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Extracting Salient Features for EEG-based Diagnosis of Alzheimer's Disease Using Support Vector Machine Classifier

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ABSTRACT

Alzheimer's disease (AD) is one of the most common and fastest growing neurodegenerative diseases in the western countries. Development of different biomarkers tools are key issues for the diagnosis of AD and its progression. Prediction of cognitive performance of subjects from electroencephalography (EEG) and identification of relevant biomarkers are some of the research problems. Although EEG is a powerful and relatively cheap tool for the diagnosis of AD and dementia, it does not achieve the standards of clinical performance in terms of sensitivity and specificity to accept as a reliable technique for the screening of AD. Hence, there is an immense need to develop an efficient system and algorithms for diagnosis. Accordingly, the objective of this research paper is to analyze different features for the diagnosis of AD to serve as a possible biomarker to distinguish between AD subject and normal subject. The research is carried out on an experimental database. Three different features such as spectral-, wavelet-, and complexity-based features are computed and compared on the basis of classification accuracy obtained. The classification is carried out using support vector machine classifier giving 96% accuracy on complexity-based features and increased performance in terms of sensitivity and specificity. The results show the improved performance in the diagnosis of AD. It is observed that the severity of AD is depicted in EEG complexity. These features used in research work can be considered as the benchmark for AD diagnosis.

KEYWORDS

Alzheimer's disease; Electroencephalography; Preprocessing; Feature extraction; Support vector machine

1. INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disease in which electrical activities of the brain become slower than normal subjects. These abnormalities observed in AD patients are detected using electroencephalography (EEG) that records the electrical activity of the brain. It is one of the well-established and well-known modalities for measuring the electrical activity generated by the population of neurons of the cerebral cortex. EEG signals are non-stationary signals in nature and hence sometimes the disease symptoms are not easily observed. Due to this, EEG signals are recorded for several hours to detect the abnormalities like dementia, AD, and any more. Recording of this EEG patterns for several hours creates a large data. Therefore, the task of detection of abnormalities from EEG becomes tedious and time-consuming for medical professionals. Thus, there is a need for computer-based automated techniques for the diagnosis of AD from large volume of medical data. The bioelectric cells are recorded in a non-invasive manner by a set of electrodes placed over the head of the subject. Basically, EEG is a multivariate signal acquired over many channels (20–128) with various sampling rates (from 200 to 1000 Hz) depending on the clinical applications [1,2]. This technique requires a lot of time since it generates a huge data which is to be stored and transmitted. EEG is one of the key diagnostic tools for neurologists, clinicians, and doctors. Along with these applications, EEG signals are widely used in Brain Computer Interface (BCI) applications [3].

Many research findings have highlighted the potential of EEG for the diagnosis of AD in recent years. Since, EEG recording systems are very cheap and mobile. In future, EEG technique can be used as a tool for screening large population with the risk of different neurodegenerative disorders such as AD, epilepsy, Huntington's disease, and much more. There are numerous dynamical changes of EEG related to normal aging, and thus, this reflection can be easily seen by the use of EEG [4]. Recent research findings have proved the EEG complexity analysis can be used to diagnose AD in early stage [5].

AD is the most common form of dementia, sixth leading cause of death in the United States. It is a neurodegenerative disease which is characterized by progression and severe memory loss with cognitive impairment. About more than 10% of Americans over an age of 65 years suffer from AD and it is predicted that the prevalence of

AD will increase in next 50 years [6]. Currently, there is no known medicine for curing AD but a number of medications are believed to delay the symptoms and cause of the disease. The diagnosis of AD is commonly carried out using laboratory tests, medical history, and mental status examinations such as Mini Mental State Examination (MMSE), clinical dementia rating (CDR), and most commonly used neuroimaging techniques such as fMRI, PET, and SPECT [7–9]. In [7] researchers used displacement field method for AD diagnosis using MRI images. The advantages of this method are (i) it is a twofold method; (ii) it easily locates the affected regions in the brain; and (iii) it is easy for classification purpose. However, this clinical assessment technique requires experienced clinicians and lengthy sessions and therefore they are non-specific, costly, and time-consuming [6]. In developing countries, i.e. medium- and low-income countries, these limitations are further worse and thus it is difficult for early diagnosis of the disease.

The progression of AD is categorized in three different stages: the first stage is termed as mild or moderate AD and the last stage is termed as severe AD. There is also mid-stage called mild cognitive impairment (MCI) or predementia which characterizes a population of elderly subjects who are compromised in their daily living and are potentially at a risk of developing AD. Comparing and referring previous research studies, 6%–25% of people are affected by MCI progresses to AD every year. Diagnosis of MCI and mild AD is difficult because most of the symptoms are often neglected as normal consequences of aging [3,5,10,11]. Different tests such as physiological evaluations (MMSE), blood tests and spinal fluid tests, neurological examinations, and imaging techniques (neuroimaging tools) are extensively used for AD diagnosis. But, EEG in recent research is observed as the potential biomarker for AD. Quantitative EEG has emerged as a promising technique for the diagnosis of AD. EEG signal reflects functional changes in the cortical regions and thus can be used to reveal the diagnosis of neuronal degeneration and functional impairment. Recent research has demonstrated the use of EEG analysis in AD diagnosis by the use of different linear and non-linear features. For instance, apparent changes are observed in power spectrum of EEG, along with this reduced spectral coherence between two brain regions is also observed. Reduction in the non-linear connection between cortical regions which shows a decreased signal complexity of EEG signals in case of AD is also observed. Many technical measures have been reviewed in the literature to provide diagnostic information about AD. The use of EEG in early diagnosis of AD is supported by observing various abnormalities such as [12–14]:

