Autism Diagnosis using Linear and Nonlinear Analysis of Resting-State EEG and Self-Organizing Map

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***Abstract*—The prevalence of autism has increased dramatically in recent years and many people around the world are facing this difficult condition. There is a need to develop an objective method to diagnose autism. Various analysis methods have been used to classify the EEG signals of people with autism, from linear methods in the time and frequency domain to nonlinear methods based on chaos theory. However, there is still no consensus on which method of EEG signal analysis can provide us with the best diagnostic accuracy and valid biomarkers for autism diagnosis. Therefore, in this study, we evaluate different feature extraction methods from EEG signals to diagnose autism from healthy individuals. For this purpose, EEG analysis was performed in time, time-frequency, frequency and nonlinear domains. Furthermore, the self-organizing map (SOM) method was used to classify features extracted from autistic and normal EEG. The data used in this study were recorded by the research team from 24 children with autism and 24 normal children. The accuracies of 92.31, 93.57, 95.63 and 97.10% were achieved through time and morphological, frequency, time-frequency and nonlinear analyzes, respectively. Indeed, the findings showed that nonlinear analysis could yield the best classification results (accuracy = 97.10%, sensitivity = 98.80% and specificity = 97.02%) in the EEG discrimination of autistic children from typical children through the SOM neural network.**

***Keywords*—Autism; EEG; linear analysis; nonlinear analysis; neural network**

I. Introduction

Autism is a severe psychiatric disease in which patients have serious problems in executive functions, social relations, cognition, normal behaviors and daily activities [1]. Its prevalence has grown in recent years drastically, and many people around the world are facing this difficult condition [2-4]. However, psychiatrists and psychologists do not deal with the definitive state of this disorder, but they have to deal with autism spectrum disorder with different biological and behavioral symptoms [5, 6]. This causes doctors to choose different screening tools to diagnose patients with autism and therapists to choose different treatment approaches for each patient [7]. But most of the existing screening and diagnostic tools are subjective, and various types of research suggest the need to develop an objective method to diagnose autism [8]. For example, a review article highlighted various biomarkers, such as hormones, to develop reliable, objective methods for diagnosing autism [9]. A systematic review focused on the application of artificial intelligence in autism screening and diagnosis through validated questionnaire-based data such as the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS) [10]. Another systematic review showed that a combination of eye-tracking technology and machine learning could be taken into account as a suitable approach for objective and early diagnosis of autism [11]. Lai et al. proposed an objective method for autism diagnosis based on automatic retinal image analysis and machine learning and reported a good accuracy of 97.4% for this purpose [12]. Zhao et al. proposed an automatic objective system based on the analysis of the movements of patients during a motor task and machine learning algorithms. They reported an accuracy of 88.37% for autism diagnosis [13]. Therefore, as we can see from the literature, many researchers around the world have tried to develop objective methods of autism diagnosis through various psychological, biological and physiological data.

In the meantime, electroencephalogram (EEG) is one of the electrophysiological data that has received much attention from researchers and has been analyzed in various ways to develop objective methods for diagnosing autism [14]. EEG indicates the pattern of neural electrical activity in different areas of the brain, providing brilliant information about brain function in various healthy and unhealthy conditions [15, 16]. Therefore, EEG signals have been targeted by computational neuroscientists and biomedical engineers for various biomedical applications [17-23]. So far, various EEG biomarkers have been introduced to diagnose psychiatric and neurological disorders [24, 25]. Bosl et al. used a combination of nonlinear EEG analysis and different machine learning techniques, achieving a 95% accuracy in screening pediatric populations at risk for autism [26]. Haputhanthri et al. extracted statistical features from wavelet analysis applied to EEG signals of children with autism, achieving a diagnostic accuracy of 93% [27]. Ahmadlou et al. proposed a fuzzy synchronization likelihood wavelet approach, achieving an EEG classification accuracy of 95.5% for autism diagnosis [28]. Pham et al. applied the higher-order spectra bispectrum method to EEG signals and achieved a high accuracy of 98.7% using a probabilistic neural network for autism diagnosis [29]. Baygin et al. utilized a combined deep lightweight feature extraction method based on one-dimensional local binary patterns and deep features of the spectrogram images generated by the short-time Fourier transform. The 10-fold cross-

validation algorithm showed an ability to identify children with autism with a support vector machine with 96.44% accuracy [30]. Alotaibi and Maharatna proposed an EEG classification system based on functional connectivity features conceptualized by graph theory and cubic support vector machine, achieving an accuracy of 95.8% for autism diagnosis [31]. Radhakrishnan et al. evaluated deep learning models for the diagnosis of autism from EEG signals, reporting an average accuracy of 81% using their methodology [32].

