ORIGINAL ARTICLE

Predicting Mini-Mental State Examination Scores Using Electroencephalography Signal Features

Vahid Asayesh [1,2*], Mahdi Dehghani [2], Majid Torabi [1,2], Sepideh Akhtari-Khosroshahi [1], Shahriar Gharibzadeh [1,3]

[1] *Asab Pajouhane Farda Research Company, Tehran, Iran*

[2] *Asayesh Rehabilitation Clinic, Tabriz, Iran*

[3] *Institute for Cognitive and Brain Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

*Corresponding Author: Vahid Asayesh
Email: vahid.asayesh@gmail.com

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Abstract

Purpose: The purpose of this study is to use linear and non-linear features extracted from Electroencephalography (EEG) signal to predict the Mini-Mental State Examination (MMSE) test score by machine learning algorithms.

Materials and Methods: First, the MMSE test was taken from 20 subjects that were referred with the initial diagnosis of dementia. Then, the brain activity of subjects was recorded via EEG signal. After preprocessing this signal, various linear and non-linear features are extracted from it that are used as input to machine learning algorithms to predict MMSE test scores in three levels.

Results: Based on the experiments, the best classification result is related to the Long Short-Term Memory (LSTM) network with 68% accuracy.

Conclusion: Findings show that by using machine learning algorithms and features extracted from EEG signal the MMSE scores are predicted in three levels. Although deep neural networks require a lot of data for training, the LSTM network has been able to achieve the best performance. By increasing the number of subjects, it is expected that the classification results will also increase.

Keywords: Mini-Mental State Examination; Electroencephalography Signal; Electroencephalography Feature Extraction; Machine Learning Algorithms.

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1. Introduction

Cognitive impairment is a spectrum that ranges from subjective cognitive decline to dementia [1]. Dementia is a clinical syndrome that includes a group of disorders related to cognitive decline that influence language, presentation, memory, social abilities, etc. [2]. In 2013, the World Health Organization (WHO) study [3] estimated the top 20 leading causes of death in 2030 showing that non-communicable diseases such as dementia will become the major threats to human lives. Diagnosing dementia involves cognitive assessment of brain functions, such as attention, memory, problem-solving, thinking, and many other mental abilities [4]. General diagnostic procedures for dementia are usually performed using valid clinical tests [5], and imaging techniques such as Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI). PET scans are not mostly available, expensive, and invasive, while fMRI is widely available but costly [6]. Electroencephalography (EEG) is a neurodynamic time-sensitive biomarker that is widely accessible, non-invasive, and inexpensive [6] which helps in detecting cortical abnormalities associated with cognitive decline and shows good performance in diagnosis dementia [7-9].

Usual techniques to detect dementia are distressing and costly. Nevertheless, early and accurate diagnosis is important to control disease progression [10]. For this reason, automatic and affordable diagnosis techniques have become an important research subject in this field. Recently, machine learning techniques have been studied for diagnosing dementia [11]. For this aim, the algorithm is trained using various cognitive impairment biomarkers to learn the relationship between the input data and the corresponding output variable (clinical diagnosis). Once the learning process is completed, the algorithm can yield predictions or classifications with new data. Automatic diagnosis was performed by coherence [12-14], spectral peaks [12, 15], Power Spectral Density (PSD) [13, 16], spectral bands [15], relative power [17], Wavelet transform [17-20], Fourier transform [21], complexity [17, 22], skewness [23], mean [23], and correlation-based [24] features which extracted from resting-state eyes closed EEG, using Support Vector Machine (SVM) [12, 14-17, 22], K-Nearest Neighbors (KNN) [19], Multilayer Perceptron (MLP) [20], Convolutional Neural Network (CNN) [23], or decision trees [18] as classifiers. These studies have compared EEG biomarkers in dementia patients, healthy controls, and patients with Mild Cognitive Impairment (MCI).

