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Computer-Aided Diagnosis of Depression Using EEG Signals

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Key Words
Brain stimulation · EEG · Emotion · Depression · Linear methods · Nonlinear methods

Abstract
The complex, nonlinear and non-stationary electroencephalogram (EEG) signals are very tedious to interpret visually and highly difficult to extract the significant features from them. The linear and nonlinear methods are effective in identifying the changes in EEG signals for the detection of depression. Linear methods do not exhibit the complex dynamical variations in the EEG signals. Hence, chaos theory and nonlinear dynamic methods are widely used in extracting the EEG signal features for computer-aided diagnosis (CAD) of depression. Hence, this article presents the recent efforts on CAD of depression using EEG signals with a focus on using nonlinear methods. Such a CAD system is simple to use and may be used by the clinicians as a tool to confirm their diagnosis. It should be of a particular value to enable the early detection of depression.

Introduction

According to the latest WHO report, depression affects more than 350 million people of all ages, making it as one of the most prevalent global diseases [1]. It is estimated that the largest proportion of people suffering from depression are women aged between 18 and 45 years [2]. In women, pregnancy and menopause are the main causes for depression. Depression can be treated using available effective treatments, but due to ignorance, untimely detection, misdiagnosis or improper medication people suffer from the disease worldwide. Untreated depression may lead to suicidal attempts. According to the 65th World Health Assembly (WHA) organized in 2012, the global burden of depression disorder is increasing and there is a need for a comprehensive, coordinated response from all health and social sectors at the country level [3].

Depression is a mental disorder characterized by persistent occurrences of lower mood states in the affected person and is usually perceived by friends or relatives. The symptoms of depression appear mostly as behavioural ones. Normally, the help of psychiatrists or

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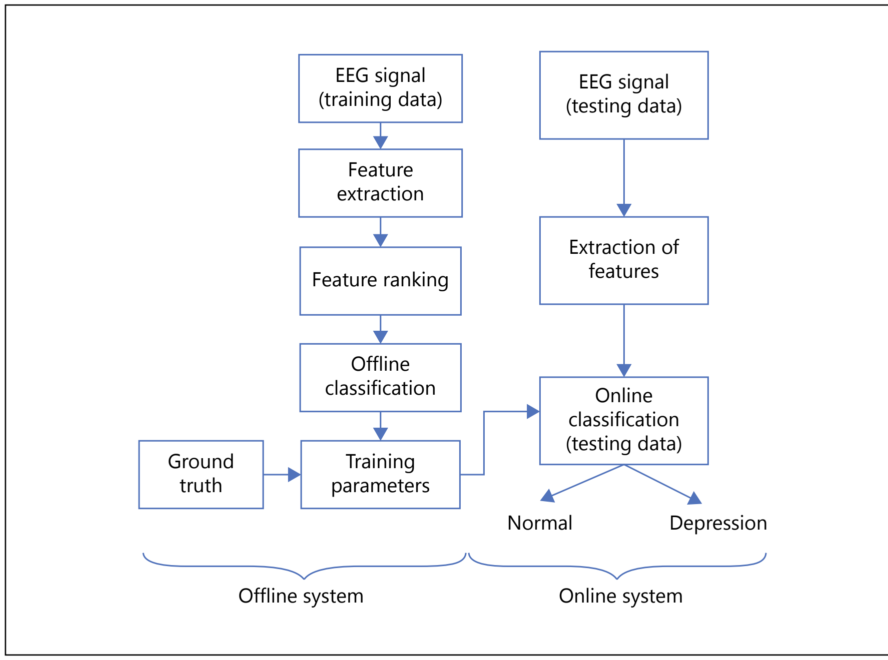

Fig. 1. Block diagram of a typical computer-aided system for EEG-based diagnosis of depression.