As can be seen in the literature, various analysis methods have been used to classify the EEG signals of people with autism, from linear methods in the time and frequency domain to nonlinear methods based on chaos theory. However, there is still no consensus on which method of EEG signal analysis can provide us with the best diagnostic accuracy and provide valid biomarkers for autism diagnosis. Therefore, in this study, we are going to evaluate different feature extraction methods from EEG signals in order to diagnose autism from healthy individuals. For this purpose, EEG analysis in time, time-frequency, frequency, and nonlinear domains were performed through various analysis techniques. This paper is organized as follows. Section II provides the procedure proposed in the current study. Section III reports the experimental results. Section IV discusses the obtained results and makes a conclusion.

II. METHODS

In this section, various analysis methods applied to EEG signals for autism diagnosis were described. Fig. 1 shows the framework adopted in this study.

A. Time and Morphological Analysis

EEG signals have specific temporal characteristics that may be affected by different neuropathologies. As a result, according to these temporal characteristics, it is possible to extract features based on the signal waveform over time, which can be used to distinguish between the two classes of autism and normal. These features are simple and require very little computation. The advantage of such features is increasing the speed of the designed system and the possibility of using it in real-time [33-35]. The following features in this category were calculated from EEG signals.

$$Absolute\ amplitude = \max|s(t)| \quad (1)$$

$$Peak - to - Peak = S_{max} - S_{min} \quad (2)$$

$$Negative\ Area = \sum_t 0.5(s(t) - |s(t)|) \quad (3)$$

$$Positive\ Area = \sum_t 0.5(s(t) + |s(t)|) \quad (4)$$

$$Total\ Absolute\ Area = |Negative\ Area| + Positive\ Area \quad (5)$$

$$Zero\ Crossing = \sum_t \delta_s(t) \quad . \quad \delta_s(t) = \begin{cases} 1 & s(t) \times s(t-1) < 0 \\ 0 & otherwise \end{cases} \quad (6)$$

$$Mean = \frac{1}{n}\sum_{t=1}^{n} s_t \quad (7)$$

$$Standard\ deviation = \left(\frac{1}{n}\sum_{t=1}^{n}(s_t - \bar{s})^2\right)^{\frac{1}{2}} \quad (8)$$

$$Energy = \sum_t |s(t)|^2 \quad (9)$$

$$Skewness = \frac{E[(S-\mu)^3]}{\sigma^3} \quad (10)$$

$$Kurtosis = \frac{E[(S-\mu)^4]}{\sigma^4} \quad (11)$$

where s(t) is the time series under analysis, n is the number of data points, μ is the mean of the time series, σ is the standard deviation, and E denotes the expectation operator.

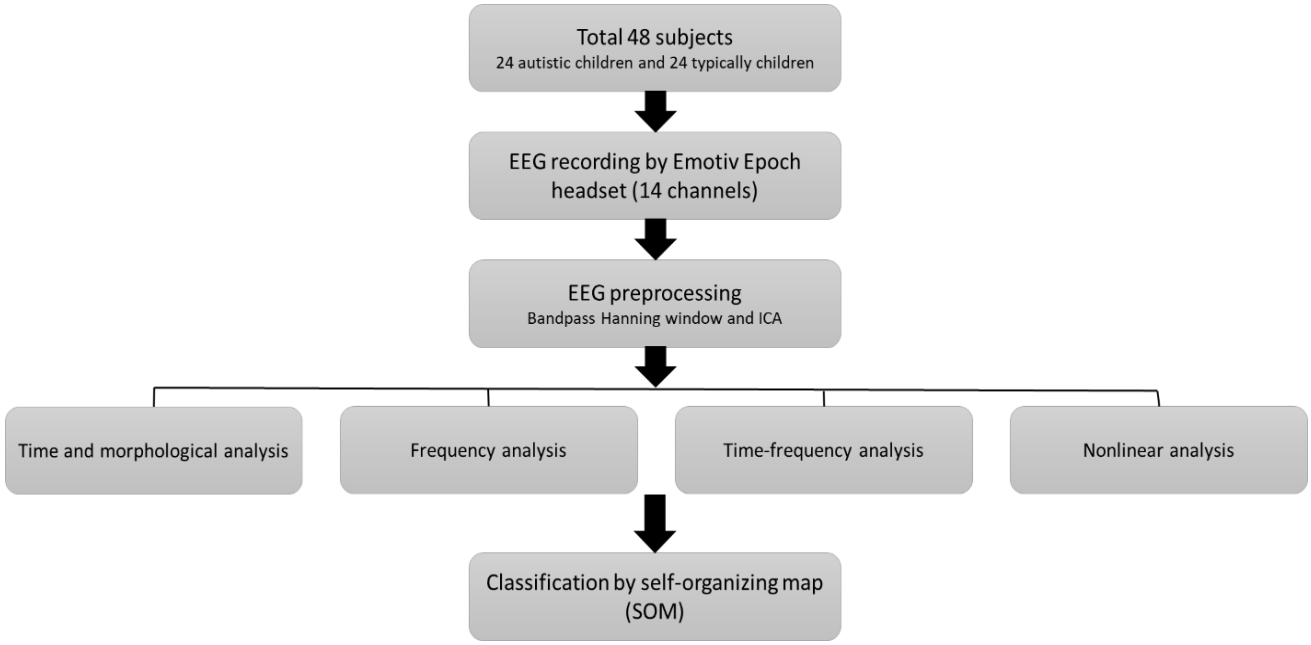

Fig. 1. Adopted framework in this study for EEG classification of autistic children and typically children.