Some articles focus on acoustic features [5] or finger-tapping measurement [25] as biomarkers to find a correlation of them with Mini-Mental State Examination (MMSE) test scores for evaluating the global cognitive decline automatically. For this aim, authors in [26] developed a predictive model for the MMSE scores using resting-state EEG parameters, including median frequency, peak frequency, and the alpha-to-theta ratio at the prefrontal regions of Fp1 and Fp2 in eyes-closed state.

Unlike most studies that investigate the classification of Alzheimer's Disease (AD), Healthy Control (HC), and MCI subjects, the purpose of this paper is to investigate whether the severity of cognitive decline could be diagnosed by linear and non-linear features extracted from the resting-state eyes-closed EEG using machine learning algorithms. Compared to the [26] in this paper, more features and electrodes have been studied.

The rest of the paper is organized as follows: In section 2, steps of recording and preprocessing of EEG data, feature extraction from them, and machine learning algorithms are explained. In section 3, the results of the classification using various algorithms are described, and in sections 4 and 5, discussion on the results and conclusion are presented, respectively.

2. Materials and Methods

2.1. Data Collection and Preprocessing

To predict the MMSE scores, first, the MMSE test was taken from 20 med-free subjects, including 14 females and 6 males with an average age of 69.85 ± 10.03 years old that referred with the initial diagnosis of dementia. All participants expressed their consent to participate in this experiment. The MMSE test [27] is widely used in clinical and research studies to measure the severity and progression of cognitive disorders. This test consists of questions in five different areas, including orientation, memory, attention, naming, following verbal and written commands, writing a sentence spontaneously, and copying a complex polygon [27], the answer to which leads to a score between 0 (greatest cognitive decline) to 30 (no cognitive decline). Based on the results of the MMSE test, the subjects were classified as T3 (MMSE: 28-30), T2

(MMSE: 24-27), or T1 (MMSE < 24) groups [26]. Then, the brain activity of subjects was recorded via resting-state eyes-closed EEG according to the international 10-20 system using Mitsar 19 channel system. The time duration of EEG recording was 5 minutes. All the EEG electrode contact impedances were maintained below 5 kΩ. To remove interferences from EEG signals, a high-pass filter with a cut-off frequency of 0.1 Hz, a low-pass filter with a cut-off frequency of 50 Hz, and a Notch filter with cut-off frequencies of 45 and 55 Hz were used.

- **Kurtosis**

Kurtosis is the higher-order moment that measures the complexity of the EEG signal [31]. It also determines that the signal is rather flat or has a peak at the mean point of the signal. The kurtosis of the signal $x(n)$ is computed based on Equation 1:

$$\gamma_2 = \frac{E[[x(n) - \mu]^4]}{[E[x(n) - \mu]^2]^2} \quad (1)$$

Where μ is the standard deviation and E is the expected value of the signal. In this study, this feature is computed in delta, theta, alpha, beta, and gamma frequency bands.

- **Skewness**

Statistically, skewness is the measure of the symmetry or asymmetry of an EEG signal [31]. This feature for a signal $x(n)$ is given by Equation 2:

$$\gamma_1 = \frac{E[[x(n) - \mu]^3]}{\sigma^3} \quad (2)$$

We used Infomax Independent Component Analysis (ICA) decomposition to remove usual eye movements such as saccades or blinking [28]. Recordings were further cleaned with an automated z-score based method, using the Fully Automated Statistical Thresholding for EEG Artifact Rejection (FASTER) plugin [29].

2.2. EEG Biomarkers

After pre-processing the EEG signals, various linear and non-linear features, according to Table 1, are extracted from them within a 5-second rectangular window [30]. In addition to the features extracted from the EEG signal, due to the relationship between cognitive decline and age, the age of the subjects is also used as a feature. These features and extraction methods are discussed in detail below.

In this Equation, E shows the expected value estimator, μ is the mean, and σ is the standard deviation of the signal. In this paper, this feature is computed in delta, theta, alpha, beta, and gamma frequency bands.

- **Interquartile Range (IQR)**

This feature shows the difference between the third and first quartiles of the signal [32]. In this work, IQR is computed in delta, theta, alpha, beta, and gamma frequency bands.

