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Early Detection of Alzheimer's Disease With Nonlinear Features of EEG Signal and MRI Images by Convolutional Neural Network

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Abstract

Background: The main purpose of this study is to provide a method for early diagnosis of Alzheimer's disease. This disease reduces memory function by destroying neurons in the nervous system and reducing connections and neural interactions. Alzheimer's disease is on the rise and there is no cure for it. With the help of medical image processing, Alzheimer's disease is determined and the similarity of the characteristics of brain signals with medical images is determined.

Methods: Then, by presenting the characteristics of effective brain signals, the mild Alzheimer's group is determined. The level of this disease should be diagnosed according to the relationship between this disease and different features in the brain signal and medical images.

Results: For 40 participants brain signals and MRI images were recorded during 4 phase protocol and after appropriate preprocessing, nonlinear properties such as phase diagram, correlation dimension, entropy, and Lyapunov exponential are extracted and classification is done using a convolutional neural network (CNN). The use of this deep learning method can have more appropriate and accurate results among other classification methods.

Conclusions: The accuracy of the results in the reminding phase is 97.5% for the brain signal and 99% for the MRI images, which is an acceptable result.

Keywords: Alzheimer's disease; EEG brain signal; MRI images; Entropy; Lyapunov exponential; Correlation dimension; Convolutional neural network

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Introduction

Alzheimer's disease is the most common caste disease in the elderly for which there is no definitive cure yet. Symptoms of this disease include memory loss, judgment and significant behavioral changes in the person. The disease results in the loss of synapses of neurons in some areas of the brain, necrosis of brain cells in different areas of the nervous system, the formation of spherical protein structures called aging plaques outside neurons in some areas of the brain, and fibrous protein structures called coils A spiral is identified in the cell body of neurons.[1] Researchers have found that using tools in artificial intelligence to extract brain biomarker's information and combine them with each other can help improve the accuracy of diagnosing or predicting cognitive diseases such as Alzheimer's disease.[2] The EEG signal of the brain is a simple, cost-effective, non-invasive method that demonstrates the electrical activity of the brain with high resolution. With the help of this signal and determining different temporal or frequency characteristics, Alzheimer's disease is diagnosed. Changes in the amplitude or range of frequency bands of delta, theta, alpha (alpha 1, alpha 2, alpha 3), beta and gamma can be a valuable way to detect the disease early. Alpha frequency band amplitude decreases slightly in Alzheimer's patients compared to healthy group, while delta band amplitude increases in this group of individuals compared to healthy individuals.[3] This trend shows that the electrical potential of the brain is an effective way to differentiate Alzheimer's patients from dementia or healthy people. Decreased brain signal dynamics, indicating a decrease in neural interactions, occurs in Alzheimer's patients.[4] In Alzheimer's disease, there is a decrease in alpha and beta bandwidth along with an increase in delta and theta bandwidth, and this shows that careful examination of frequency bands is a tool to identify Alzheimer's patients. On the other hand, due to the nonlinear changes in the brain signal and the chaotic nature, the extraction of nonlinear features is also appropriate. Reducing signal complexity, which indicates a decrease in the level of neuronal interactions in Alzheimer's disease, can be used as a method of detecting Alzheimer's disease. Complex dynamic systems such as the brain require nonlinear analysis due to the proliferation of their interactions and

neural connections and rapid changes. Phase diagram, which is a method for converting 1-dimensional signal to multidimensional, and based on the previous example, the current sample and the next sample of the signal, this process of drawing changes in multidimensional can be a suitable way to identify brain dynamics. On the other hand, the degree of convergence and divergence of this dynamic and the trend of changes can be determined by the correlation dimension, entropy and Lyapunov exponential features. The positive value of Lyapunov exponential and a finite non-integral D2 indicate the nonlinear and chaotic behavior of the brain signal. [5] P300 is a specific type of ERP, or in other words, a component of ERP that appears in specific situations. According to research, a P300 wave appears in the recorded brain signal when the brain encounters a new (unusual) stimulus while processing a series of normal stimuli. Of course, to produce a P300, it is necessary to define a specific task for the individual to perform only in response to the target stimulus, for example, to ask the subject to count the number of these stimuli. For acoustic stimulation, the average P300 wavelength is about 300 milliseconds, which was chosen because of its positive polarity and its 300 millisecond delay, but for other stimuli, such as visual stimulation, this time may be up to about 1000 milliseconds Also increase. But in general, the average delay is between 300 and 1000 milliseconds. Spatially, this signal is recorded from three channels on the midline of the head, namely Fz, Cz, Pz. Research has shown that in comparison between these three channels, most cases of P300 have the highest amplitude in the parietal region (Pz) and the lowest amplitude in the frontal region (Fz). Of course, it is necessary to pay attention to the fact that age, gender and many psychological characteristics such as intelligence and personality, etc. affect the amplitude and delay of this wave. In addition, the magnitude of this wave varies with the amount of information provided by the stimulus, meaning that the greater the mental task required of the individual on unusual stimuli, the greater the amplitude of the extracted P300 wave.[6] Electroencephalography (EEG) is a measurement of the electrical potential of the brain that can measure the electrical activity of the cerebral cortex in a multi-channel manner, while quantitative EEG (qEEG) is the analysis of EEG digitally and is called brain mapping. The method visually shows the amount of cortical interactions in each area and by this method the amount of cortical activity is determined as a color map. In the diagnosis of Alzheimer's disease, due to reduced interactions and reduced nervous system function, this process of changes in the EEG can be identified slightly accurately.[7] The use of cerebrospinal fluid (CSF) and the determination of gray matter and white matter volume are some of the features of image processing that are used to diagnose mild Alzheimer's disease.[8] In addition to using brain signals, medical images can also be helpful in early detection of Alzheimer's disease and the extent of changes in different areas of the brain. Cortical atrophy means the gradual destruction of the nerve cells that make up the upper regions of the brain, specifically the structures found in the cerebral cortex, mostly due to a reduction or loss of oxygen and nutrients in these areas. Due to the large number of conditions that can lead to the degeneration of higher structures of the brain, cortical atrophy is one of the most studied types. These causes include a wide range of neurodegenerative diseases, such as Alzheimer's disease, whose main effect is the destruction of nerve cells and consequent loss of brain mass.[9] Medial temporal lobe atrophy (MTA) is one of the changes used to diagnose Alzheimer's disease. The temporal lobe is located in the lower part of the brain. Any damage or atrophy in this area usually causes the most characteristic symptoms of neurodegenerative diseases, as they are all related to memory and thought processes.[10] The aim of this study is to identify Alzheimer's disease with nonlinear features of EEG signal due to dynamic properties and temporal changes in proportion to disease progression and in addition extracting features of MRI images to determine the extent of spatial changes in the brains of Alzheimer's patients. By identifying the location of changes, it could be determined the best and most effective channel for recording brain signals in these patients. In summary, MRI images and brain signals from participants in three channels were recorded in order to accurately evaluate the memory function by sound stimulation and assess the learning rate in reminder and stimulus modes. Then, with proper preprocessing of the EEG signals and MRI images, proper and nonlinear features from these images and signals are extracted due to their fit with Alzheimer's disease changes. At last, the convolutional neural network (CNN) which is one of the deep learning methods has been used for detection.