a. Slowing of EEG signals: It is associated with the increase in relative power of the low-frequency bands (delta, 0.5–4 Hz, and theta, 4-8 Hz), along with the reduction in power of the high-frequency bands.
b. Reduced complexity: It is associated with an increase in regularity of the signal which is measured with some non-linear measures such as sample entropy, approximate entropy, Tsallis entropy, multiscale entropy Lempel-Ziv entropy, and much more. Basically, it is observed that EEG signals of AD patients are more regular as compared to normal subjects. But, till present no study has predicted this biological phenomenon.
c. Loss of synchrony measures: Synchrony refers to simultaneous appearance of rhythmic distinct patterns over the various regions of head; either unilateral (on the same side) or bilateral (both sides of brain regions). The statistical independence in EEG recordings around different regions or channels seems to be low in case of AD patients. A variety of different synchrony measures have been reported in the literature such as Granger causality, Pearson correlation coefficient, phase synchrony, stochastic event synchrony, and much more for measuring the loss of synchrony.

But, these effects may tend to vary from patient to patient, which makes the diagnosis of AD a difficult task. So, the main objective is to develop a suitable biomarker for the diagnosis of AD which can predict the conversion from MCI subject to AD.

In this paper, we investigate the use of different linear and non-linear features for the diagnosis of AD. Along with the proposed features, their effects on EEG signals of AD patients are discussed. In the proposed research work, the goal is also to improve the diagnostic accuracy for classification between two groups.

2. MATERIALS AND METHODS

2.1 Participants

Data used in the study was obtained from Smt. Kashibai Navale General Hospital and Research Centre, Pune (India), consisting of both AD patients and healthy controls. Patients were selected from consecutive, community residing elderly persons 55–80 years of age with the report of a decline in cognitive as well as behavioural functioning. Diagnosis of the patients was made by

experienced neurosurgeons based on Indian version of *Mini Mental State Examination (MMSE) and Clinical Dementia Rating (CDR)*. Multichannel EEG recordings were obtained from 100 participants who were resting with their eyes closed separated into two groups. The first group composed of 50 subjects; 30 males and 20 females (mean age: 60 years, 7.92 SD), with an indication of functional cognitive and behavioural decline over the last 12 months. The second group composed of 50 participants of normal subjects consisting of 35 males and 15 females (mean age: 60.5 years, 7.94 SD), with no indication of functional cognitive decline. In addition to the AD cohorts, patients belonging to the first group were having functional, behavioural, and cognitive decline over the last 12 months. Patients belonging to the abnormal group were also checked for diabetes, kidney disease, thyroid disease, lung and liver disease, or vitamin B12 deficiency, as these can also cause cognitive decline. The EEG recordings and the study were approved by the ethical committee of the hospital and participants as well as AD patients.

2.2 EEG Data Acquisition and Recording

EEG signals were recorded from RMS (Recorders and Medicare Systems Prt. Ltd.) EEG machine with 12-bit resolutions and a sampling rate of 1024 Hz. The impedance of the machine was maintained below 10 Mohms and the electrodes (Referential Montages) were placed according to the International 10–20 systems as recommended by the American EEG Society. Biauricular referential electrodes were also attached as they also play a crucial role in examining the EEG signal of AD patients. The power grid interference was eliminated by low-pass filtering. As there is evidence of an interhemispheric disconnection in AD and dementia, a virtual hemisphere bipolar montage is also taken into consideration. The obtained signals are termed as "bipolar signals". The bipolar signals recorded in the study were Fp1-Fp2, F3-F4, F7-F8, C3-C4, T3-T4, P3-P4, T1-T6, and O1-O2. During EEG examination and recordings, patients were awake and relaxed with the eyes closed. The artefacts of EEG signals such as muscle activity and eye blinking were removed manually. The artefacts in this method were removed by experts on basis of the visual inspection. The experts observed the EEG signal and eliminated the unwanted parts in it by visual inspection on the basis of following criteria: (i) abnormal high amplitude of EEG signal and (ii) abnormal wave shape of the signal such as drifts, eye blinks, and sharp waves. As this artefacts removal is done manually, no computational method is required.