- **Range**

EEG signals were processed using Power Spectral Density (PSD) to extract frequency bands, including delta (1-3 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (15-20 Hz), and gamma (20-30 Hz) ranges [33].

- **Covariance**

In statistics, covariance is a measure of the relationship between variables. This feature evaluates how much the variables change together. In this paper, covariance is calculated in delta, theta, alpha, beta, and gamma frequency bands.

- **Entropy**

Entropy measures quantify the random process uncertainty [34]. In other words, this feature measures the regularity /randomness of the EEG signal and is calculated based on Equation 3 in the delta, theta, alpha, beta, and gamma frequency bands.

Table 1. Features extracted from the EEG signal

• Kurtosis, Skewness, Interquartile Range (IQR), range, covariance, entropy, and coherence in the delta, theta, alpha, beta, and gamma frequency bands.
• Delta/theta, delta/alpha, delta/beta, delta/gamma, theta/alpha, theta/beta, theta/gamma, alpha/beta, alpha/gamma and beta/gamma power ratios.
• Theta, alpha, alpha rhythm frequency (AF), beta, gamma, and broadband median frequencies.
• Theta, alpha, alpha AF, beta, gamma, and broadband absolute powers.
• Theta, alpha, alpha AF, beta, gamma, and broadband relative powers.
• Alpha and alpha AF spectral peaks.
• Individual Alpha spectral Frequency (IAF).

$$E(X) = -\sum_{n} x(n) \log x(n) \tag{3}$$

- **Coherence**

Coherence refers to the normalized covariance of signals in the spectral domain and is defined as the square of the cross-spectrum of the electrodes divided by the product of the power spectra of the individual electrodes [35]. In the case of EEG, this feature shows the degree of functional connectivity among the cortical areas. In AD patients, EEG coherence shows whether the cognitive decline is associated with changes in functional connections between brain regions [6]. In this paper, this feature is computed in delta, theta, alpha, beta, and gamma frequency bands.

- **Power Ratio**

This feature compares the power of different frequency bands. The power ratio of delta-to-theta, delta-to-alpha, delta-to-beta, delta-to-gamma, theta-to-alpha, theta-to-beta, theta-to-gamma, alpha-to-beta, alpha-to-gamma, and beta-to-gamma are used in this study.

- **Median Frequency**

Median frequency is a frequency at which the EEG signal power spectrum is divided into two regions with equal amplitude. This feature is computed in broadband, AF, theta, alpha, beta, and gamma frequency bands.

- **Absolute Power**

This feature is defined as the total energy intensity at different frequency bands. In this study, absolute power is computed in broadband, AF, theta, alpha, beta, and gamma frequency bands.

- **Relative Power**

This feature quantifies the proportion of power that is contained in an EEG sub-band compared to the total power of the signal. In this study, relative power has been computed for alpha AF, broadband, theta, alpha, beta, and gamma frequency bands [17]. The relative power in the fast rhythms decreased in AD and MCI patients while it is increased in the slow rhythms [6].

- **Spectral Peak**

This feature is the frequency at which the PSD of the average power in it has the highest magnitude. Spectral peaks of AF and alpha frequency band were used as features in this paper.

- **Individual Alpha Spectral Frequency (IAF)**

IAF is defined as the frequency associated with the strongest EEG power within the alpha range.

The combination of these features is used as input to the machine learning algorithms. In order to create a hybrid feature, each feature is placed in a row of the matrix as shown in Figure 1.

$$\begin{bmatrix} \text{Kurtosis in delta frequency band} \\ \text{Kurtosis in theta frequency band} \\ \vdots \\ \text{Skewness in delta frequency band} \\ \text{Skewness in theta ferequency band} \\ \vdots \\ \text{Individual alpha frequency band} \\ \text{Subjects age} \end{bmatrix}$$

Figure 1. The procedure of the combination of different features to obtain a hybrid feature matrix

2.3. Machine Learning Algorithms

Machine learning algorithms are trained using the extracted features from the training dataset to detect the MMSE scores of the test dataset. These algorithms include SVM, MLP, CNN, Long Short-Term Memory (LSTM), and logistic regression which are discussed below.