B. Frequency Analysis

Frequency features actually represent the rate of change in the signal. Methods such as the Fourier transform are used to convert the signal from the time domain to the frequency domain. Here, the Welch method was utilized to extract EEG sub-bands, including delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), sigma (12-16 Hz), beta (16-30 Hz) and gamma (30-45 Hz). This method is Fourier transform-based algorithm to estimate the power spectral density. After signal sub-bands extraction and power spectrum density estimation, we calculated mean, standard deviation, skewness, kurtosis, absolute power and relative power from each sub-band as frequency features.

C. Time-Frequency Analysis

We utilized this type of analysis to assess signals in the time and frequency domains concurrently. For this purpose, wavelet transform was used, which provides a time-frequency representation of EEG signals with good frequency and time localization. This technique decomposes time series into shifted and scaled versions of the basic wavelet function. The wavelet function can be written as:

$$\psi_{a.b}(t) = 2^{a/2}\psi\left(2^{a/2}(t-b)\right) \quad (12)$$

where ψ(t) denotes the wavelet function, a is the scale parameter, and b is the shift parameter. The discrete version of this algorithm decomposes EEG signals into high- and low-frequency components at each level, known as detail and approximation coefficients [19]. In the current work, the Haar wavelet was employed to represent the time-frequency sub-components of the signals. After calculating the detail and approximation coefficients, we calculated the mean, standard deviation, variance and entropy as time-frequency features.

D. Nonlinear Analysis

Due to the nonlinear characteristics of EEG, nonlinear analyzes may reveal more details about the neuropathological mechanisms involved in autism. In the current study, we tried to calculate various nonlinear features for the signals, including large Lyapunov exponent, Lempel-Ziv measure, approximate entropy, sample entropy, Higuchi fractal dimension, and detrended fluctuation analysis. In this subsection, the mathematical notation of these nonlinear features was explained.

1) Large lyapunov exponent: This feature is a chaotic concept to assess the trajectory divergence in dynamical systems. Lyapunov exponent determines the exponential divergence rate between the two adjacent trajectories. The mathematical notation of this exponent can be written as:

$$\lambda = \frac{1}{n}\ln\left(\frac{d_n}{d_0}\right) \quad (13)$$

where d_n and d_0 denote the divergence/distance between sequential data points in the n^{th} and initial times, respectively.

2) Lempel-Ziv measure: It is a complex feature to estimate new paradigms in EEG signals. This method converts a signal to a binary one by median thresholding and scans the binary signal for new subsequences in sequential symbols [36].

$$LZ = \frac{\log_2(n)\cdot c(n)}{n} \quad (14)$$

where n is the number of data points and c(n) denotes the number of new subsequences.

3) Approximate entropy: It is a measure to estimate the randomness of EEG fluctuations over time.

$$ApEn(m.r.N) = \ln\left[\frac{C_m(r)}{C_{m+1}(r)}\right] \quad (15)$$

where $C_m(r)$ denotes the repeating paradigms of length m in a signal of N data points according to the similarity index r. In this work, we set m = 2 and r = 0.2 standard deviation of EEG signals [37].

4) Sample entropy: Sample entropy: It is a modified algorithm of approximate entropy that reduces the self-matching bias in the entropy calculation [38]. This algorithm depends on the length of the data and yields relatively consistent results in various conditions.

$$SampEn(m.r.N) = -\ln\left(\frac{A^m(r)}{B^m(r)}\right) \quad (16)$$

where r, m and N indicate tolerance, embedding dimension and the number of samples, respectively. $B^m(r)$ represents the probability that two series of data samples of length m have a distance smaller than the tolerance r, and $A^m(r)$ indicates a similar probability for two series of data samples of length m+1.