Materials and Methods

Clinical Diagnosis of Candidates

In this research, 20 men and 20 women with age in range of 60 to 88 years (mean of 68.43 ± 8.86 years) have participated wherein each gender based on literacy they equally selected 10 illiterate and 10 literate and all of them are right-handed.

At first, the participants must be evaluated by a physician with criteria such as clinical tests. One of the appropriate criteria for labeling subjects is the Mini-Mental State Examination (MMSE) memory test. Of course, there is another test such as Dementia Rating Scale (DRS), which is not needed due to the length of the test and proper evaluation of the memory test. It is then labeled according to the score earned by the subject in the test and according to the threshold considered below. The considered groups are: (1) Healthy, (2) Mild patient,

(3) Severely ill.

When running the test, the important point is that according to the questions raised, we must consider the difference between the literate and the illiterate groups. The range for both groups is shown in Table 1.

There were 19 healthy participants with MMSE scores from 23 to 30 with a mean of 27.57 and a standard deviation of 2.29. Eleven participants were in the group of mild patients with an MMSE score range from 19 to 22 with a mean of 20.71 and a standard deviation of 0.95. The last 10 participants were in the severely ill group with an MMSE score range of 3 to 18 with a mean of 13 and a standard deviation of 6.09.

Brain Signal Recording

After clinical test, 3 channels of Fz, Pz, Cz are used unipolarity to record the brain signal because the aim is to record the total brain activity and to study the activity of EOG and its effect on the electrical activity of the brain for a single channel bipolar Alzheimer's patient. The electrical activity of the eye has been recorded. On the other hand, using an audio stimulation in the form of the Oddball protocol, the amplitude and latency of the P300 component in the ERP signal can be measured.[11] In patients with mild Alzheimer's disease, the amplitude of this component is reduced and the delay rate is more than 300 ms. [12] Recording the brain signal from the subject includes the following steps: (1) Teaching the subject, (2) Closing the eyes for 1 minute, (3) Record open eyes for 1 minute and (4) Recording while performing the task assigned to the subject, this includes: (a) Remembering the displayed shapes. (b) Counting target and non-target sounds in the audio audible sample. The subject is instructed by the doctor in the steps of recording the signal after labeling and it is explained that during the recording of the signal, she maintains her composure and this recording does not cause any harm. After preparing the subject and keeping calm, the process of recording the brain signal begins. Initially, the brain signal is recorded for 1 minute with the eyes closed. The brain signal is then recorded in the open eye for 1 minute, and after showing Figure 1, the subject is asked to close his eyes and recall the images for 1 minute, during which time the brain signal is recorded. This state is called the reminder period. Then two sounds with two frequencies of 1 kHz and 1.5 kHz are called standard sound and target sound. 30 target sounds are randomly placed among the 90 standard sounds. The subject is asked to press the right key if he hears the target sound and the left key if he hears a non-target sound. The interval between sounds is about 2 seconds and the playing time of all sounds is about 10 minutes. Figure 2 shows a number of research subjects during brain signal recording.

Table 1. Determine the Threshold for Illiterate and Illiterate People

Condition	Literate	Illiterate
Healthy	23 ≤ MMSE < 30	22 ≤ MMSE < 30
Alzheimer's patient	0 < MMSE < 23	0 < MMSE < 22
Mild Alzheimer's	20 ≤ MMSE < 23	19 ≤ MMSE < 22
Severe Alzheimer's	0 < MMSE < 20	0 < MMSE < 19

Table 2. Mean MTAi and Mean IA between Healthy, Mild and Severe Alzheimer's Disease Groups

Group	Mean MTAi	Mean IA
Healthy	2.3	1.7
Mild Alzheimer's disease	4.5	2.5
Severe Alzheimer's disease	5.7	3.3

MRI Images

Early diagnosis of Alzheimer's disease and differentiation for mild cognitive impairment (MCI) are possible with MRI images. Among the deep learning methods, CNN is used for MRI images to diagnose mild Alzheimer's disease.[13] In preparing MRI images, at least 1.5 Tesla and the thickness of the slices should be 3 mm and the number of slices should be 48 so that acceptable images can be seen to examine the lesions of aging coils and spiral plaques. The database of Tehran Imaging Center has been prepared. Figure 3 shows an MRI image in three different sections of the skull. Table 2 shows the average temporal lobe atrophy and average asymmetry in healthy group and Mild and severe Alzheimer's disease groups.