3. PREPROCESSING

EEG signals are basically non-stationary, noisy, and susceptible to blinking effects, eye movements, and muscle activity artefacts which worsen the performance of AD diagnosis. To overcome such artefacts and certain problems associated with recordings, preprocessing step is essential. Many research works have focused on artefact-free EEG segments for analysis which are commonly termed as "epochs". They are obtained by visual inspection by expert clinicians. It requires human experts and thus makes it low cost which introduces possible biases and errors. To overcome this problem, Artefact Removal Algorithms (AAR) were used. These are further classified as "semi-automated" and "automated" depending on the need of the human intervention. Artefact removal algorithm such as independent component analysis (ICA) is considered as semi-automated since components of signal associated with artefacts are manually identified by human and are then removed before the new signal is reconstructed. In this paper, both semi-automated as well as automated artefact removal techniques are discussed and used. Blind source separation (BSS), wavelet-based denoising, and wavelet-enhanced independent component analysis (wICA) are some examples of automated artefact removal techniques. Since, they do not require the human intervention for manually removing the unwanted part of the component in the signal. For the diagnosis of any disease using EEG, the advantages and drawbacks of the artefact removal techniques are unknown. The reason is certain algorithm may remove the important part of the signal which can be needed for accurate diagnosis [15]. In this paper, a semi-automated method such as ICA and automated artefact removal method such as wavelet-based denoising techniques are used for artefact removal depending on the state-of-art methods applicable in research work and database used. Let us discuss the above methods.

3.1 Independent Component Analysis

ICA is the effective tool used for obtaining noise-free signal. The important use of this technique is to perform the dimensionality reduction and separate the relevant information of the signal. EEG signals consist of high-dimension data, in such cases ICA helps out for obtaining noise-free signals to increase the quality of signal. ICA is a statistical technique in which the observed random data is linearly transformed into components which are maximally independent from each other and have "interesting" distributions [16]. In general, mathematical formulation of ICA is given by,

$$x = As + n \tag{1}$$

where A is the *mixing matrix*, x is the sensor vector, s is the source vector, and n is the noise, which is to be eliminated by filtering. It is assumed that the component variables used are statistically independent of each other and independent components must have non-Gaussian components.

3.2 Wavelet-based Denoising

In the present study, we have used one-dimensional, wavelet-based denoising technique for preprocessing the input signal. In basic terms, the model for noisy signal is given by,

$$s(n) = f(n) + \sigma e(n) \tag{2}$$

where n is equally spaced, $e(n)$ is the Gaussian white noise, and σ is the noise level whose value is considered to be 1. The main objective of this denoising technique is to suppress the noise part of the signal and to recover the original signal $f(n)$. The denoising procedure requires three steps which are decomposition, detailed coefficients thresholding, and reconstruction. In decomposition, a certain wavelet is chosen at level N and it is then decomposed at that particular level. Then the particular signal is reconstructed depending on the corresponding original approximation coefficients and modified detailed coefficients. In present research, we have not considered the noise influences from other channels; since our intention was to get filtered EEG signal for analysis. In the present research work, Daubechies wavelet (db3) at level 3 and soft thresholding technique are used for smoothing the given EEG signal. The reasons behind using Daubechies mother wavelet are (i) they possess wide smoothing characteristics; (ii) they are well understood; and (iii) the changes in the EEG signals are easily seen [17–20]. Based on the above reasons, we have used the wavelet-based denoising technique for signal preprocessing.

4. FEATURE EXTRACTION

EEG signal is processed both in time and frequency domain at a clinical level. It is required to analyze the signal in both time as well as frequency domain since EEG signal is non-stationary and brain rhythms exist in time domain. In this research work, analysis of EEG data is done in time, frequency, and time–frequency domain. The algorithms proposed in this research work and data analysis are implemented using MATLAB software. In this section, we discuss the theory of each feature such as spectral-, wavelet-, and complexity-based features in each subsection. In this research work, these features are used which provide comparatively better results when implemented on EEG signals for the diagnosis of AD and to conclude which of the proposed features provides better results in terms of classification accuracy.

4.1 Spectral-based Features

To investigate the slowing effect in EEG signal of AD patients, computation of relative EEG power in each EEG frequency bands is done. It is observed that relative power is high in low-frequency bands (delta and theta bands), i.e. frequency range between 0.5 and 8 Hz. This is termed as slowing of EEG signal [21,22]. This irregularity of EEG signal is quantified by the standard measure such as Lempel Ziv complexity [20,22]. EEG spectrum is helpful in understanding the brain activity. EEG signal is basically divided into specific frequency bands such as: 0.5–4 Hz (delta), 4–8 Hz (theta), 8–12 Hz (alpha), and 30–100 Hz (gamma). Neurodegenerative diseases such as MCI and AD affect the spectrum of EEG signal. Recent studies have shown that AD and MCI cause EEG signal to slow down. It is seen that in case of EEG signals of AD patients power in low-frequency bands (delta and theta bands, 0.5–8 Hz) is increased, whereas power in high-frequency bands (alpha and beta bands, 8–30 Hz) is decreased.

The Power Spectral Density (PSD) function helps in the assessment of spectral characteristics of EEG activity of each epoch. It is computed as Fourier transform of its autocorrelation function [23]. The PSD is normalized by the total power in the frequency range of 0.1–40 Hz to obtain a normalized PSD [23]. It is given as,

$$\mathrm{RP} = \sum_{f\mathrm{low}}^{f\mathrm{high}} \mathrm{PSD}_n(f) \tag{3}$$

The above equation is used for calculating the power in each band of the signal.

