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Electroencephalogram (EEG)-based computer-aided technique to diagnose major depressive disorder (MDD)☆

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ABSTRACT

Recently, Electroencephalogram (EEG)-based computer-aided (CAD) techniques have shown their promise as decision-making tools to diagnose major depressive disorder (MDD) or simply depression. Although the research results have motivated the use of CAD techniques to help assist psychiatrists in clinics yet their clinical translation has been less clear and remains a research topic. In this paper, a proposed machine learning (ML) scheme was tested and validated with resting-state EEG data involving 33 MDD patients and 30 healthy controls. The EEG-derived measures such as power of different EEG frequency bands and EEG alpha interhemispheric asymmetry were investigated as input features to the proposed ML scheme to discriminate the MDD patients and healthy controls, and to prove their feasibility for diagnosing depression. The acquired EEG data were subjected to noise removal and feature extraction. As a result, a data matrix was constructed by the columns-wise concatenation of the extracted features. Furthermore, the z-score standardization was performed to standardize each column of the data matrix according to its mean and variance. The data matrix may have redundant and irrelevant features; therefore, to determine the most significant features, a weight was assigned to each feature based on its ability to separate the target classes according to the criterion, i.e., receiver operating characteristics (roc). Hence, only the most significant features were used for testing and training the classifier models: Logistic regression (LR), Support vector machine (SVM), and Naïve Bayesian (NB). Finally, the classifier models were validated with 10-fold cross-validation that has provided the performance metrics such as test accuracy, sensitivity, and specificity. As a result of the investigations, most significant features such as EEG signal power and EEG alpha interhemispheric asymmetry from the brain areas such as frontal, temporal, parietal and occipital were found significant. In addition, the proposed ML framework proved automatic identification of aberrant EEG patterns specific to disease conditions and provide high classification results i.e., LR classifier (accuracy = 97.6%, sensitivity = 96.66%, specificity = 98.5%), NB classification (accuracy = 96.8%, sensitivity = 96.6%, specificity = 97.02%), and SVM (accuracy = 98.4%, sensitivity = 96.66%, specificity = 100%). In conclusion, the proposed ML scheme along with the EEG signal power and EEG alpha interhemispheric asymmetry are proved suitable as clinical diagnostic tools for MDD.

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1. Introduction

Major depressive disorder (MDD) is a chronic, recurrent, and a life-threatening mental illness commonly termed as depression. In the USA, it has been reported as highly prevalent (13.2% to 16%) and has been found as a leading cause of functional disability [1]. According to World Health Organization (WHO), in the year 2020, it has become the 2nd most leading cause of disease burden worldwide [2]. An accurate and early diagnosis is recommended by clinicians in order to avoid increased risk of treatment failure with

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an increase in the time of onset. In addition, an early diagnosis will further help during the treatment process and helps to improve patients quality-of-life [3]. Currently, the diagnosis includes structured questionnaires that are administered as an interview session between health practitioners and the MDD patients. However, the subjectivity involved due to the heterogeneity of MDD and the potential errors incurred by human factors may not be ignored and could result into a misdiagnosis.

Recently, machine learning (ML) techniques have received considerable attention due to their capability to mine non-invasive neuroimaging data to establish the computer-aided (CAD)-based solutions that facilitate during the diagnosis [4–6]. For example, mining functional magnetic resonance imaging (fMRI) data with ML methods has shown promising research results [7,8]. Specifically, the support vector machine (SVM) has been emphasized as a method of choice for the diagnosis of depression [9]. On the other hand, the automated EEG-based ML methods are proved feasible to discriminate the depressed patients from healthy controls [10–14]. In addition to depression, the classification algorithms are found useful for neurological diseases such as schizophrenia, and Alzheimer's disease [15]. In the context of depression, classifier such as artificial neural networks (ANN) is trained to classify the depressed and healthy controls [16,17]. Recently, a depression diagnostic index is proposed based on nonlinear features extracted from EEG data [11]. Electroencephalogram (EEG) offers high temporal resolution and lower cost than fMRI which makes it suitable for portable and remote clinical applications involving monitoring epileptic patients [18,19], quantifying different sleep stages [20], indexing for anesthesia monitoring [21], and diagnosing patients with alcohol addiction [22]. Furthermore, EEG data acquisition is faster than fMRI and a trained nursing staff could handle the EEG-based CAD system.

