

Deep Learning in the EEG Diagnosis of Alzheimer's Disease

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Abstract. EEG (electroencephalogram) has a lot of advantages compared to other methods in the analysis of Alzheimer's disease such as diagnosing Alzheimer's disease in an early stage. Traditional EEG analysis method needs a lot of artificial works such as calculating coherence between different pair of electrodes. In our work we applied deep learning network in the analysis of EEG data of Alzheimer's disease to fully use the advantage of the unsupervised feature learning. We studied EEG based deep learning on 15 clinically diagnosed Alzheimer's disease patients and 15 healthy people. Each person has 16 electrodes. The time domain EEG data of each electrode is cut into 40 data units according to the data size in a period. In our work we first train the deep learning network with 25 data units on each electrode separately and then test with 15 data units to get the accuracy on each electrode. Finally we will combine the learning results on 16 electrodes and train them with SVM and get a final result. We report a 92 % accuracy after combining 16 electrodes of each person. In order to improve the deep learning model on Alzheimer's disease with the upcoming new data, we use incremental learning to make full use of the existing data while decrease the expenses on memory space and computing time by replacing the existing data with new data. We report a 0.5 % improvement in accuracy with incremental learning.

1 Introduction

1.1 Background of Study in Alzheimer's Disease (AD)

Alzheimer's disease (AD) is the most common cause of dementia all over the world. It's not a familial disease, so it has more than 15 million people affected worldwide sporadically. It not only takes a lot of health expenditures and costs of care but influent caregivers' normal life and work as well. Alzheimer's disease puts a heavy burden on society. A lot of work and research have been done on diagnosing it as early as possible.

There are a lot of methods used in the analysis of Alzheimer's disease (AD). Neuroimaging like CT and MRI plays an important part in the diagnosis of Alzheimer's disease. But there are also some other causes of dementia, such as subdural hematoma and brain tumor. Since the changes of early stage Alzheimer's

patient is subtle. It takes a long time to diagnosis it under clinical follow up testing and analyzing but the accuracy is still comparatively low, with sensitivity of around 80 % and specificity of 70 % according to Sarah Hulbert and Hojjat Adeli in [14].

Luckily, researches by computer aided methods such as Electroencephalogram (EEG) and magneto encephalogram (MEG) has been used in diagnosis of Alzheimer's disease (AD) these years. The advantage of using computer is that it will help clinicians diagnose the disease earlier and easier. This means we will have a higher chance of slowing down the development of the disease.

1.2 EEG Analysis of Alzheimer's Disease (AD)

The EEG analysis of Alzheimer's disease has been used as a tool for differential diagnosis and early detection of AD for decades since Hans Berger first observed pathological EEG sequences in a historically verified AD patient. EEG abnormalities which reflect anatomical and functional damages of the cerebral cortex are frequently shown in AD, that's the main reason why EEG has been intensively researched. Researchers have studied EEG diagnosis of AD with different methods.

One of the most important methods is to diagnose AD by analyzing the brain coherence with EEG. EEG coherence is supposed to give information about connections between different recording electrodes and is used as the evidence of structural and functional connections between cortical areas underlying the recording electrodes. A lot of studies have discovered a pattern of decrease in AD coherence. Sankari et al. in [13] studied on the intrahemispheric, interhemispheric and distal brain coherence in AD patients and discovered a pattern of decrease in AD coherence. Absolo et al. in [1] used sample entropy in the diagnosis of AD and got the accuracy of 77.27 %. Sankari and Adeli in [13] present a probabilistic neural network model which uses features extracted in coherence and wavelet coherence studies in AD and reported a classification accuracy of 100%. T. Locatelli in [15], evaluate whether short-distance or long-distance coherence is more affected and the possible diagnostic value of coherence analysis in AD.

The second method for EEG analysis is Entropy method. It's helpful in the analysis of Alzheimer's disease because the brain is a nonlinear dynamical system. Entropy methods don't require large data sets. There are different entropy methods used for the analysis of EEG data such as approximate entropy (ApEn), sample entropy (SampEn), and multiscale entropy (MSE). Absolo et al. in [1] used sample entropy to differentiate between groups of AD patients (11) and HCs (11). They report an accuracy of 77.27 % on distinguishing AD patients and Healthy people at all four electrodes using receiver operating characteristic plots to test the accuracy of the SampEn method.

Another method is wavelets. Polikar et al. in [11] compare different types of wavelets for analysis of event-related potentials and get the highest average classification of 78.2 % for Daubechies wavelets. Ahmadlou et al. in [3] use fractal dimension (FD) to model the dynamical changes in the Alzheimer's disease

patient's brain. They use the two global features and linear discriminant analysis (LDA) to classify ADs and HCs and report a high classification accuracy of 99.3% with sensitivity of 100% and specificity of 97.8%. Sankari et al. in [12] investigate wavelet coherence of EEG records obtained from AD patients and HCs. Sankari and Adeli in [13] present a probabilistic neural network model for the classification of AD patients and HCs using features extracted in coherence and wavelet coherence.