4.2 Wavelet-based Features

Decomposition of EEG signals is computed by means of wavelet technique. We have decomposed the signal at five levels for separating the signal into different bands of frequency. Since, we require only five bands of EEG signals for analysis in the present study. In such a case, for certain coefficients mean power and variance values are computed for those particular coefficients. In case of AD patients, it is observed that the value of mean and variance reduces as compared to normal patients [24].

Mean and variance are given by,

$$\text{Mean} = \frac{1}{n} \sum_{i=0}^{n-1} x_i, \quad i = 1 \ldots N \tag{4}$$

where x_i's are the computed coefficients of the signal at each sub-band, n is the number of coefficients at each band, and N is the number of bands.

Similarly, variance is calculated by using the following formula,

$$\text{Var}\ (X) = \frac{1}{n} \sum_{i=1}^{n} (x_i - \mu)^2 \tag{5}$$

where μ is the expected value. The above calculated values of mean and variance are taken for classification purpose.

These features depict the reduced complexity in case of EEG signals of AD patients. Hence, we used these features for analysis.

4.3 Complexity-based Features

After the filtering and preprocessing of EEG signals, EEG signals were divided into samples of 3–5 seconds. Jarque–Bera test was used for testing the signal for normality condition per epoch [25,26].

The Jarque–Bera statistical test is given by,

$$\text{JB} = \frac{n}{6}\left(s^2 + \frac{(k-3)^2}{4}\right) \tag{6}$$

where n is the sample size, s is the sample skewness, and k is the sample kurtosis. The features of the epochs were computed depending on the values of h and p, which denotes the normality conditions. The statistical parameters were also tested and p – values are also calculated. Let us now discuss the different complexity based features used in the feature extraction.

4.3.1 Spectral entropy

Spectral entropy (SE) indicates the amount of irregularity and disorder in the spectrum of EEG. Higher complexity is achieved if higher amount of SE is observed in the spectrum of signal [26]. It is computed in following manner:

1. For the given signal $x(t)$, compute $S(f)$ PSD considering Fourier transform of its autocorrelation function of the signal $x(t)$.
2. Depending upon the frequency of interest, extract the Power in the spectral band from 0.5 to 30 Hz.
3. After the calculation of spectral band power, normalize the power in the given band of interest.
4. SE is computed by using formula,

$$\text{SE} = \sum_{f=0.5}^{40} S(f) * \ln \frac{1}{s(f)} \tag{7}$$

4.3.2 Spectral centroid

Spectral Centroid (SC) measures the shape of the spectrum. Higher value of SC equals the large amount of energy of the signal concentrated within higher frequencies specifically in between 12 and 30 Hz [26]. Basically, it measures the spectral shape and position of the spectrum. It is computed as follows:

a. Let $x_i(n)$, $n = 0,1,\ldots, N-1$ be the sample of the ith frame, with $X_i(k)$, $k = 0, 1, \ldots, N-1$ being the discrete Fourier transform (DFT) coefficients of the sequence.
b. Compute the SC of the ith frame as:

$$C\ (i) = \frac{\sum_{k=0}^{N-1} k\,|\,X_i(k)\,|}{\sum_{k=0}^{N-1} |\,X_i(k)\,|} \tag{8}$$

4.3.3 Spectral roll-off

Spectral roll-off (SR) represents the frequency below which a certain percentage (usually 80%–90%) of the magnitude distribution of the spectrum is concentrated in the spectrum. [26]. It is computed as follows:

a. Let $x_i(n)$, $n = 0, 1, \ldots, N-1$ be the samples of its frames, and $X_i(k)$, $k = 0, 1, \ldots, N-1$ are the corresponding DFT coefficients of each frame.
b. Compute the SR as the sample that satisfies,

$$\sum_{k=0}^{k(i)} |\,X_i(k)\,| \;=\; \frac{P}{100} \sum_{k=0}^{N-1} |\,X_i(k)\,| \tag{9}$$

where the range of parameter P is taken between 80 and 100.

4.3.4 Zero crossing rate

The rate at which the signal changes its sign is termed as zero crossing rate (ZCR). It denotes the number of times the signal changes its value, from positive to negative and vice versa, divided by the total length of the frame [26]. ZCR for each frame is computed as:

a. Let $x(n) = 0,1, \ldots N-1$ be the samples of the frame.

b. ZCR for any frame is computed as:

$$Z\ (i) = \frac{1}{2N}\ \sum_{n=0}^{N-1} |\ \mathrm{sgn}[x_i(n)] - \mathrm{sgn}[x_i(n-1)]\ | \tag{10}$$

where

$$\mathrm{sgn}[x_i(n)] = \begin{cases} 1, & x_i(n) \geq 0 \\ -1, & x_i(n) < 0. \end{cases}$$

We have seen that EEG signals of AD patients exhibit slowing effect. Hence, the computed ZCR values tend to be less complex since the signal does not change its sign due to this effect.

5. METHODOLOGY

The methodology consists of different parameters and methods taken for study. The brief details of the proposed methodology are explained in this section. There is an immense need for the development of new techniques for early diagnosis of AD, and in this regard a number of different brain imaging techniques facilitate providing noninvasive ways for the visualization of brain atrophy. The earlier diagnosis of any disease is not only challenging but is also necessary for further treatment of the patient. The detailed block diagram used in research work is shown in Figure 1.