5) Higuchi fractal dimension: Consider a time series S(N) = S(1), S(2),…,S(N) as an input. Higuchi algorithm builds a new time series based on S(N) as follows:

$$S_m^k = \left\{S(m).S(m+k).S(m+2k)\ldots.S\left(m+\left\lfloor\frac{N-m}{k}\right\rfloor k\right)\right\}.\ for\ m = 1.2.3\ldots.k \quad (17)$$

where m is the first sample of the time series and $\left\lfloor\frac{N-m}{k}\right\rfloor$ represents the integer part of the series. Length $L_m(k)$ for S_m^k is obtained by:

$$L_m(k) = \frac{\sum_{i=1}|S(m+ik)-S(m+(i-1)k|(N-1)}{\left\lfloor\frac{N-m}{k}\right\rfloor k} \quad (18)$$

where N represents the number of total samples in the time series and $\frac{(N-1)}{\left\lfloor\frac{N-m}{k}\right\rfloor k}$ represents the normalization coefficient. The total mean length, L(k), is calculated for k_1 to k_{max} for all k.

6) Detrended fluctuation analysis: The DFA criterion is used to reveal the correlation of the time series with itself in the long-term time range [39]. To calculate the DFA in the time series, it must first be aggregated according to the following relationship.

$$y(k) = \sum_{i=1}^{k}[x(i) - x_{average}] \quad (19)$$

Then y(k) is divided into equal segments of length n. One line fits each segment. This line is denoted by $y_n(k)$, and $y_n(k)$ is subtracted from y(k).

$$F(n) = \sqrt{\frac{1}{N}\sum_{k=1}^{N}[y(k) - y_n(k)]^2} \quad (20)$$

To obtain the DFA, one must obtain the equivalent of F(n) for a suitable number of n. Then its graph is drawn in a logarithmic scale, and the slope of the scaling area is introduced as DFA.

E. Classification

In the current work, the self-organizing map (SOM) method was used to classify features extracted from autistic and normal EEG. This method is a popular unsupervised neural network with many applications in prediction, classification and clustering problems [40]. In this algorithm, a vector of weights is defined for every neuron i. The dimension of this vector is equal to the dimension of the input data. Firstly, a winner neuron is specified by the following equation:

$$i^*(t) = argmin\{g_i(x(t))\} \ . \ g_i\big(x(t)\big) = \|x(t) - w_i(t)\| \quad (21)$$

where $w_i(t)$ is the weight vector that must be updated based on the following equation:

$$\Delta w_i(t) = \alpha(t)h(i^*.i;t)[x(t) - w_i(t)] \quad (22)$$

where h(.) denotes the neighborhood function with the following definition:

$$h(i^*.i;t) = \exp(-\|r_i(t) - r_{i^*}(t)\|^2/\sigma^2(t)) \quad (23)$$

$\|r_i(t) - r_{i^*}(t)\|$ defines the distance between i and i^*, σ(t) is the neighborhood radius, and α(t) is the learning rate parameter.

To be classified by SOM, the output neurons must be labeled. After training the SOM, a winner neuron is devoted to each training vector. Then, the label of each training vector is determined. Eventually, the label of the winner neuron is defined based on the most frequent class labels of the training vectors. In this work, the initial neighborhood parameter was defined as 3, which was reduced to 1 after 100 iterations. Moreover, α(t) was set at 0.8.

F. EEG Data

The data used in this study were recorded by the research team from 24 children with autism and 24 normal children. Participants ranged in age from 4-9 years, and all patients received a diagnosis of autism based on DSM-5 diagnostic criteria by experienced clinicians. The patient enrollment was administered in a psychiatric clinic. The research project was done in accordance with the principles of the Declaration of Helsinki (1996) and the current Good Clinical Practice guidelines. The goal and an overview of the project were characterized by the participants and their parents during the initial contact. For those who agreed to participate, all the necessary information was provided prior to signing written informed consent. Information about the subjects was utilized anonymously and for the purpose of the study.

EEG was recorded for 10-18 minutes for each participant in one session. Given the difficulties of working with autistic patients and the difficulties of recording EEG from these patients in the awake state, the Emotiv Epoch headset device was employed in this research. Since the Emotiv Epoch headset is a wireless EEG device, the signal recording was conducted in autistic patients more easily. This EEG device uses a Bluetooth module for wireless communication. The Emotiv Epoch headset and Software Development Kit include 14 electrodes (AF3, AF4, F7, F8, F3, F4, FC5, FC6, T7, T8, P7, P8, O1, O2 based on 10-20 international system) along with DRL/CMS references at P4/P3 locations. The sampling rate in this device is 128 Hz. The impedance of the electrode is reduced through saline liquid and alcohol pads. Emotive software was utilized to record EEGs and convert their format to MATLAB format.

After signal recording, in the signal pre-processing step, a band-pass Hanning window with a finite duration and frequency range of 1-45 Hz was applied to the EEGs through MATLAB software. Furthermore, electrode interpolation was done through adjacent channels for low-quality electrodes. EEGs were re-referenced to the common average and then were decomposed via independent component analysis. Components with motion and muscle artifacts were identified and were then eliminated according to time courses and frequency scalp maps. The cleaned components were reconstructed, and a 50-second cleaned EEG signal was prepared for each participant.