Figure 4 shows the atrophy of the temporal lobe on the right side of the image and the atrophy of the hippocampus on the left side of the image. In most Alzheimer's patients, atrophy of the inner part of the temporal lobe in patients

Figure 1. Images Displayed for Each Participant.

Figure 2. Images of a Number of Research Subjects During Brain Signal Recording.

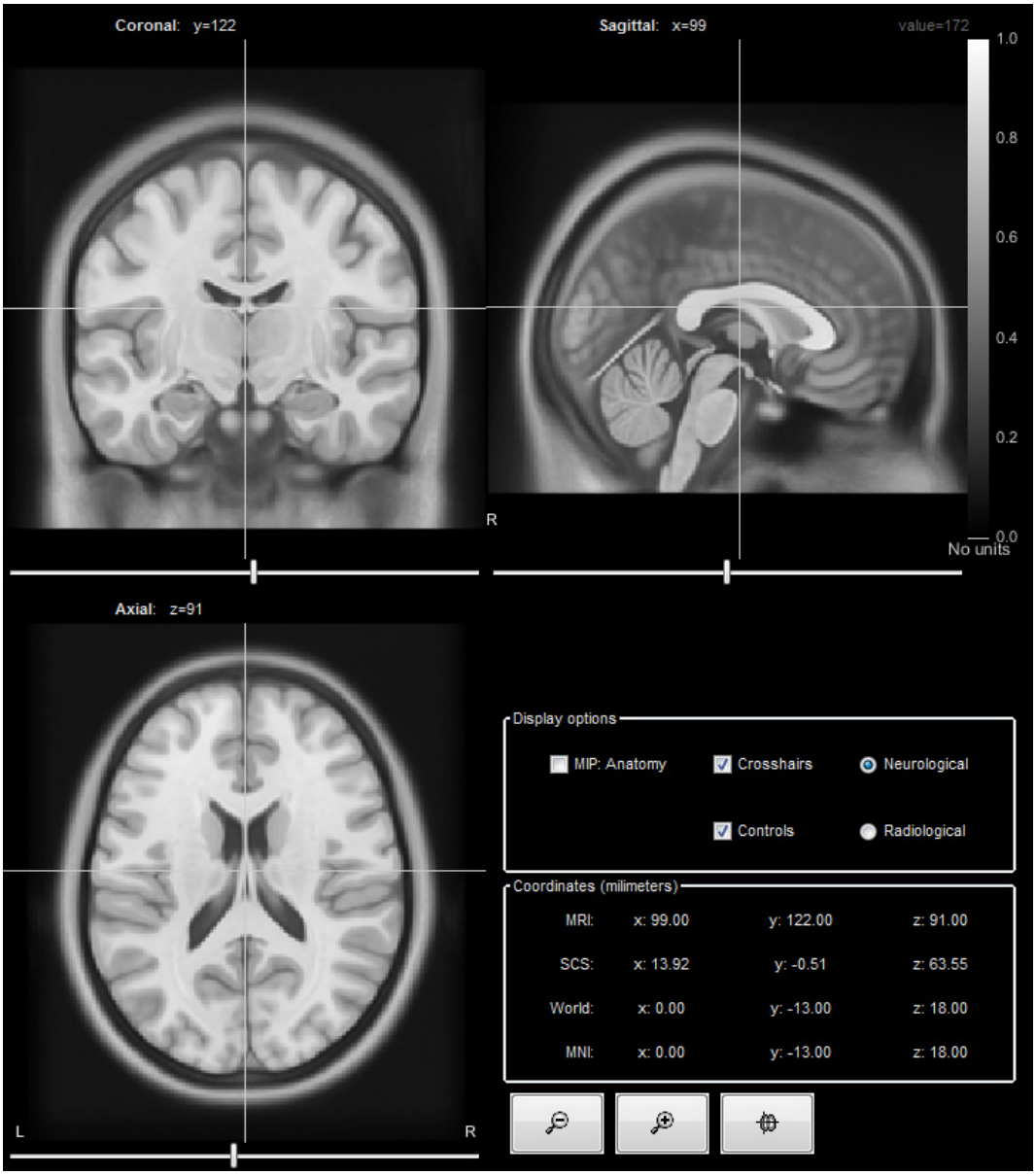

Figure 3. MRI Image in Three Different Sections for Proper Processing.

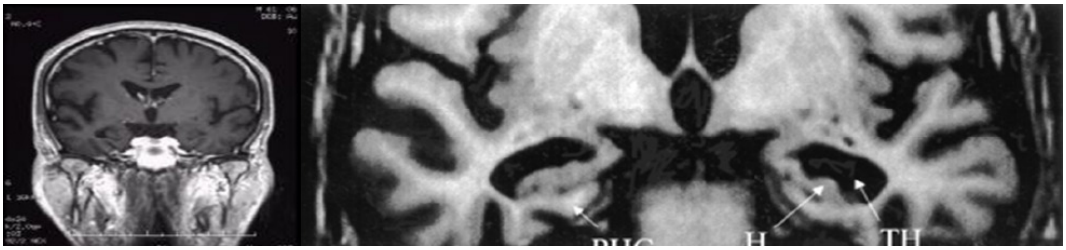

Figure 4. Temporal Lobe Atrophy on the Right and Hippocampal Atrophy on the Left.

with cognitive impairment can be detected up to several years before the onset of clinical symptoms.

In patients with Alzheimer's, hippocampal atrophy will occur with a reduction of 10% to 50% and Para hippocampus with up to 40% compared to healthy individuals. Clinically, a reduction in hippocampal volume of up to 25% causes mild Alzheimer's disease. In Alzheimer's disease, atrophy of the inner temporal lobe and parietal lobe is seen.