The EEG-based AD diagnosis is followed by suitable methodology. Initially, EEG signal from patient is acquired through the EEG electrode. Basically, 10–20 electrode placement system is used for acquiring the EEG signal. In order to enhance the EEG signal, ICA is used to clean the signal. Wavelet-based denoising is also done in order to enhance the quality of the signal for feature extraction. Once the signal is processed and interfaced with computer, analysis of signal is done by using standard tools such as MATLAB. By using suitable feature extraction methods, various algorithms are used for differentiating the signal. The features extracted are given as the input for classification purpose. Various classifiers are available in domain of pattern recognition and machine learning. Linear discriminant analysis and support vector machine are some of the classifiers that can be used for diagnosis. Figure 1 shows the methodology used for early diagnosis of AD using EEG signals. Along with this, the EEG signals of temporal, frontal, central, and parietal lobes of both controls and AD patients are taken into consideration for the study. In short, the first phase of the proposed approach prepares the input signal for further analysis of the signal. The second phase includes the preprocessing of the EEG signals to remove unwanted parts from signals which include the noise content removal such as eye blinking activity and muscle activity. Features are extracted in the third phase of the process. The fourth and final phase classifies the signal as belonging to a normal subject group or AD group. The computation of different features is explained in the preceding subsection.

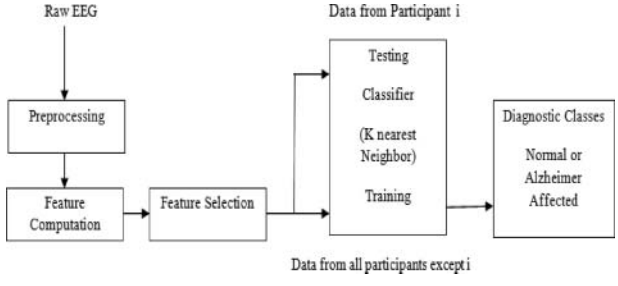

Figure 1: System methodology [27,28]

5.1 EEG Relative Power

The spectral power features, i.e. relative EEG power can be computed for each epoch for different EEG electrodes which can be considered for analysis. In this present study, we have computed the same for different EEG electrodes such as T3 (temporal), F3 (frontal), C3 (central) and P4 (parietal). The following algorithm is used for the computation of power features in each sub-band of EEG signals.

Step. 1: Load the sample data of EEG signal.
Step. 2: Declare the sampling frequency and obtain the length of the EEG signal.
Step. 3: Declare the wavelet decomposition function (Daubechies wavelets).
Step. 4: Obtain different EEG bands.
Step. 5: Obtain the frequencies of EEG bands using detrend and FFT functions.
Step. 6: Compute the power in each band of EEG signal using the power density function.
Step. 7: Stop.

From the above algorithm, it gives the idea of calculating the power-based features in each sub-band of each signals. First, the filtered EEG signal is decomposed into various bands using the wavelet decomposition tool. In this process, "Daubechies" mother wavelet (db2, level 5) is used for decomposing EEG signal into five sub-bands [29]. The reasons behind the use of Daubechies wavelet is discussed in Section 3.2. The EEG signal is decomposed using the above Daubechies wavelet at level 5.

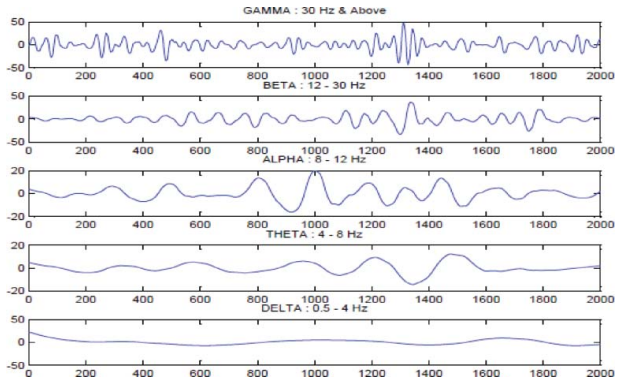

Figure 2. Classification of EEG signals into different sub-bands

Accordingly, EEG signal is decomposed into five bands with the following frequencies: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz). Further, the power in each sub-band of the EEG signal is computed by means of power density functions. Figure 2 shows the classification of EEG signal in various bands. The relative EEG power is computed as in Equation (3).

5.2 Wavelet-based Features

The decomposed EEG signal at a particular level is selected. The wavelet-based features include the calculation of mean and variance of each coefficient at a certain level. The values of mean and variance are calculated as given in Equations (4) and (5).

5.3 Complexity-based Features

In present work, computation of four different complexity-based features namely SE, SR, SC, and ZCR are computed for EEG signals. Firstl, the epoch of 2–3 seconds of EEG signals of about 150 samples was imported into the MATLAB. The signal was then filtered by means of wavelet-based denoising and ICA between 0.5 and 30 Hz. The signals were then tested for Jarque–Bera test to check whether they originate from normal distributions. MATLAB Statistical toolbox has an inbuilt function to check this condition. Hence, we have incorporated the use of the same function to check this condition in our study. If the value of p is less than 0.001 then the signal is allowed to proceed for further analysis. But, in our case, all signals were tested accordingly and satisfied the test. This test can also be used for the analysis of evoked resting potential (ERP-P300) EEG signals.