- **SVM**

SVM is one of the supervised learning methods. In the simplest type of this classifier, the training data set can be categorized linearly with at least one hyper-plane. Linear classifiers are inefficient for real problems that have a nonlinear structure. One of the abilities of SVM is to be converted to a non-linear learner, which is done by mapping the features to a higher-dimensional space [36]. The SVM used in this research is nonlinear with a cubic kernel.

- **MLP**

An Artificial Neural Network (ANN) is a mathematical computational model that models the operation of biological neural systems. In 1958, Rosenblatt [37] introduced the first neural network called perceptron. Perceptron is the basic unit of the concept of deep learning and an artificial neuron that, when combined with other components, is able to solve complex problems in accordance with human function. Perceptron can be considered as a binary classification algorithm that can be used to divide a set of input signals into two categories, 0 and 1. Unlike other common classification algorithms, this algorithm is inspired by the basic processing unit of the human brain (neuron) and has the ability to learn and solve complex problems. When several perceptrons are combined in layers, an ANN called the MLP is created. The MLP network used in this research consists of a hidden layer with 60 neurons.

• LSTM

LSTM is an artificial recurrent neural network that is used in the field of deep learning. This network has a feedback connection; thus, it can process not only single data points but also entire sequences of data [38]. In the LSTM network used in this research, after the input layer, there is a dropout layer with a probability of 0.3, LSTM layer with 70 neurons, a dropout layer with a probability of 0.2, and fully connected, softmax, and classification layers.

• CNN

CNN is a class of ANNs that is designed to adaptively learn spatial hierarchies of features through backpropagation by using multiple blocks, such as convolution, pooling, and fully connected layers [39]. In the CNN used in this work, after the input layer, there are convolutional layers with filter size 5, batch normalization, max pooling, dropout with a probability of 0.5, fully connected, softmax, and classification layers.

• Logistic Regression

Regression methods describe the relationship between a response variable and one or more explanatory variables. The logistic regression model is the most frequently used regression model for the analysis of data. The goal of an analysis using this model is to find the best fitting to describe the relationship between a dependent or response variable and a set of independent or predictor variables [40].

3. Results

Machine learning algorithms are trained using three sets of features, including only non-linear and connectivity features (kurtosis, skewness, IQR, range, covariance, entropy, and coherence), only frequency domain features (power ratios, IAF, spectral peak, central frequency, absolute and relative powers), and hybrid features (non-linear and connectivity features + frequency domain features) those extracted from the EEG signals of 15 subjects (training phase) to recognize the MMSE scores of 5 other subjects (testing phase) using 5-fold validation method.

The criteria for evaluating classification results are accuracy, sensitivity, and specificity. The accuracy of a machine learning classification algorithm is one way to measure how the algorithm classifies a data point correctly. According to Equation 4, accuracy is the number of correctly predicted data points out of all the data points.

$$ACC = \frac{TP + TN}{TP + TN + FP + FN}. \quad (4)$$

In this Equation, *TP*, *TN*, *FP* and *FN* respectively show True Positive, True Negative, False Positive, and False Negative values.

According to Equation 5, sensitivity is the metric that evaluates a model's ability to predict the true positives of each available category.

$$TPR = \frac{TP}{TP + FN} \quad (5)$$

Based on Equation 6, specificity is the metric that evaluates a model's ability to predict the true negatives of each available category.

$$TNR = \frac{TN}{TN + FP} \quad (6)$$

The classification accuracy, specificity, and sensitivity using different classifiers and three sets of features are shown in Table 2. Also, Figure 2 shows the best features

Table 2. MMSE score classification results using different sets of features and machine learning algorithms