Brain Signal Preprocessing

For proper signal processing, the first step is proper EEG signal preprocessing in order to filter the signal from interfering factors and all kinds of disturbances and noise. For this reason, 5 steps have been considered for this purpose: elimination of deviation from the baseline, elimination of high and low frequency artifacts, elimination of electrical noise, reduction of sampling rate and segmentation.

- Remove deviations from the baseline
- Remove high and low frequency artifacts
- Eliminate city electricity noise
- Reduce sampling rates
- Segmentation

The recorded EEG signal has a set of artifacts and noise. Although the variety of artifacts in the EEG signal is high, it can be divided into two main parts: high frequency artifacts due to EMG of the head and neck muscles and low frequency artifacts due to electrode movement and transpiration. To eliminate these artifacts and the noise of the city's electricity, an intermediate filter with cut-off frequencies of 0.5 to 45 Hz has been used.[14] Figure 5 shows the EEG signal in the Fz, Cz, and Pz channels after eliminating city noise and other time and frequency interactions.

Nonlinear Features of EEG

Another approach to EEG signal analysis is the nonlinear and chaotic view of the signal type. From this point of view, tools describing the dynamics and absorption medium should be used for a system and nonlinear chaotic signal. The parameters that express the behavior of chaotic species are twofold. The first group is those who emphasize the dynamics of chaotic behaviors, such as Lyapunov's view and entropy. These parameters describe how the system behaves over time and in close paths as time goes on. The second category emphasizes the geometric nature of motion paths in state space, such as the correlation dimension. In this view, the system is allowed to move in the adsorption bed at the appropriate time and then the geometric dimension of the adsorption bed is obtained. One of the most important tools used to understand the behavior and dynamics of time series, especially time series of vital signals that are mainly extracted from nonlinear systems, is the phase diagram.[15] Figure 6 shows the two-dimensional phase curve and Figure 7 shows the three-dimensional phase curve of the Fz, Cz, and Pz channels. The EEG signal of the healthy subject is shown with the eyes closed.

Lyapunov exponent shows the average view of the convergence or divergence of the neighboring trajectory in the phase space, which also shows the sensitivity of the dependence on the initial conditions. The correlation dimension indicates the number of independent variables needed to describe the dynamics of the system and is another way to check the chaotic signal. The higher the value of this parameter means the more complexity of the nonlinear system. Figure 8 compares the correlation dimension of Pz, Cz, and Fz channels between 3 groups of healthy subjects, mild patients and severe patients. As it can be seen, the amount of this feature has decreased with the severity of the disease, which is more evident in the Pz channel.

Medial Temporal Lobe Atrophy

In patients with a clinical diagnosis of Alzheimer's disease, atrophy of the inner part of the temporal lobe is evident.[16] In the autosomal dominant form of Alzheimer's disease, atrophy of the inner part of the temporal lobe in patients, compared with controls, can be detected up to 3 years before the onset of clinical signs of cognitive impairment. In patients with Alzheimer's disease, hippocampal atrophy was reduced (10%-50%), the amygdala was reduced to 40%, and parahippocampus was reduced to 40% compared with the control group, which was standardized for age. There is compelling evidence that atrophy of the internal structures of the temporal lobe, especially the hippocampus and entorhinal cortex, occurs early in the course of the disease and even before the onset of clinical symptoms.[17] The severity of changes in

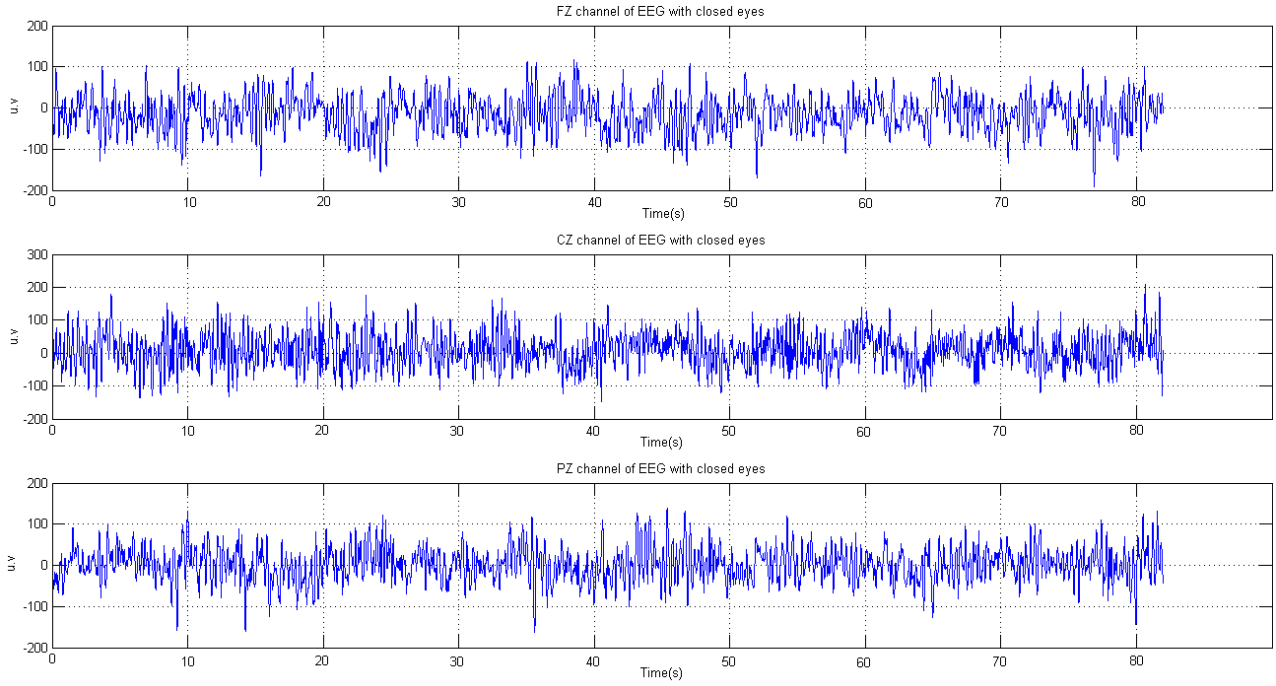

Figure 5. Display Three Channels Fz, Cz, Pz After Preprocessing.