III. Experimental Results

After data conditioning, all mentioned analyzes were applied to EEG signals and different described features were extracted in both typically and autism groups. Fig. 2 shows an example of an EEG signal recorded from a child with autism before pre-processing. Fig. 3 shows the time-frequency representation of two channels, P7 and P8, for normal and autistic children obtained from wavelet analysis. As shown in this figure, there are clear differences in the frequency content of the EEG signals of normal and autistic children over time. In addition, Fig. 4 to 6 show the nonlinear features (i.e., sample entropy, DFA and Lempel-Ziv measure) extracted from EEG signals of normal and autistic children in the O1 channel. These graphs show that there is a clear difference between the nonlinear dynamics of the EEG signals of the two groups. The noteworthy point is that the values of nonlinear features in the normal group were generally higher than in the autism group.

In the next step, we tried to classify different features extracted from EEGs through various analyzes. In this step, the leave-one-subject-out cross-validation method was utilized to validate the efficiency of every analysis method as well as the performance of the SOM classifier for autism diagnosis. In this cross-validation method, a subject was left out to test, and the rest of the subjects were utilized to train the SOM. As a result, after implementing the 48 tests, the average accuracy was calculated over all the obtained accuracies. Specificities, sensitivities and averaged classification accuracies for each type of analysis are depicted in Table I. Accuracies of 92.31, 93.57, 95.63 and 97.10% were achieved through time and morphological, frequency, time-frequency and nonlinear analyzes, respectively. Indeed, the findings showed that nonlinear analysis could yield the best classification results (accuracy = 97.10%, sensitivity = 98.80% and specificity =

97.02%) in the EEG discrimination of autistic children from typical children through the SOM neural network.

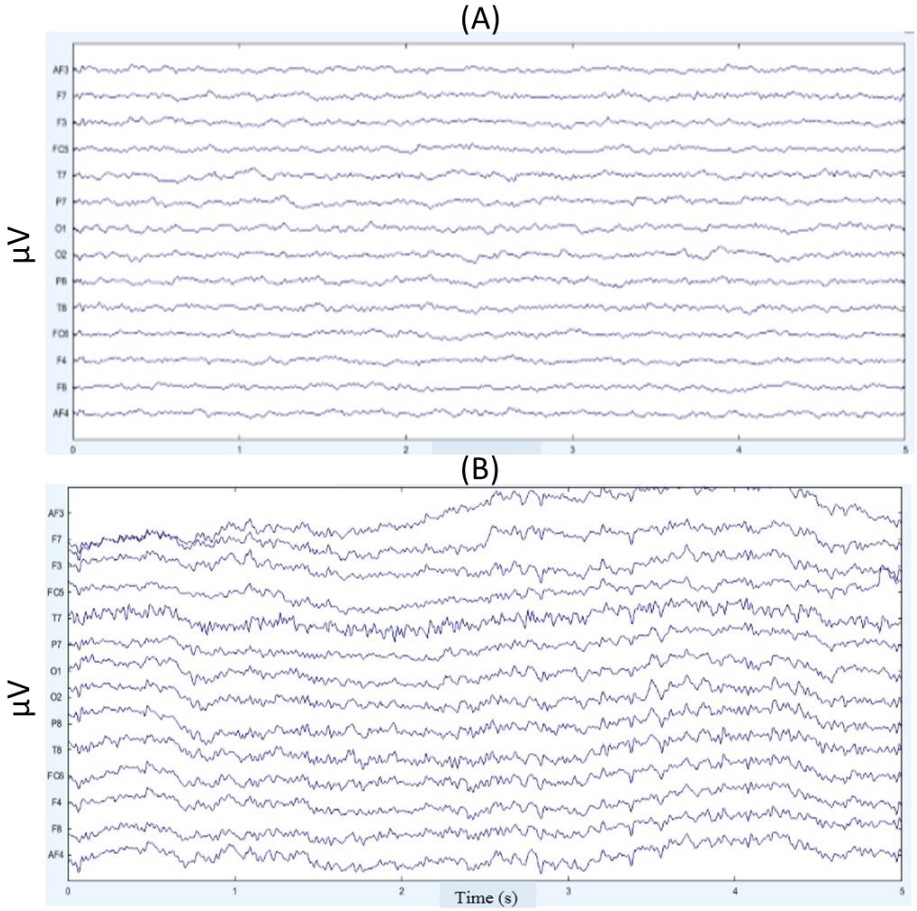

Fig. 2. An example of EEG signals recorded from (A) a healthy child and (B) a child with autism.