Classifier	Features set								
	Non-linear and Connectivity			Frequency domain features			Hybrid features		
	ACC.	TPR	TNR	ACC.	TPR	TNR	ACC.	TPR	TNR
SVM	60%	33.3%	25%	50%	31%	33%	64%	53.3%	53.3%
Logistic regression	44%	28.8%	28.6%	48%	40%	39.2%	64%	48.8%	53.2%
MLP	52%	51.1%	49.2%	36%	33.3%	29.8%	56%	40%	40%
CNN	52%	33.3%	32.1%	52%	42.2%	42.2%	56%	44.4%	45%
LSTM	56%	31.1%	20.3%	56%	44.4%	44.4%	68%	64.4%	62.4%

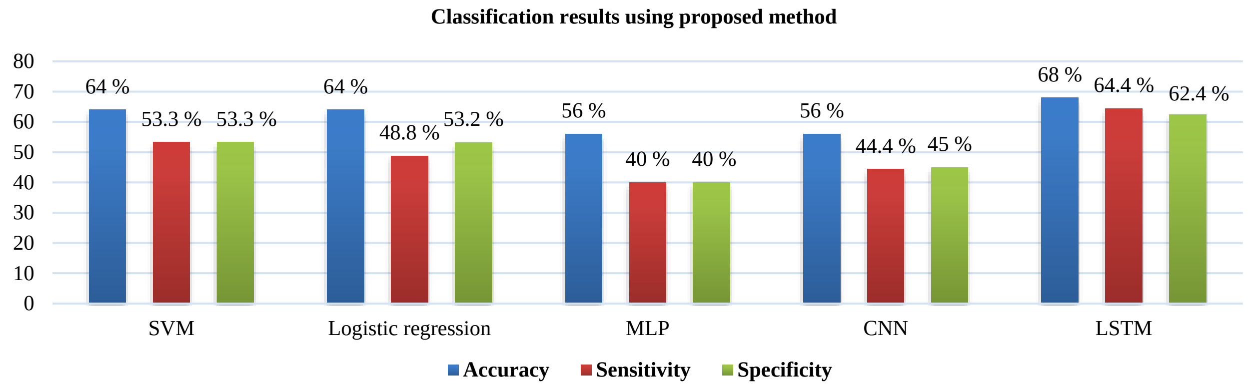

Figure 2. MMSE scores classification results using different machine learning algorithms and the proposed method

(hybrid features) classification results. Based on this figure, the highest classification result is related to the LSTM network with 68% accuracy. Sensitivity and specificity are also in the acceptable range in all classifiers. Figure 3 shows the results of the experiments using the features discussed in the base paper [26], including median frequency, peak frequency, and alpha-to-theta power ratio and the points (Fp1 and Fp2) used in this paper.

In this case, also, LSTM has achieved the best result with 44% accuracy.

Comparing the results shown in Figure 2 and Figure 3, it can be concluded that the use of the proposed hybrid features and more points has improved the automatic detection of MSME scores by 24% in terms of accuracy.

4. Discussion

From a signal processing view, EEGs yield multivariate non-stationary and non-linear representations of the underlying neural activities. In this paper, machine learning approaches are proposed to EEG engineered features for automatic classification of dementia severity. Three sets of features were generated: only non-linear and connectivity features, only frequency domain features, and hybrid features. The extracted features were fed to the machine learning algorithms (SVM, Logistic regression, MLP, CNN, and LSTM) to perform classification. The results show that the hybrid features (non-linear and connectivity + frequency domain features) are to better discriminate among different groups. To the best of our knowledge, this is the first work that uses EEG features to classify dementia severity. Studies in this field are often concerned with extraction features from speech signals [5] or biomarkers such as finger tapping [25], or examining the significant relationship between the frequency domain features of the EEG signal and the severity of dementia [26]. Three major effects of cognitive decline have been observed in the EEG signal: slowing in terms of a shift in the power spectrum to lower frequencies, reducing complexity and coherence [26]. Choi *et al.* [26] focused on the median frequency, spectral peak, and alpha-to-theta power ratio to explain the slowing of the brain rhythms which have been reported to be suitable classification biomarkers for AD and MCI. They showed that these features are correlated with dementia severity so that by