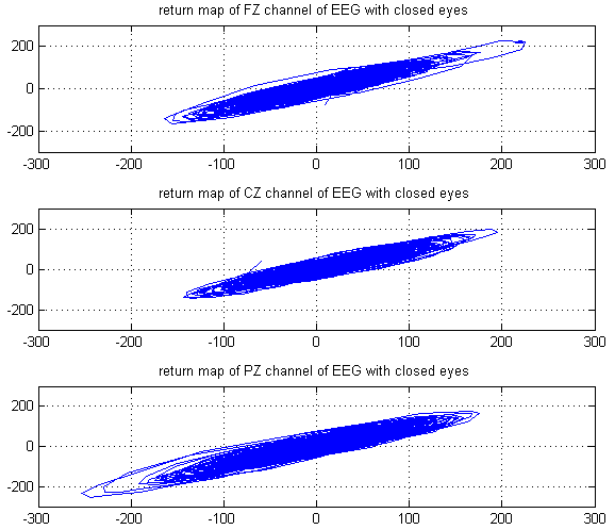

Figure 6. Two-Dimensional Phase Curve of Fz, Cz, Pz Channels EEG Signal of Healthy Subject in Closed Eye.

imaging of healthy elderly people makes it difficult to use MRI as a definitive diagnostic method. By the time mild symptoms appear, the volume of the hippocampus may have decreased by more than 25%. Clinically, a reduction in hippocampal volume is associated with the severity of clinical signs and symptoms of memory loss, the patient's score on cognitive evaluation tests, and pathological findings. However, another group believes that there is no clear association between lesions in the course of dementia, including lesions of hyperexcitability of white matter on MRI, and the severity of the symptoms of post-adjustment cognitive impairment for age. Figure 9 shows how to determine atrophy in MTA images.

The following equation shows how to determine the MTA:

A. Internal temporal loop area
B. Hippocampus and parahippocampus
C. Unilateral lateral ventricle

$MTAi = (A - B) \times 10/C.$

$$C_{left}: Area = 187.3\,mm^2, Avg = 691.1, Dev = 128.3$$
$$C_{right}: Area = 173.1\,mm^2, Avg = 648.2, Dev = 146.2$$
$$A_{left}: Area = 324.7\,mm^2, Avg = 323.9, Dev = 238.1$$
$$A_{right}: Area = 325.5\,mm^2, Avg = 245.3, Dev = 191.3$$
$$B_{left}: Area = 200.3\,mm^2, Avg = 190.8, Dev = 121.6$$
$$B_{right}: Area = 220.1\,mm^2, Avg = 160.4, Dev = 118.3$$

When MTAi is calculated, two values are determined that Each corresponds to a hemisphere. Match asymmetry relation the figure is as follows:

IA (index of asymmetry) = (lMTAi − dMTAi)/(lMTAi + dMTAi) × 100

Measurement of CSF, gray matter, and white matter volume from MRI images has been used to diagnose mild Alzheimer's disease.[18] Determining the range of CSF, gray matter volume, and white matter volume, and quantifying them in 48 slides are determined by MRI images, for example in Figure 10 of one of the slides.

Feature Selection

After appropriate signal and image preprocessing, phase diagram properties, entropy, Lyapunov exponent, correlation dimension, entropy and image properties