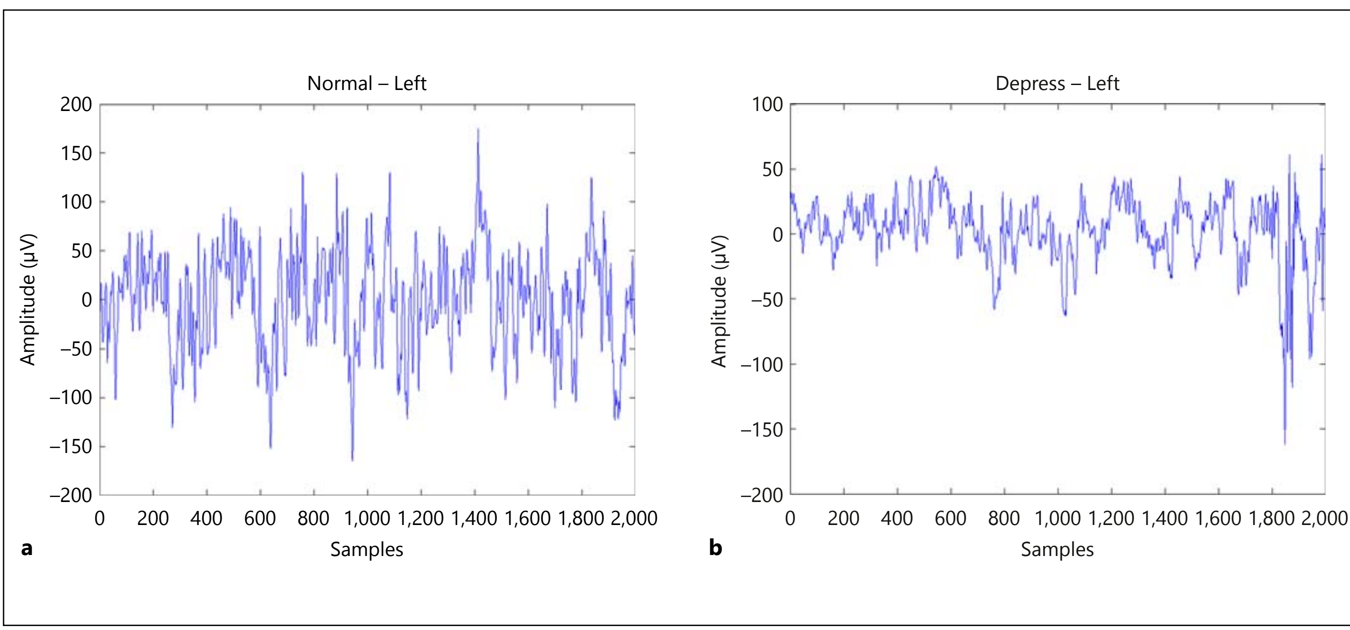

Fig. 2. Sample EEG signals used in this research from the left brain hemisphere: **a** normal; **b** depression.

counsellors is sought for diagnosis and treatment. The identification of depression in the early stage is crucial to prevent it from reaching a severe and irreversible state. Electroencephalogram (EEG) may be used as a tool for making an objective diagnosis of depression. This article presents the recent efforts on computer-aided diagnosis (CAD) of depression using EEG signals. Figure 1 shows a typical CAD system used for the classification of normal and depression EEG signals. Figure 2 shows sample normal and depression EEG data obtained from the left

(FP1-T3) and right (FP2-T4) hemispheres of the brain. The flow of this review article is as follows: section 2 provides highlight on general EEG studies of depression using the clinical interpretation of EEG signals' features. Section 3 discusses the various studies conducted in the detection of depression from EEG signals using linear methods. The final section 4 focusses on the use of nonlinear methods by different researchers to extract the EEG signal features for CAD of depression.