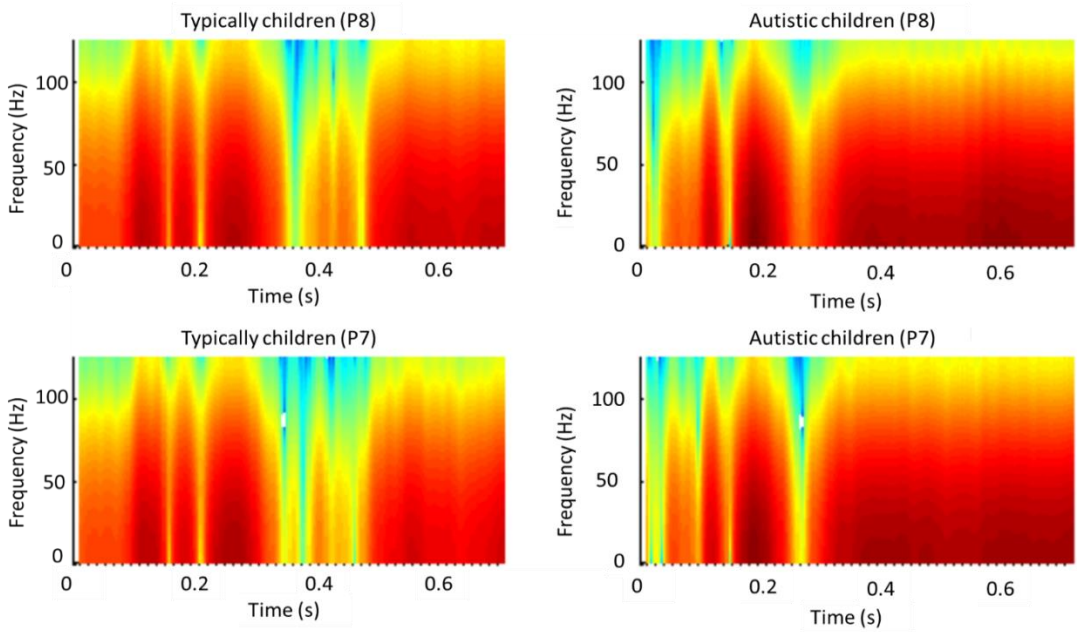

Fig. 3. Time-frequency representation of two channels, P7 and P8, for normal and autistic children.

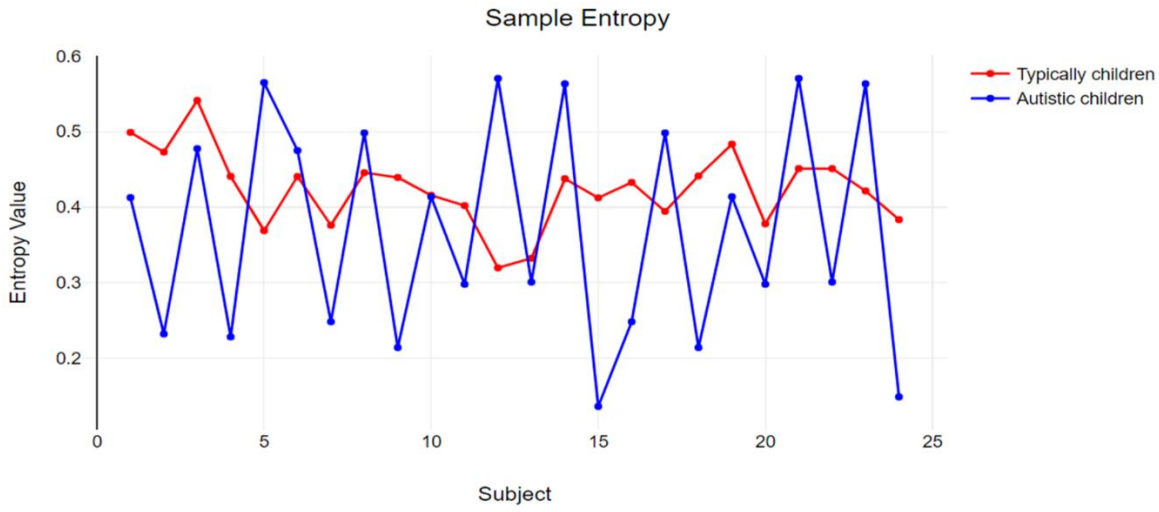

Fig. 4. Calculated sample entropy at the O1 channel for typical and autistic children.