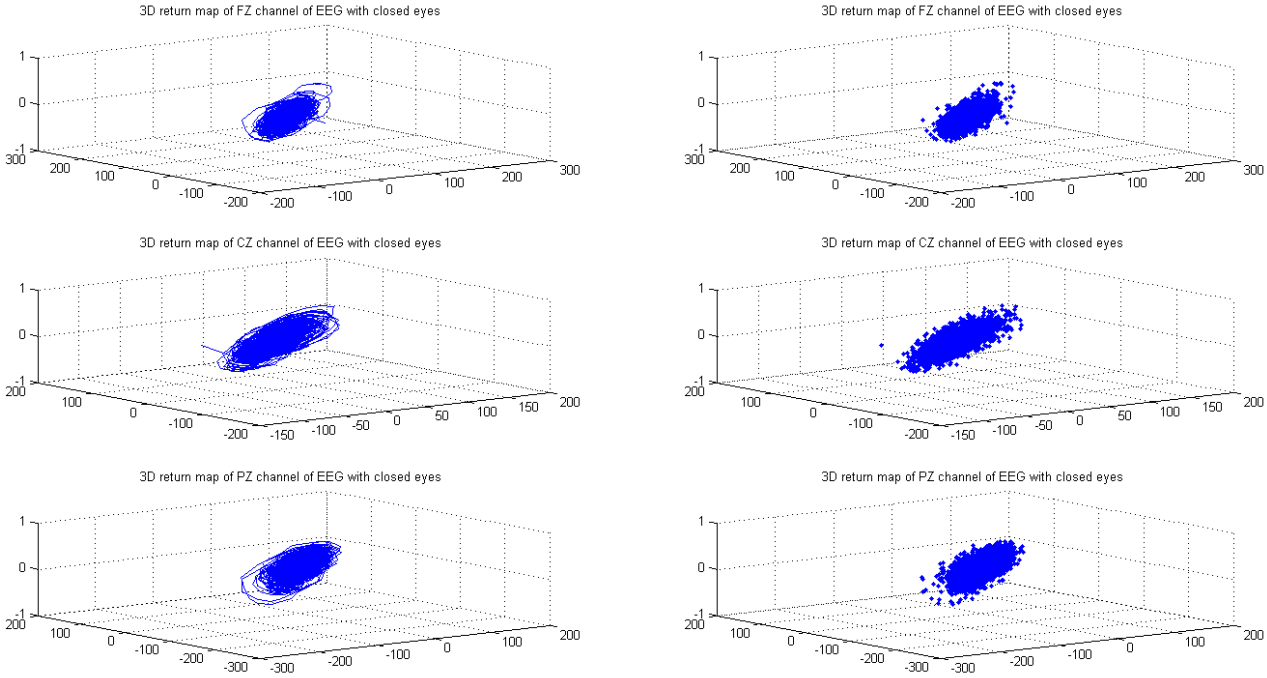

Figure 7. Three-Dimensional Phase Curve of Fz, Cz, Pz Channels EEG Signal of Healthy Subject in Closed Eye.

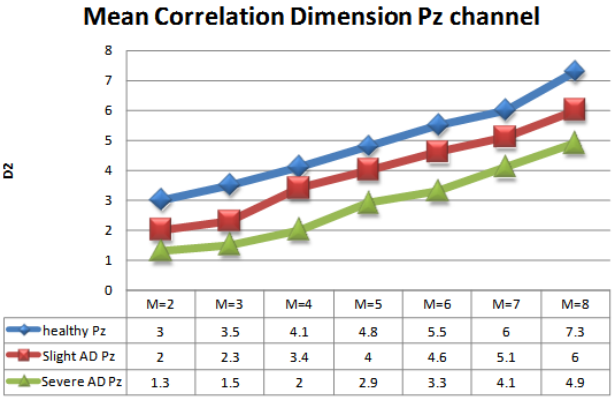

Figure 8. Dimensional Comparison of Pz Channel Correlation for Three Groups of Healthy Subjects, Mild Patient and Severe Patient.

such as statistical properties, MTA, ash volume and white matter volume, gray mater volume and asymmetry in MRI images of both sides of the hemisphere have been used to diagnose Alzheimer's disease. In this study, three EEG channels Fz, Cz, Pz were examined in each period, and 37 features in the closed-eye mode, 37 features in the open-eye mode, 37 features in the reminder period, and 45 features in the stimulation period were extracted. Analysis of these features and the obtained results expressed in continue.

Classification Methods

Deep learning is actually machine learning because learning for the machine performs at complex levels of performance, representation, or abstraction so that the machine has a better understanding of reality and it can

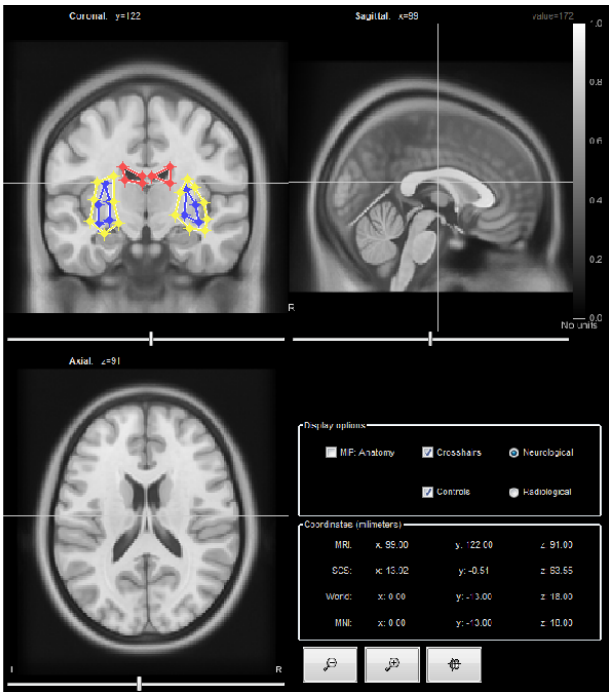

Figure 9. How to Determine Atrophy in MTA Images.

recognize different patterns. The CNN is a type of deep learning that can be used when the data volume is large. The most common form of architectural design, CNN consists of alternating layers of convolution with extraction layers. The recent study used stacked autoencoders (SAE) , which is the total number of fully connected layers to the case, followed by a fully connected layer to all cases. [19] The processing system we use here for classification is