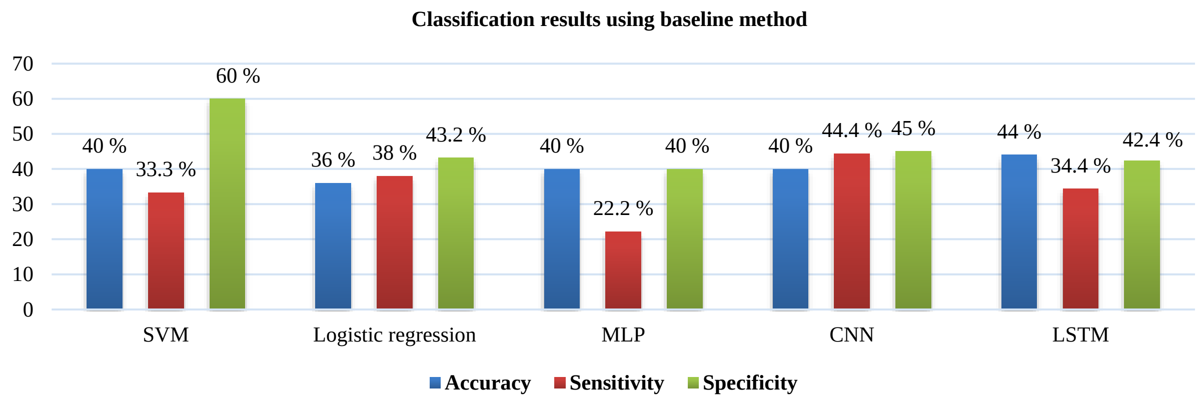

Figure 3. MMSE scores classification results using different machine learning algorithms and baseline paper method

decreasing MMSE scores from T1 to T2 level, these features are decreased too. Figure 3 shows the classification results between T1, T2, and T3 groups using these features. Comparison of these results and the results of classification using only frequency domain and hybrid features shown in Table 2 and Figure 2 indicates the superiority of both proposed features. The most usual findings in EEG analyses of AD are the displacement of background frequency into delta and theta ranges and the decrease of the alpha central frequency [12], also, the direct correlation between the degree of cognitive impairment and the power of low frequencies activities in the EEG. Authors in [13] have further proved that AD patients show an increase in low frequency bands (delta and theta) power with simultaneous decrease in high frequency (alpha and beta) power along with the development of the disease. Moreover, it has been shown that the amount of power in various frequency bands correlated with the severity of AD. These results led the authors to use the frequency features proposed in the present paper. Comparison of the classification results using the baseline paper [26] features (Figure 2) and the proposed frequency features (Table 2) shows the better performance of the proposed model. It seems that the frequency domain features traditionally used for separation AD, MCI, and HC have been able to distinguish between different severity of dementia. However, these features are not sufficient to display all EEG signal information. It is extensively reported that AD is considered a disconnection syndrome, characterized by widespread degeneration of synapses and the death of neurons [41]. EEG coherence is a promising approach to evaluate functional cortical connections between different cortical areas of the brain. Also, non-linear features such as skewness and kurtosis are statistical quantities that measure the complexity of the EEG signals and measure signal element distribution [31]. Therefore, the use of non-linear and connectivity features helps to improve the performance of classifiers.

The proposed features in addition to increasing the accuracy of the classifiers, also increase the specificity and sensitivity which means that the classifiers are not over-fitted and provide reliable discrimination between different categories. This is due to the increase in the content available (features length) for classification. Among the various classification algorithms, LSTM has performed better than others due to its suitable structure for string processing.

One of the weaknesses of this work is the small number of subjects. Obviously, with the increase in the number of subjects, machine learning algorithms especially deep learning-based methods (CNN and LSTM) can show better performances.

5. Conclusion

In this research, by training and testing different machine learning algorithms using linear and nonlinear features extracted from EEG signals and a combination of them with the subject's age, the MMSE score is predicted in three levels. Although deep neural networks require a lot of data for training, in this work, the LSTM neural network, which is suitable for processing time series with a limited amount of data, has been able to achieve the best performance with 68% accuracy. By increasing the number of subjects, it is expected that the classification results will also increase.

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