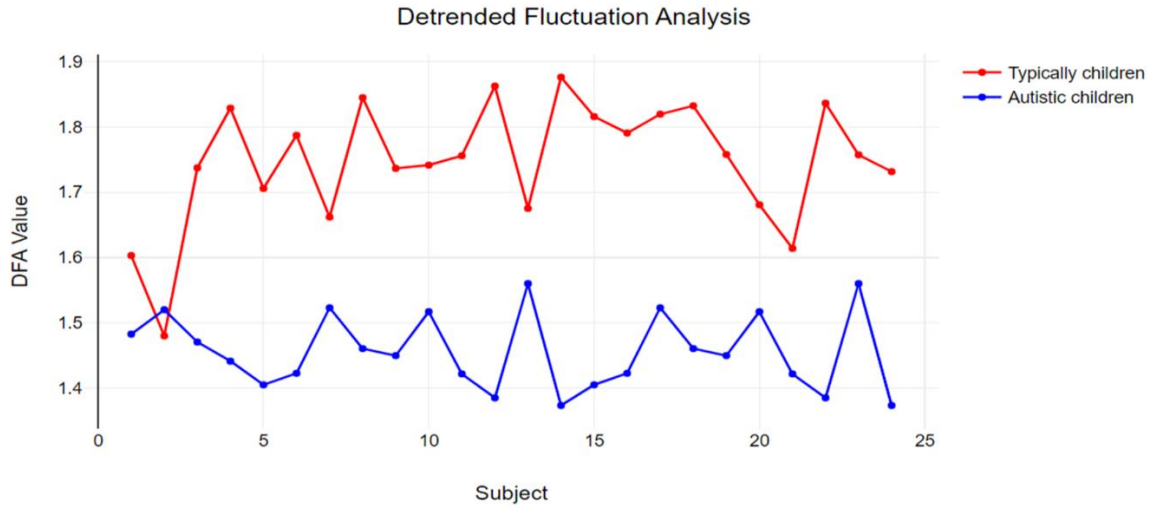

Fig. 5. Detrended fluctuation analysis at O1 channel for typically and autistic children.

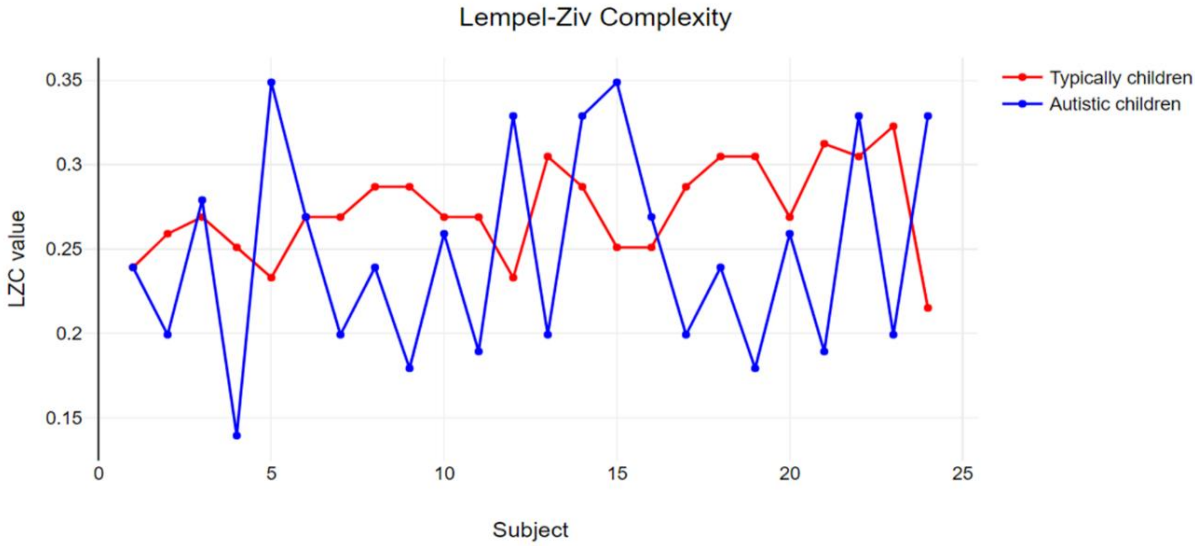

Fig. 6. Calculated Lempel-Ziv measure at O1 channel for typically and autistic children.

TABLE I. ACCURACY, SENSITIVITY AND SPECIFICITY FOR DIFFERENT ANALYZES USING SOM CLASSIFIER

Type of analysis	Accuracy (train) (%)	Accuracy (test) (%)	Sensitivity (%)	Specificity (%)
Time and morphological analysis	94.78 ± 4.25	92.31 ± 3.59	90.36	93.39
Frequency analysis	96.13 ± 3.36	93.57 ± 4.61	93.00	94.69
Time-frequency analysis	97.71 ± 2.06	95.63 ± 2.48	95.89	94.26
Nonlinear analysis	99.54 ± 2.14	97.10 ± 1.95	98.80	97.02