6. EXPERIMENTAL RESULTS

The above-listed features were computed on an experimental EEG database consisting of two groups' subjects (males and females aged between 55 and 80 years): AD patients and age-matched healthy subjects, i.e. normal subjects. We incorporated the use of three different features for correctly classifying the data between two groups. The EEG data was imported in MATLAB for further analysis. The fluctuations present in the signals were removed by the use of suitable artefact removal techniques as discussed in Section 3 of this paper. For this purpose, signals were analyzed using the semi-automated and automated artefact removal techniques. MCI category is generally an illness but it is not severe to exceed clinical criteria for AD. This is a standard research problem for the early diagnosis of AD to identify MCI and normal subject. Similarly, discriminating MCI from normal subject is generally more difficult.

6.1 Standard Analysis of the Signals

Figures 3 and 4 depict time–frequency computation of EEG signals for the subjects belonging to two categories (normal and AD) with respect to frontal electrode. EEG signals of temporal, frontal, central, and parietal lobes of both normal and AD patients were taken into consideration for the study as these electrodes play a significant role in AD diagnosis.

Figures 3 and 4 show the time–frequency bumps observed in the EEG signal of the normal subjects and AD patients. In case of AD patients, the EEG signal shows the slowing effect due to the neuronal loss observed in the brain regions (cerebral cortex); but this phenomenon (or effect) is not observed in case of normal subjects. Dauwels et al. [14] has already justified this concept in their research work. But, we have practically observed and verified the bumps exhibited in case of our database. We also computed the relative power by means

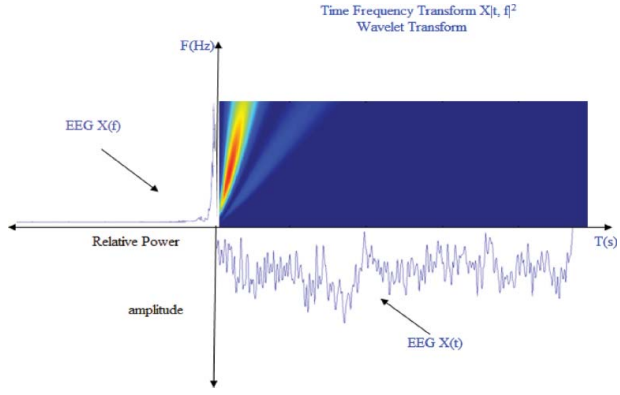

Figure 3: Practical results obtained for slowing of the EEG signal in normal subjects: EEG signal shown in time-domain, frequency domain, and time–frequency domain

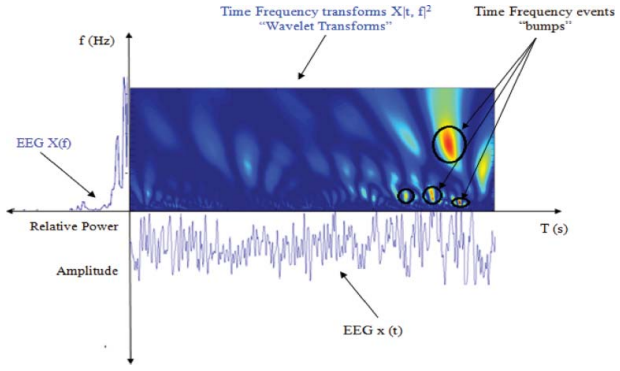

Figure 4: Practical results obtained for slowing of the EEG signal in AD patients: EEG signal shown in time-domain, frequency domain, and time–frequency domain $|X(t,f)|$

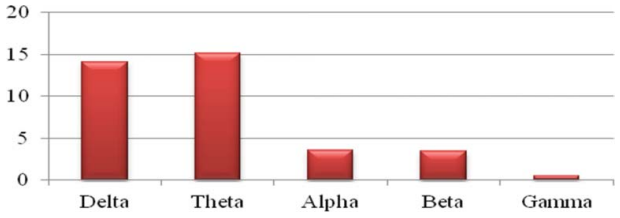

Figure 5: Computations of relative power in EEG sub-bands in AD patients

of time–frequency maps. Time–frequency maps of this EEG is often sparse. In this, most energy is contained in specific regions of time–frequency maps termed as "bumps". It is observed that transient oscillations in the EEG signals of MCI and AD patients occur more often at low frequencies compared to the normal subjects. This is the signal of severe AD, in which the signal is slower. Thus, cognitive deficits are tremendously affected in this stage. The above figures also show the time–frequency representation using wavelet transform; along with it relative power is also calculated which is decreased in delta and theta bands in case of AD patients. These bumps are not observed in case of normal subjects since they do not exhibit slowing effect. Figures 5 and 6 highlight the computation of relative power in each EEG sub-band in case of normal subjects and