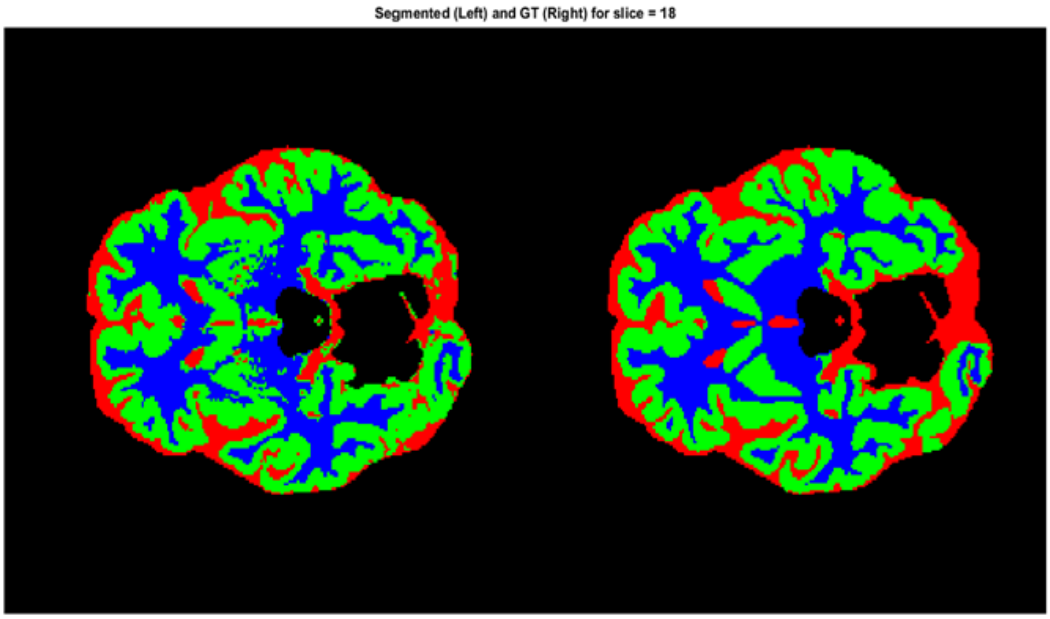

Figure 10. Cerebrospinal Fluid, Gray and White Matter Volume in the Image.

based on an in-depth learning framework for classifying multivariate time series called deep-channel multi-channel neural networks (MC-DCNN).[20] Traditional CNNs usually consist of two parts.[21,22] One of them is the feature extraction module, which can automatically learn features from raw data. The second module is a fully connected training MLP that classifies based on features learned from the previous section. Finally, it can execute one step from exactly the entire processing structure. In this work, the CNN input is generated by an EEG time factor preprocessing step.[23]

Results

Each EEG channel is divided into non-overlapping windows of 10 seconds and recording three channels of brain signals in CNN input, it consists of $10 \times 3 = 30$ inputs. The CNN we propose here has two hidden convolutional layers. The input vector convolves with 3 masks of 30 elements (one per channel) generating 3 features for each channel. The activation layer with nonlinear logistic sigmoid activation functions has a length of 60. Then, the pooling layer generates a sub-sampled representation of 3 elements (each one is generated taking the maximum of over 3 entries). The second convolutional layer is generated through the first (compressing) layer of an auto-encoder MLP. In particular, the auto-encoder MLP compresses the 3 outputs of the previous layer in 30 elements that form the input of the final classification NN (30-7-3). The classification NN is trained by supervised learning (backpropagation). The output of the network is a couple of bits (actually, a soft-max nonlinearity is used, thus the sum of the two outputs is constrained to unity), that correspond to the MCI or AD label. 10% of data is used for testing, and 20% for validation, and 70% for train. To re-evaluate the performance accuracy, we can also use the predicate function to calculate the matrix configuration, and before that, the evaluation is determined for the trained data. Loss diagrams and performance are shown in Figures 11 to 12.

The CNN confusion matrix for recall modes is shown in Figure 13. In addition, the classifier's evaluating criterions such as precision, sensitivity, specificity, and F-score are shown in Table 3.

The results of feature extraction from MRI images show that the mean rate of atrophy in the group of severe Alzheimer's patients is higher than the group of mild Alzheimer's patients and the healthy group. This average is 5.7 in the group of severe Alzheimer's patients, 4.5 in the group of mild Alzheimer's patients and 2.3 in the healthy group. Also, the characteristic of asymmetry between the two hemispheres shows that in the group of severe Alzheimer's patients it is more than the group of mild

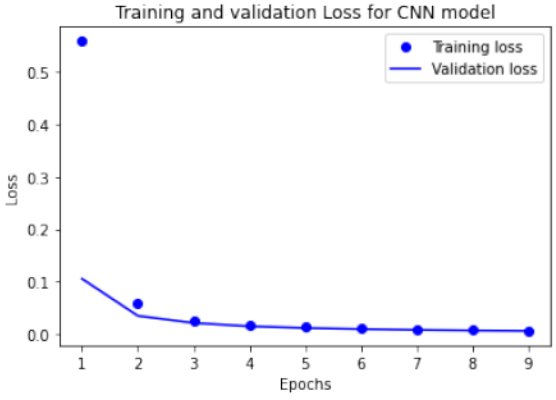

Figure 11. Training and Validation Loss for CNN Model.

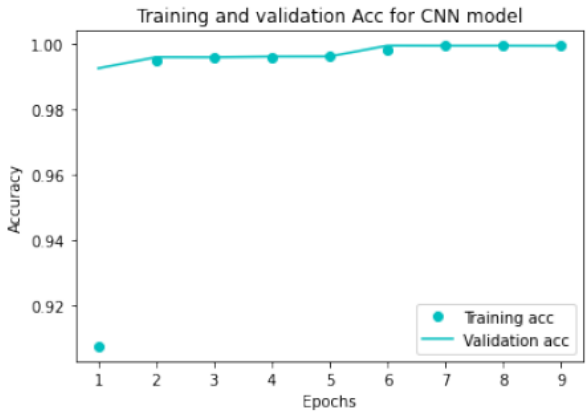

Figure 12. Training and Validation ACC for CNN Model.

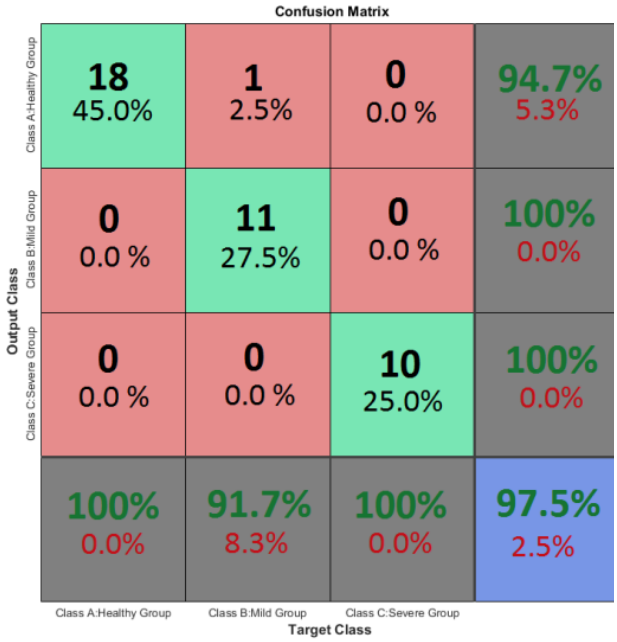

Figure 13. Convolutional Neural Network Confusion Matrix for Recall Mode.