IV. DISCUSSION AND CONCLUSION

Autism is a neurodevelopmental condition that is related to different neural and neurotransmission impairments in various brain areas. These functional abnormalities of the brain are supposed to play a critical role in the neuropathology of autism [41, 42]. Therefore, the search for a reliable biomarker through EEG analysis is a hot topic in autism research. In the present study, we aimed to explore the different types of EEG analysis for feature extraction for autism diagnosis. For this purpose, time and morphological, time-frequency, frequency and nonlinear features were extracted from EEG signals of typical and autistic children at resting-state. The obtained findings revealed that nonlinear features achieved the best classification results for autism diagnosis. Indeed, the proposed nonlinear features integrated with the SOM classifier yielded an average accuracy of 97.10% in detecting autism cases, which is a good result for improving research achievements in this field. This type of quantitative analysis is more consistent with the nonlinear and chaotic properties of brain signals. This finding is in line with previous studies [43-47]. In other words, based on the findings of the present study, it is recommended that future studies focus more on various nonlinear EEG analysis methods and their optimization in order to diagnose autism. Since none of the previous EEG studies on autism have conducted a comparative study between different linear and nonlinear analysis methods, the findings of the present study as the first example in this field can be a roadmap for future research. However, this study, like many other studies, has limitations. The limited sample size is one of the important limitations of the current research, which reduces the generalizability of the obtained findings. In this study, only five nonlinear analysis methods were investigated, while there are many more nonlinear methods and future studies should investigate different methods. In addition, we only analyzed resting-state EEG, while other recording protocols may have helped to improve the results.

Table II summarizes the characteristics of the studies on autism diagnosis using EEG analysis and machine learning. As shown in this table, previous studies used different methods for feature extraction from EEG signals, from linear frequency analysis to various nonlinear approaches such as recurrence quantification analysis and fractal dimension. The obtained results showed that future studies should work on the nonlinear dynamics of EEG signals and the combination and optimization of nonlinear features for autism diagnosis. Support vector machine (SVM) is the most frequently used classifier in these works to classify EEG features. Moreover, some studies used neural networks such as radial basis function and probabilistic neural networks for this purpose. Most studies have achieved an autism classification accuracy of 90% or higher, which shows the high potential of this approach for the objective diagnosis of autism. However, most of these studies suffer from important limitations that reduce their generalizability. Small datasets, complex implementation processes and low accuracy are some of these limitations. In addition, the results obtained in the present study compared to previous works show that the nonlinear approach adopted along with the SOM classification has a very good ability to diagnose autism.

TABLE II. CHARACTERISTICS OF THE STUDIES ON AUTISM DIAGNOSIS USING EEG ANALYSIS AND MACHINE LEARNING

Study	Population	Feature Extraction	Classifier	Results
Ahmadlou et al. (2010) [48]	Nine autistic and eight non-autistic children	Higuchi and Katz fractal dimension, wavelet-chaos neural network	Radial basis function (RBF)	Accuracy = 90%
Bosl et al. (2011) [49]	46 infants at high risk for autism and 33 healthy controls	Modified multiscale entropy	Support vector machine (SVM)	Accuracy = 90%
Ahmadlou et al. (2012) [28]	Nine autistic and nine healthy children	Fuzzy synchronization likelihood	Enhanced probabilistic neural network	Accuracy = 95.5%
Sheikhani et al. (2012) [50]	17 autistic children and 11 healthy children	Short-time Fourier transform	KNN	Accuracy = 96.4%
Jamal et al. (2014) [51]	12 subjects in each autism and normal group	Brain connectivity	Linear discriminant analysis (LDA) and SVM	Accuracy = 94.7%
Eldridge et al. (2014) [52]	19 autistic children and 30 healthy children	Modified multiscale entropy	SVM, Logistic regression, Naïve Bayes	Accuracy = 79%
Bosl et al. (2018) [26]	99 infants with an older sibling diagnosed with autism	Wavelet analysis, Sample entropy, DFA, Recurrence quantitative analysis	SVM	Accuracy = 95%
Heunis et al. (2018) [45]	Seven autistic children and seven non-autistic children	Recurrence quantitative analysis	SVM	Accuracy = 92.9%
Kang et al. (2018) [53]	52 autistic children and 52 non-autistic children	Fast Fourier transform	SVM	Accuracy = 91.38%

Haputhanthri et al. (2019) [27]	Ten autistic children and five non-autistic children	Wavelet analysis	Logistic regression, SVM, Naïve Bayes, Random forest	Accuracy = 93%
Pham et al. (2020) [29]	40 autistic children and 37 healthy children	higher-order spectra (HOS) bispectrum	LDA, SVM, k-nearest neighbor (KNN), probabilistic neural network (PNN)	Accuracy = 98.7%
Baygin et al. (2021) [30]	61 autistic subjects and 61 healthy subjects	one-dimensional local binary pattern and deep features of the spectrogram images	SVM	Accuracy = 96.44%
Alotaibi et al. (2021) [31]	12 autistic children and 12 healthy children	Brain connectivity	SVM	Accuracy = 95.8%
Our proposed approach	24 autistic children and 24 healthy children	Time, time-frequency, frequency, and nonlinear analysis	Self-organizing map (SOM)	Accuracy = 97.1%

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