Random Forest, KNN	78.0	N/A	N/A
[55]	2019	Frequency features	12	4	SVM, KNN	62.52	N/A	N/A
[56]	2017	Time series	43	2	SVM	67.46	78.95	57.14
Proposed method	2021	FE	88	4	NB	86.93	92.46	95.32

SAD groups. It is assumed that, the slow-frequency bands are less sensitive to cortical activities because they mainly oscillate from the sub-cortical brain regions (e.g., amygdala, insula) [64].

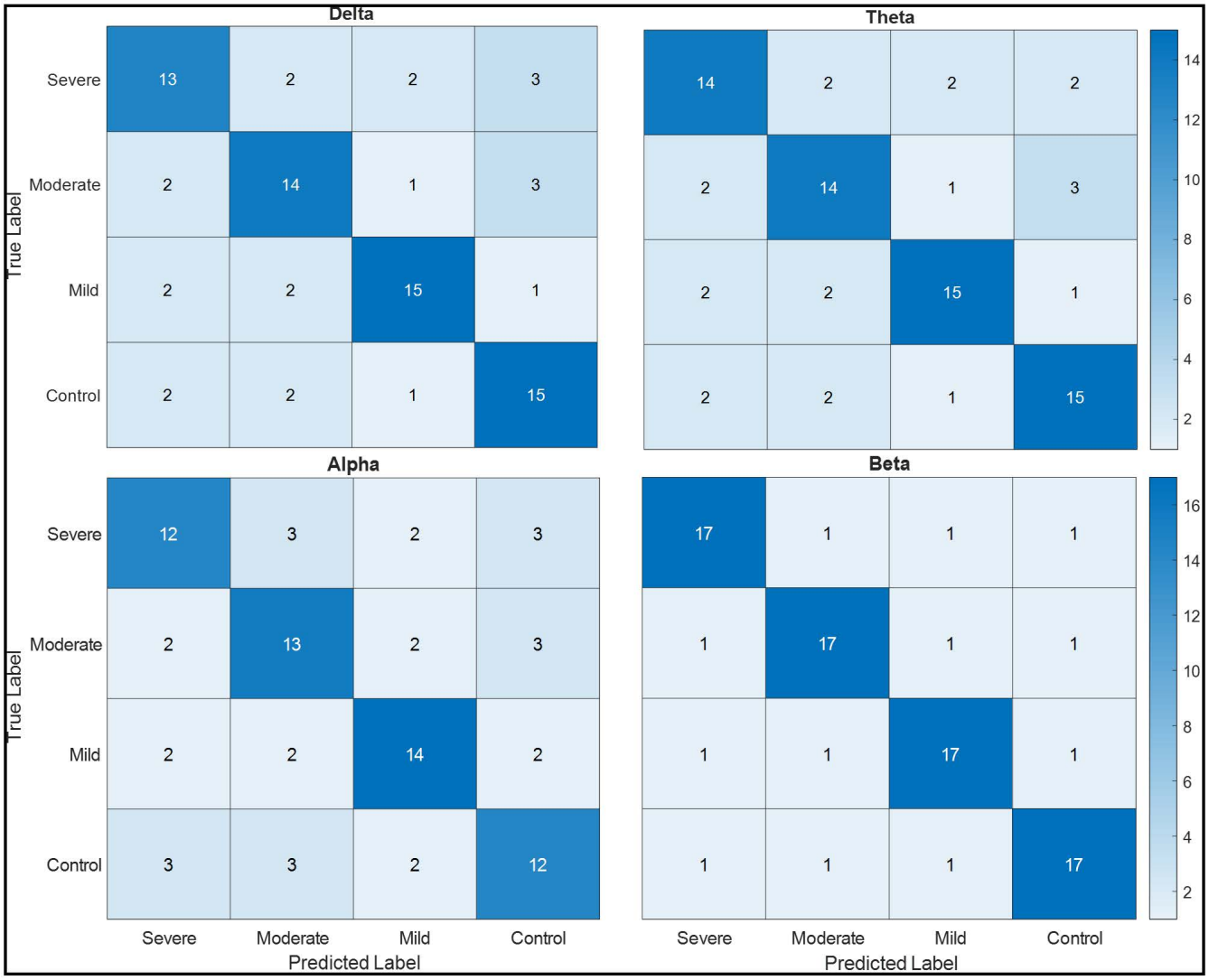

FIGURE 5. Normalized confusion matrix of the best classifier (NB) accuracies using the FE features for all SAD groups and HCs. The top left is representing the confusion matrix for delta band, the top right is representing the confusion matrix for theta band, the bottom left is representing the confusion matrix for alpha band, and the bottom right is representing the confusion matrix for beta band.

C. CLASSIFICATION PERFORMANCE

The application of different machine learning classifiers is assisting in creating the most appropriate classifier for mental health state diagnosis (e.g., SAD). The features extracted from FE measures have successfully classified the severity of SAD by categorizing its grading to (severe, moderate, mild, and HC) with high accuracy. Fuzzy Entropy features showed classification accuracy above 86% in fast-waves (beta) and above 70% in slow-waves (delta and theta) using NB and LDA classifiers as summarized in Table 4. Meanwhile, the previous investigation in classifying two classes of SAD (anxious and HCs) had achieved 72.0% using SVM, we have achieved higher classification accuracy in four different classes of SAD [52]. Furthermore, Pantazatos et al, achieved accuracy with 88.0% in classifying 16 SAD patients and 19 HCs using functional connectivity features [65]. Although other classifiers exhibited quiet equivalent accuracies, NB outperformed the other classifiers in all the frequency bands as mentioned earlier [66]. Basically, NB is a probabilistic method that is based on Bayesian theorem with assumptions of a feature of a particular group that is independent of any other features. The NB classifier requires less training data for the classification and it's based on maximum likelihood [67]. Similarly, in our analysis, both the averaged specificity and sensitivity computed by the NB classifier using FE (95.32% and 92.46%, respectively) were significantly greater than those computed using the other classifiers. The prediction performance of the NB classification is summarized by the confusion matrices in Fig 5. Table 5 is presenting a comparison of the current study and related classification literature. Taking into consideration the difficulty of classifying 4 classes in one state (resting-state),