Table 3. The Values of Precision, Sensitivity and Precision in Different Groups in Recall Mode for Convolutional Neural Network

Group	Precision	Sensitivity	Specificity	F-Score
Healthy	100%	94.7%	100%	97.27%
Mild	91.7%	100%	100%	95.6%
Severe	100%	100%	94.7%	100%

Alzheimer's patients and the healthy group. This value is 3.3 in the group of severe Alzheimer's patients, 2.5 in the group of mild Alzheimer's patients and 1.7 in the healthy group. The results of processing and extraction of features from EEG signals show that among the closed-eye, open-eye, reminder and stimulation periods, the accuracy of the results of the reminder period by the CNN is 97.5%.

Discussion and Conclusion

Nonlinear changes in the brain signal of Alzheimer's patients are an important and influential issue. The reduction in the complexity of the brain signal pattern is the result of reduced information transmitted between cortical regions. The brain signal in Alzheimer's disease has other characteristics such as reduced mean frequencies and reduced complex and correlated activities. Abnormal symptoms of the disease affect the EEG signal, including a decrease in rhythms (slow signal) and a decrease in dependence between different areas of the brain. Increased theta and delta activity and decreased beta and alpha activity and decreased beta and alpha band dependence are other symptoms of this disease. The use of EEG signal is important for several reasons. The first reason is that Alzheimer's disease is a cortical disease whose abnormalities is well visible in this brain signal and has been comparable to the normal signal. Abnormal states of Alzheimer's disease in the brain signal directly reflect the functional and anatomical defects of the damaged cerebral cortex. Therefore, research on EEG signal dynamics in relation to neuronal injury has been very important. Another reason is that non-invasiveness can be considered a privilege according to the signal analysis and study of the mechanism of the disease. In this way, cortical synaptic function is evaluated. Flexible states of synapses are considered a crisis for brain function, especially in learning and memory. Interference of synaptic connections is the cause of many neurological diseases. The study of nonlinear dynamics of this signal in Alzheimer's disease indicates nonlinear brain activity in different stages of the disease. Nonlinear dynamics analysis of this signal shows a decrease in the complexity of the brain signal pattern and a decrease in connections due to a decrease in the nonlinear cell dynamics between cortical regions. The next two features are correlation and Lyapanov's appearance, which indicates the feature space and the convergence or divergence of this space is slightly reduced in this disease. Nonlinearity is a prerequisite for chaotic behavior in dynamically known systems in nature. For a neural network such as the brain, this nonlinear dynamic is the result of complex cognitive tasks. On the other hand, we see significant changes in reducing connections and interactions of different brain signal channels in Alzheimer's patients in higher frequency bands, greater sensitivity to correlation, decrease in conformity and increase in correlation dimension in beta frequency band, decrease in synchronization in alpha and beta frequency bands. And gamma, increased compliance and connections in the theta frequency band, decreased functional connections and decreased compliance in the high alpha and beta frequency band in the brain signal of Alzheimer's patients. The studied courses are closed-eyed, open-eyed, reminder and stimulation, and among these 4 courses, the best course for evaluating and extracting features is the reminder

and stimulation course. On the other hand, among the three channels Fz, Cz, Pz to record brain signals, the Pz channel shows better features for diagnosing Alzheimer's disease. The two indicators of amplitude and latency of the P3 component are very important in the process of identifying Alzheimer's disease, but on the other hand, it is important to note that these two indicators are closely related to various parameters of the Oddball protocol. The amplitude and latency index of the P3 component of the ERP signal depends on the amplitude of the excitation signal, the frequency of the excitation signal, the excitation intervals, and especially the probability of the occurrence of two excitation classes.[24] For example, if the frequency of target stimuli decreases or the intervals between stimuli increase, the amplitude of the P3 component increases in healthy individuals. Another important point is that the amplitude and delay of the P3 component change with age and the stages of Alzheimer's disease and even forms of dementia. On the other hand, the range of this component is directly related to the way memory works, that is, the more a person enjoys a more appropriate state of memory, the range of this component increases. The delay of this component has been reported in various sources of approximately 300 ms, which can vary depending on the condition of the subject and the recording of this component, but another important point is that the delay is 300 ms, or in other words a delay of less than 300 ms represent better mental performance. The use of deep learning methods, including channel neural network, can have more appropriate and accurate results among other classification methods. The accuracy of the results in the reminder period is 97.5% for the brain signal and 99% for the MRI images, which is an acceptable result. By properly selecting features and combining them effectively using two CNN networks and an MLP network, recursive classifiers have higher accuracy results than other deep and recursive learning methods such as R-CNN and fastR-CNN.[25] Because nature the features in MRI images are spatial and physical and the features of brain signals are temporal and dynamic, so for EEG and MRI the custom recursive classifier is designed and finally combined by the MLP neural network. In the case of using two CNN networks and one MLP network, the accuracy of the results has increased compared to the case of using a CNN network by combining the features of brain signals and medical images.

Also, the use of deep learning methods for MRI images is less accurate between the three groups of healthy people, mild patients and severe patients than when EEG signals are used with MRI.[26]

Data Availability

The data are available upon request.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

Ethical Statement

All participants were informed about the procedure and their satisfaction has been obtained. In addition they evaluated by a physician with clinical tests. A local ethics committee entitled "Theses Committee" certified the study in terms of ethical considerations.

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