General EEG Studies of Depression

Studies show that patients with depression have hemispheric asymmetry in their brain signals when compared to non-depressed subjects [4–7]. A preliminary study by Nandrino et al. [8] shows that the decrease in complexity [9] of brain functioning in patients with depression is a sign of a lower level of interaction with the environment. The study reports that the EEG dynamics is more predictable, that is, less complex, in depressed patients than in normal subjects. Pezard et al. [10] confirmed and extended the conclusion of Nandrino et al. [8]. Their study showed that patients differ significantly in their dynamical response to therapeutic interventions during first and recurrent episodes. Deslandes et al. [11] assessed the differences in EEG signal asymmetry of depressed and normal elderly subjects and observed the connections between depressive symptom measures and quality of life. They reported that EEG signal asymmetry at the alpha band in clinically depressed elderly adults are similar to that of younger depressed subjects when compared to normal subjects.

The resting frontal EEG alpha asymmetry is reliably assessed in clinically depressed patients; thus, it serves as a trait marker of risk for depression and other emotion-related psychopathology [12]. Debener et al. [13] explains the relationship between alpha EEG asymmetry and depression in patients on two separate occasions between 2 and 4 weeks apart. Their results show that the increased variability of anterior EEG asymmetry can be used as a characteristic feature or marker for depression detection from EEG signals. Recently Stewart et al. [14] used resting frontal EEG asymmetry as a marker of depression and showed that it is predominant in women.

Even though multiple courses of antidepressants are used to treat individuals with depression, the relationship between earlier treatment and the brain's response to future treatment is not known. Antidepressant drugs present notable variations in human brain activity or function and are reflected in the EEG. The effects of drugs on the EEG vary and are often dose dependent. The effects of drugs include accentuation of beta activity, background slowing with decreased amplitude and frequency of the alpha rhythm, and intermixed theta and delta activity [15, 16].

The most common changes in EEG characteristics due to medications are slight increase of theta and excess beta activity. The medication causes an augmentation of voltage of beta activity on the EEG signal. Central nervous system (CNS) stimulants such as cocaine, methylphenidate and antidepressants may excite significant beta activity at low voltage [17, 18]. High doses of several types of medications such as, lithium, phenothiazines and antidepressants, may evoke spikes due to delta and increase theta [17, 18].

Antidepressants with thymoleptic properties (e.g. impramine) generate a decline of alpha activity and an elevation of both slow and fast activities [19], while the antidepressant without thymoleptic properties (e.g. amitriptyline) produces slightly more distinct EEG pattern. In contrast, antidepressants with thymoretics properties (e.g. desipramine), induce decline of fast beta and an elevation of alpha activities. The antidepressant medications induce slight decline in the prefrontal brain activity [20].

A study by Davidson et al. [21] suggested that pronounced corresponding right anterior EEG activity acted as an indicator for the evolution of depression and anxiety problems. It was investigated and proved by experimental results that anterior and posterior EEG asymmetry patterns predicted the future occurrence of depression symptoms [22]. The study predicted that those with comparatively less right posterior EEG activity may complain higher depressive symptoms after a year [22], whereas particularly the frontal asymmetry of EEG alpha power indicated the risk for depression [23]. Using EEG signal processing, depression levels and evolution of depression to various disorders like sleep disorders and alcoholism were studied [24].

Linear Methods

A number of EEG studies based on linear methods found frontal asymmetry [14, 25–27] but reported different results in depressed patients. A bilateral increase in the frontal lobe alpha band activity [28], an increase in the frontal beta band activity [28, 29], and a reduction in the slow wave activity during sleep [30, 31], are results observed by different researchers.

Knott et al. [32] suggested the EEG power as a useful tool for investigating brain regional mechanism in depressed patients. They reported that EEG measurements (amplitude, frequency and power) obtained using linear methods in depressed patients appeared to describe a pattern of aberrant inter-hemispheric asymmetry and a profile of frontal activation.