the current results have shown high identification precision and are convenient for research into the classification of the severity of SAD. Future work should include different types of entropy measures to validate the SAD findings such as sample and multi-scale entropy. It is recommended to select the most active regions which are highly involved in the active SAD network such as default mode network [68], [69], occipital cortex, and salience network (SN), in order to improve the accuracy performance [68]. In addition, combining EEG with different modalities (e.g., fNIRS and fMRI) is believed to better study both temporal and spatial brain activities of SAD [70]–[73]. Though we achieved a satisfactory classification performance using traditional machine learning algorithms, the application of deep learning classifiers in future studies may improve the SAD diagnosis accuracy. The general perceived patterns of these results motivates the implementation of the modern diagnosis of EEG signals and other neuroimaging modalities to study human mental disorders (e.g., SAD, stress and depression).

VI. CONCLUSION

In summary, FE values were utilized to extract the non-linear features of EEG signals under resting-state, concentrating on the alterations in the irregularity of EEG signals between SAD groups and HCs. We found that the EEG complexity of patients with SAD was less than those of the normal control in all frequency bands. The increment in FE measures revealed an enhancement in the eventuality of the time series generating new characteristics in the brain. From the perspective of EEG complexity, the increase in FE values indicates greater activity and vigilant states in human brain. The empirical findings exhibited that features extracted from FE measures can achieve higher classification performance. Thus, the complexity of brain signals is believed to mediate the symptoms of SAD and can be considered as a potential target for clinical diagnosis and future research.

VII. DISCLOSURE STATEMENT

The authors declare no competing interests.

ACKNOWLEDGMENT

The authors would like to thank the Centre of Graduate Studies of Universiti Teknologi PETRONAS, for providing EEG dataset and also would like to thank the medical research ethics committee in Royal College of Medicine Perak-Universiti Kuala Lumpur for their assistance in designing the social anxiety experiment.

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