In the literature, various nonlinear features such as detrended fluctuation analysis (DFA), Higuchi fractal, correlation dimension and Lyapunov exponent are extracted from EEG signal and have shown promises during the MDD diagnosis, e.g., a recently performed study has achieved 90% accuracy for discriminating the MDD patients and healthy controls [12]. MDD has been associated with cognitive deficits and functional impairments [23,24] localized to areas such as frontal and temporal. According to a recent review, abnormalities such as MDD tends to exhibit decreased left frontal activity (measured as increased interhemispheric alpha power/amplitude) [25]. In a study, greater left frontal activity is associated with less depressive symptoms [26]. In addition, EEG alpha interhemispheric asymmetry is concluded as a risk marker for MDD because of the finding that the study participants with lifetime depressive symptoms has shown less relative frontal activity when compared with subjects with no depression [27].

The importance of EEG alpha interhemispheric asymmetry in the diagnosis of depression is evident from various studies [28–30]. For example, psychomotor retardation during depression is linked with EEG alpha interhemispheric asymmetry [28]; EEG frontal asymmetry has been considered as a marker for vulnerability of depression [29]; decreased interhemispheric alpha waves are reported during depression [30]. In addition, altered structure of EEG oscillatory pattern is reported in MDD [25]. Hence, these evidences add to the confidence on the EEG alpha interhemispheric asymmetry, as a feature, to be used for automatic diagnosis of depression.

In addition to alpha band, activity in other bands such as theta band has shown relevance such as a decreased frontal theta activity has also been reported [31–33]. Moreover, hypo-activation of the left frontal [34,35] and hyperactivation in the right frontal regions [31] have been observed during MDD. Despite all research findings, the clinical applications of the frontal EEG alpha interhemispheric asymmetry and frontal midline theta activity have been largely unclear [36]. Hence, in context of diagnosing MDD, a further investigation involving features such as EEG alpha interhemispheric asymmetry, and EEG spectral power of different frequency bands is required.

To fill-up this gap, this study proposes a novel ML technique including EEG-derived features (spectral power computations for different EEG frequency bands and EEG alpha interhemispheric asymmetry) as input data. In this research, it has been hypothesized that the linear features such as EEG power computed form different frequency bands and EEG alpha interhemispheric asymmetry can discriminate the MDD patients and healthy controls with high classification efficiencies even in the absence of nonlinear EEG features. For this purpose, the proposed ML method is validated with resting-state EEG data acquired from the MDD patients and healthy controls. The feature selection involved 2 steps, 1) ranking features in descending order according to receiver operating characteristics (roc) criterion, 2) selecting subsets including top-ranked features to train and test classifier models, and to determine the upper limit of a minimum number of features necessary to provide highest accuracies among other subsets. As a result, a reduced set of features is used to test and train the classifiers such as logistic regression (LR), support vector machine (SVM) and naïve Bayesian (NB). The classifiers provide the functional model to relate the EEG significant features to the outcome target groups, i.e., MDD patients and healthy controls.

2. Materials and methods

2.1. Study participants

In this study, two groups of participants were recruited: 1) 33 MDD patients (Age, Mean = 40.33, SD = ±12.861), and 2) 30 age-matched healthy subjects as control group (Age, Mean = 38.227, SD = ±15.64). The participants were recruited from the outpatient clinic of hospital Universiti Sains Malaysia (HUSM), Malaysia. The experiment design was approved by the ethics committee, HUSM. The participants agreed to sign the consent forms of participation and were fully aware of the experimental procedure adopted for experimental data acquisition. Furthermore, according to the recruitment criteria of this study, the MDD participants should have confirmed diagnosis based on the symptoms of depression as mentioned in the Diagnostic and Statistical Manual for depression (DSM-IV) [37]. The diagnosis was performed by senior psychiatrists in the psychiatric clinic, HUSM. In this study, the MDD participants with psychotic symptoms, pregnant patients, alcoholics, smokers and patients having epileptic problems were excluded. On the other hand, the healthy controls were screened for possible mental or physical illness and were found disease naive.

2.2. Experimental data acquisition

The EEG data acquisition involved vigilance-controlled monitoring during the recordings, i.e., 5 min EEG data recordings during eyes closed (EC) and 5-min recordings during eyes open (EO) conditions involving a 19-channel EEG cap with linked-ear (LE) reference. The experimental data were recorded at the same time of day and the participants were instructed to abstain from coffee intake, and other drug abuses. The EEG sensors were placed on the scalp according to the international 10–20 electrode placement standard [38]. The 19-electrodes covering the scalp included the frontal (Fp1, Fp2, F3, F4, F7, F8, Fpz), temporal (T3, T4, T5, T6), parietal (P3, P4, P7, P8), occipital (O1, O2), and central (C3, C4) regions. Moreover, the 19-channels EEG cap was attached to an amplifier from Brain Master Systems with configurations such as 0.5 Hz to 70 Hz filter, with a 50 Hz notch filter, and a sample rate of 256 samples per

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