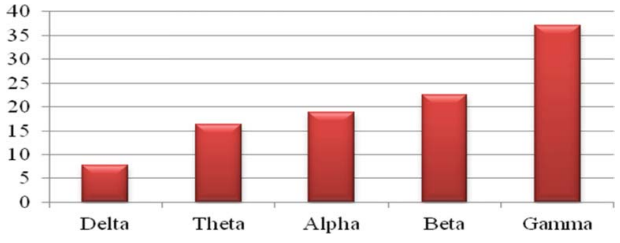

Figure 6: Computations of relative power in EEG sub-bands in normal patients

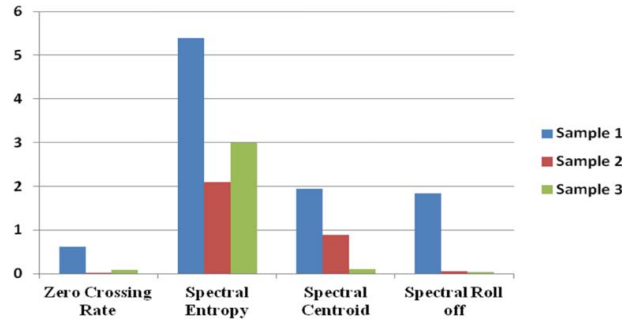

Figure 7: Results indicating the values obtained after computation of each complexity-based feature

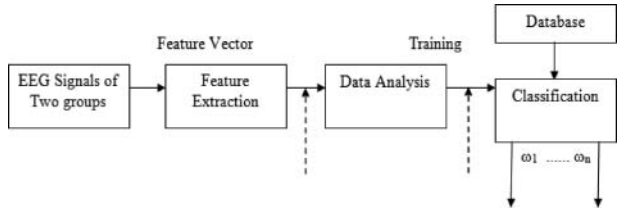

Figure 8: Supervised statistical recognition flow

AD patients. It is observed that spectral power in low-frequency bands of AD patients is increased, whereas it is reduced in high-frequency bands. Thus, EEG spectrum provides us useful information clearly stating the changes occurring in AD patients.

Similarly, complexity features for each electrode of EEG signals were computed and then classified by the use of suitable classifier. In case of wavelet-based features, mean and variance were computed of certain coefficient at level N.

Complexity-based features were computed and given as an input for classification. Figure 7 indicates the computation of complexity-based features in case of AD and normal subjects. It is observed that an AD subject tends to be less complex as compared to normal subjects.

6.2 Classification

Machine learning is a technique of programming to optimize a performance criterion based on past experience. It uses the statistical theory to build mathematical models, since the task is to make inference from a sample database. It is a twofold process: in training mode, efficient algorithms are required to solve the optimization problems, and to store and process the massive amount of data we generally have. Second, once a model is learned, its representation and algorithmic solution for inference needs to be efficient as well. In general applications, the efficiency of the learning algorithm,

space, and time complexity is important. Pattern recognition is one of the common aspects of artificial intelligence; it is also a significant field for the development, validation, and comparison of different learning techniques such as statistical or structural, supervised or unsupervised, and inductive or deductive [30,31]. We have considered the supervised learning approach in our study, which requires a large database. Figure 8 shows the supervised statistical recognition flow.

In our study, we have a database of two groups consisting of AD patient and normal subjects and we have to classify the patients between these two groups. Thus, there is a need to implement the machine-learning algorithms in the present study for classification. In this research work, 100 samples of EEG data are used; out of which 50 signals consist of AD patient while 50 consist of normal subjects. Similarly, 50% of data is used for testing purpose and remaining 50% of data is left out for testing. In literature different classifiers exist such as linear discriminant analysis (LDA), neural networks (NNs), and random forests. But in this study, support vector machine (SVM) classifier is used for classification purpose. Since in case of EEG classification problem, dimension of space is high because the dimension of the patterns increase with the number of features selected. In other way, MATLAB software provides the efficient tools for classification purpose in which the classification of two data groups can be done efficiently by use of inbuilt functions. Classifiers are also used in various applications such as data mining, pattern matching, and pattern recognition. Some classifiers are implemented by the use of special toolboxes in a variety of applications such as WEKA source toolbox which is available for classification using JAVA platform. In present study, MATLAB-based classification is done for distinguishing the subject between two groups. Let us study the classifiers in detail.

The principle behind the use of SVM is to find an optimal hyperplane which linearly separates data points belonging to two classes in case of higher dimensionality data [30,31]. It is a simple, intuitive, and efficient method of classification used by researchers and scientists for classification of data. This classifier makes a decision on comparing a newly labelled sample (testing data) with the baseline data (training data). In this study, classification performance calculation is based on leave-one-subject-out (LOSO) cross-validation approach. A LOSO cross-validation paradigm is much useful as it avoids over fitting problem during classification and ensures the generality of the classifier to unseen data. Based on this approach and classifier, a patient is labelled as normal or AD infected depending on the classification output. In this study, MATLAB pattern recognition toolbox was used for KNN and support vector machine classification. On the basis of training and testing, diagnostic accuracies of the semi-automated system are computed and compared.