Nonlinear Methods

EEG signals are complex, nonlinear, and non-stationary in nature. The features of the signal vary with the age, diet, and mental state of the subject [33]. Linear methods may not be able to exhibit the complex dynamical variations in the EEG signals obtained from the highly complex and nonlinear-depressed brain system. Chaos theory and nonlinear dynamic methods are used to extract bispectrum, power spectrum, phase entropies, wavelet energy and entropy, correlation dimension, fractal dimension, largest Lyapunov entropy, approximate entropy, Hurst's exponent features have recently been used successfully for seizure detection and epilepsy diagnosis [34–41], diagnosis of the Alzheimer's disease [42], and study of depression [43–45] and sleep stages [46, 47]. Thus, the authors advocate the use of nonlinear methods to extract the EEG signal features for CAD of depression.

A CAD system for EEG-based diagnosis of depression involves feature extraction, ranking, and classification steps. Different nonlinear methods can be used to extract features from the EEG signal to differentiate a depressive EEG from a healthy one such as Fractal Dimension (FD) [48, 49], Recurrence Quantification Analysis (RQA) [50, 51], Higher-Order Spectra (HOS) [52–54], sample entropy [55, 56], approximate entropy [57], Largest Lyapunov Exponent (LLE) [58], Hurst's exponent (H) [59] and Detrended Fluctuation Analysis (DFA) [60].

The purpose of feature ranking is to identify and rank the significance of the extracted features of the two groups (normal and depression). Most commonly the Student t-test [61] is used for this purpose, where a low p-value indicates the significance of the extracted features and the t-value is used to rank the features with higher values indicating clinically more significant features.

The highly ranked features are fed to a classification algorithm such as Support Vector Machine (SVM) [62–64], Decision Tree (DT) [65], K-Nearest Neighbour (KNN) [65]. The ten-fold cross validation method is often used to train and select the best classifier, which achieves high classification accuracy with a minimum number of features. A few studies have applied nonlinear methods namely FD [66], wavelet-based energy [43] and entropies [44] to extract EEG signal features and artificial neural networks (ANN) [43] to classify EEG signal features into depression and normal behaviour. Ahmadlou et al. [66] investigate EEGs obtained from patients with Major Depressive Disorder (MDD) using the wavelet-chaos methodology developed by Adeli and associates earlier for EEG-based diagnosis of epilepsy [67] and Higuchi's and Katz's fractal dimension (HFD and KFD) [68, 69] as measures of complexity and nonlinearity. They compared frontal lobes (left and right) HFDs and KFDs in EEG full-band and various sub-bands of MDD and control groups with the goal of discovering relevant differences in terms of FDs between the two groups. They used the discovered FDs as input to a classifier, the enhanced probabilistic neural network (EPNN) [70–72], to differentiate the MDD from healthy EEGs. They reported an accuracy of 91.3% for MDD and healthy subjects' classification based on beta sub-band HFDs and concluded that the complexity of frontal EEG at beta sub-band may be used as a marker for diagnosis of MDD and for monitoring of its treatment.

Puthankattil et al. [43] extracted Relative Wavelet Energy (RWE) parameters from the Discrete Wavelet Transform (DWT) [73–78] coefficients and used ANN [79–81] to classify the EEG signal into normal and depressed classes. They claim an overall classification accuracy of 98.11% in discriminating the two classes. Ahmadlou et al. [82] presented a novel nonlinear method 'Spatiotemporal Analysis of Relative Convergence (STARC)' for the analysis of brain dynamics. The statistically significant STARC features selected using the analysis of variance (ANOVA) test are fed into the EPNN classifier to differentiate the MDD EEGs belonging to male and female patients respectively. They report 'significant differences of relative convergences of EEGs of intra-left temporal and front-left temporal lobes at delta band between male and female patients'. Faust et al. [44] present a depression diagnosis support system using entropies extracted from the Wavelet Packet Decomposition (WPD) [83–85] coefficients of the EEG signal [61] and claim a classification accuracy of 99.5% in discrimination of normal and depression EEG signals using the Probabilistic Neural Network (PNN) classifier.

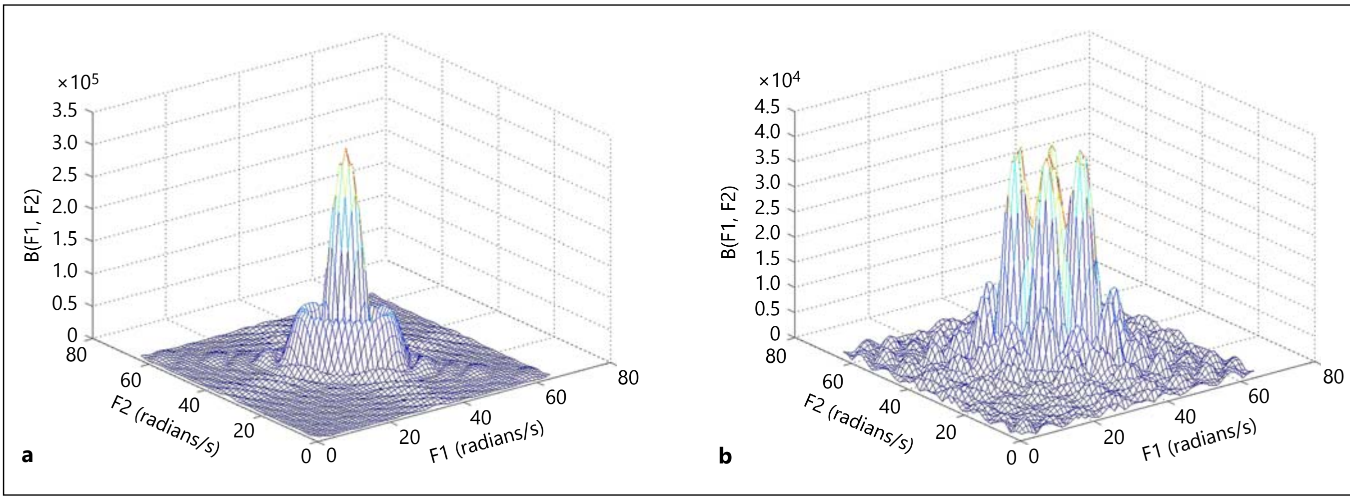

Fig. 3. Sample bispectrum magnitude plots of EEG signals from the left brain hemisphere shown in figure 2: **a** Normal; **b** depression.

Table 1. Summary of studies reporting on computer-aided EEG-based diagnosis of depression in chronological order

Authors	Features used	Analysis method	Performance/conclusion
Debener et al., 2000	Clinical features (EEG alpha asymmetry)	Statistical analysis	Increased variability of anterior EEG asymmetry may be a characteristic feature for depression
Knott et al., 2001	Clinical features (power, frequency, asymmetry and coherence measures)	Statistical analysis	Accuracy = 91.3%
Puthankattil et al., 2012	RWE	ANN classifier	Accuracy = 98.11%
Ahmadlou et al., 2012	KFD and HFD	Enhanced PNN classifier	Accuracy = 91.3%
Ahmadlou et al., 2013	STARC	Statistical analysis	Significant difference between EEGs of male and female with MDD
Hosseinifard et al., 2013	Higuchi fractal, correlation dimension, DFA, LLE	KNN, discriminant analysis, logistic regression	Accuracy = 90%
Faust et al., 2014	WPD and entropies	PNN	Accuracy = 99.5%
Acharya et al., 2015	FD, LLE, sample entropy, DFA, Hurst's exponent, HOS, RQA	SVM, KNN, DT, NC, PNN	Accuracy = 98%

Bachmann et al. [86] compared the linear and nonlinear methods for the depression detection based on EEG signals. The linear method used to extract the features was the EEG frequency band power and the nonlinear method used was the HFD method. The authors claimed an accuracy of 88 and 94% using the linear and nonlinear methods, respectively, in detecting depression from the EEG signal. Table 1 presents a summary of studies reporting on computer-aided EEG-based diagnosis of depression.