Based on the features calculated and classifier used, we have calculated the accuracy of classification based on following terminology [32]. This is also termed as confusion matrix.

$$\text{Accuracy} = \frac{(\text{TP} + \text{TN})}{(\text{TP} + \text{TN} + \text{FP} + \text{FN})} \tag{11}$$

$$\text{Sensitivity} = \frac{\text{TP}}{(\text{TP} + \text{FN})}. \tag{12}$$

$$\text{Specificity} = \frac{\text{TN}}{(\text{FP} + \text{TN})} \tag{13}$$

where TP stands for true positive (correctly classified AD patients), TN stands for true negative (correctly classified normal subjects), FP stands for false positives (misclassified normal patients), FN stands for false negative (misclassified AD patients) [32].

In our study, we have trained 50 EEG signals from temporal, frontal, parietal, and central electrodes randomly. Out of which remaining 50 EEG signals were left out for testing comprising of both normal and AD-affected persons. For classifying each EEG datum between the two groups, the feature dimensions were the same for all feature sets. The reason behind this is that each feature is tested individually during classification and on the similar basis the results were obtained. The following diagnostic accuracies were obtained after classification of

Table 1: Comparison of diagnostic accuracy obtained using individual features

Feature	AD individuals correctly classified	NC individuals correctly classified	NC individuals misclassified	AD individuals misclassified	Classification accuracy (in %)
Spectral	22	21	4	3	86
Wavelet	23	21	4	2	88
Complexity	24	24	1	1	96

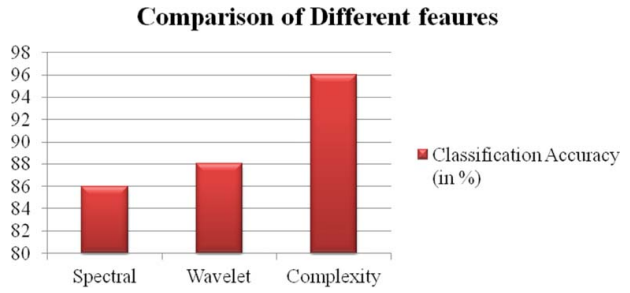

Figure 9: Graphical representation for comparison of diagnostic accuracy

each feature used in the study. Table 1 summarizes the comparison of different features along with different classification accuracies obtained and Figure 9 interprets the graphical representation of the obtained classification accuracies.

7. CONCLUSIONS AND DISCUSSIONS

On the basis of the above results and features used, we have evaluated different EEG-based spectral and wavelet features to observe and study them if they carry any diagnostic useful information for the diagnosis of AD. The objective of current study was to provide better results in terms of classification rates and/or diagnostic accuracy. Although the proposed features in this paper are not novel, but some improvements in results in terms of classification rates are observed. In medical concept, it is signified that AD affects the neuronal activity of the patients. Each individual feature was computed and classified by the use of both the classifiers discussed. In this study, it was claimed that AD patients has less EEG signal complexity as that compared to the normal subjects. The above-used features show decreased features values for AD patients, which practically confirm our hypothesis. The difference in the wavelet-based feature values among the cohort are small, but indicates its significance on the electrodes of EEG. The AD group features consists of lower values, suggesting that AD subjects tends to be less complex. The complexity features used carry significant information in the typical electrodes namely central, parietal, temporal, and frontal lobes. Appearance of plagues and neurofibrillary tangles in cortex region and decrease in volume of hippocampus slows down the EEG of AD patients [21,26]. It is observed that there exists a higher amount of spectral content in higher frequencies (namely alpha and beta) for normal group. This is predicted as the high level of complexity in normal subjects. It is to highlight that genetic modification of stem cells in AD patients also makes the slowing of EEG signals more regular. It is also observed that neural connectivity gets increased in the brain cells and Aβ (Beta Amyloid) protein gets degenerated. The stem cell increases the level of neprilysin. It is an enzyme that breaks the level of Aβ protein and lowers the brain activity of AD patients [32,33]. Hence, an alpha and beta activity also reduces and complexity gets reduces as the signal becomes slow.

Comparing the obtained results in terms of diagnostic accuracy, complexity-based features serve better in terms of accuracy, sensitivity, and specificity as compared to wavelet and spectral features.

Our future work in this study includes the automated diagnosis and classification of EEG data using various classifiers such as NNs, LDA, and many more to increase the diagnostic accuracy for distinguishing between AD and normal groups. In this study, we investigated the use of spectral-, wavelet-, and complexity-based features for automated diagnosis of AD. It is to highlight that when we combine these features with one another they provide more diagnostic information. From the results and research findings, it concludes that the above-discussed features can be effectively used for AD diagnosis using EEG signals since efficient information is extracted for diagnosis. The extracted information contained in the signal can be compared to classify the signal between two or more classes. Our future work also involves distinguishing EEG signal between different stages of AD such as MCI since discriminating MCI subjects from normal subjects is generally more difficult and tedious. In future, multichannel EEG recordings from various lobes may be more appropriate to classify AD from normal subjects [34].

In this manner, it is truly to say that EEG signals play an important role for early detection as well as diagnosis of AD and dementia.

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DISCLOSURE STATEMENT

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