Even though a number of papers have been published using the nonlinear methods, there are other nonlinear methods [48–60, 87–98] that are worth exploring for the EEG-based diagnosis of depression. As an example,

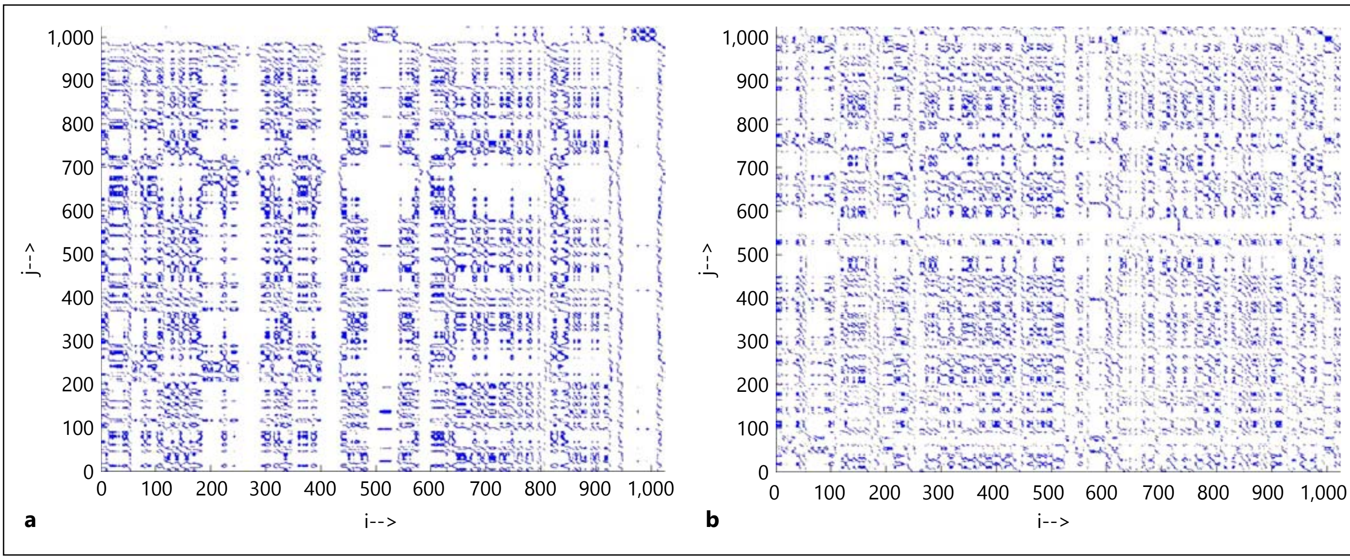

Fig. 4. Sample recurrence plots of EEG signals from the left brain hemisphere shown in figure 2: **a** Normal; **b** depression.

figures 3a and b show sample bispectrum magnitude plots of EEG signals from the left brain hemisphere for normal and depression subjects shown in figure 2, respectively. Similarly, figures 4a and b show sample recurrence plots of EEG signals from the left brain hemisphere for normal and depression subjects shown in figure 2, respectively. More peaks were observed in the bispectrum plot (fig. 3) between 0 and 20 Hz in the depression EEG signal compared with the normal EEG signal. Further, it was observed that the recurrence plot (fig. 4) was unique for each class; it is more rhythmic for the depression class.

Conclusion

In this article, a review of EEG-based diagnosis of depression was presented with a focus on CAD using nonlinear methods. Such a CAD system is simple to use and may be used by the clinicians as a tool to confirm their diagnosis. It should be of particular value for the early detection of depression. In a companion article [99], the authors presented a novel depression diagnosis index using the EEG signal and the following nonlinear methods HOS and RQA.

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