The last but also important method is Graph theory. These methods use nodes, or vertices, to represent objects, edges to represent relationships, and weights assigned to edges to represent the strength of those relationships. Generally, three types of networks can be created using the graph theory: (1) small-world networks (Han et al. in [8], which are characterized by large clustering of nodes and small path lengths between nodes, (2) ordered networks, which have large clusters and large path lengths, and (3) random networks, which have small clusters and small path lengths. The underlying goal of this method is to measure the connectivity in various brain networks and the change in the connectivity transferring from HC to AD. Ahmadlou et al. in [2] present a chaos-wavelet methodology using a recently developed concept in graph theory called visibility graph (VG) by applying two classifiers to the selected features and discovering effective classification features and mathematical markers. The used classifiers include a radial basis function neural network (RBFNN) (Zhou et al. in [16]) and a two-stage classifier consisting of principal component analysis (PCA) (Al-Naser and Soderstrom in [4]; Meraoumia et al. in [10]) and the RBFNN. They obtained a diagnostic accuracy of 97.7% using the discovered features and a two-stage classifier (PCA-RBFNN). McBride et al. in [9] compute the inter channel coherence for each pair of 30 EEG electrodes and perform graphical analysis using network features. They use LOO (leave-one-out) cross-validation method and the ML technique SVM as a classifier to differentiate AD from HC and MCI under various resting conditions.

The EEG methods we talked above are proved to be very helpful in the diagnosis of Alzheimer's disease. While those methods have good performance in the analysis, there are still several problems we should consider about. Firstly, how can we improve the accuracy when there are so much noise in the EEG data of a patient. We can reduce the influence of noise by decreasing the sensitivity of the analyzing model as well as by trying to find more features which can represent the data best. Secondly, most diagnosis with EEG data are operated after the whole set of data is totally collected and we can only use it once. How can we make full use of the previous data to help improve the diagnosis this time, in other words, how can we make the outdated data inheritable? We try to make full use of the experiment data by getting the features of it and initialize the learning model with features we used. Deep learning has the advantage of learning features in a unsupervised way. And training data of deep learning network can be flexible, which makes the EEG analysis easier and handy.

1.3 Deep Learning Networks

Deep learning has been researched for many years but there was not too much progress until 2006 when Geoffrey E. Hinton published an article called A Fast Learning Algorithm for Deep Belief Nets on the journal Science. The reason why deep learning is so popular among machine learning researchers is that it has shown great learning and classification performance in many areas, such as speech voice recognition, handwritten character recognition. Deep learning is helpful in machine learning because deep learning can extract useful features layer by layer automatically rather than artificially according to G.E. Hinton in [5]. In their work, they constructed a deep auto encoder by layer wise pretraining with pixel vectors of a picture and doing back propagation with the label of the picture through the whole auto encoder to fine-tune the weights for optimal reconstruction. On a widely used version of the MNIST handwritten digit recognition task they report the error rate is 1.2%.

1.4 Our Contribution in EEG Diagnosis of Alzheimer's Disease

We applied deep learning algorithm in the EEG analysis of Alzheimer's disease to explore the possibility of making analyzing process easier by unsupervised feature learning. Firstly, by using the handy machine to collect patients' brain data without harming the patients or invading their bodies, we collected EEG data of 30 people from hospital. There are 15 Alzheimer's disease patient and 15 healthy people. After denoising under some thresholds and filters we got the processed data. Secondly, we built the deep learning structure for EEG analysis. The existing deep learning networks are often used to learn figures and we need to adapt it to EEG data by changing the input layer. G.E. Hinton in [5] used the input vector of 784(28×28) data as the input layer but we will choose 500 or the data size which can be divided by 500 as the input vector according to the period of EEG data. The amount of hidden layers and amount of nodes in each layer also need to be considered as factors which influence the performance of deep learning network in EEG analysis. We carried out the experiment under different settings of hidden layer amount and nodes amount. And we choose the best setting as our experimental learning structure. Finally, we tried to combine 16 electrodes to get better analysis results. We used SVM to train the learning results on each electrode and got an accuracy of 92% on the combined electrodes of a person. With the help of deep learning algorithm, we need less data because we can get more learning feature in a unsupervised way, what's more, we can do the learning process as long as we have an integrated data units instead of waiting for the whole EEG data be collected. By using incremental learning, we don't have to save all of the existing EEG data of Alzheimer's disease patients and update the learning model with new data. So the analysis of Alzheimer's disease's EEG data becomes easier to handle and will be used more commonly because all we need is the a machine to collect EEG data.

2 Deep Learning Used in EEG Diagnosis of Alzheimer's Disease

2.1 Theories of Deep Learning Network

Deep learning is a machine learning model which has many hidden layers except the input layer and output layer. It's built to simulate the human brain's working mechanism on learning. Deep learning theory originates from artificial neural network. The difference between deep learning and artificial network is as follows. The neural network initials the weights randomly and trains the whole network by back propagation while deep learning uses layer-wise greedy learning algorithm to initial the learning network and trains the network layer by layer wise network like Restricted Boltzmann Machine. And then use the supervised learning algorithm to optimize the parameters.

The structure of a deep learning network is a several-layer learning network. It includes the input and output layers as well as few hidden layers. The nodes in the same layer are independent and the connections between nodes from two layers are valued by weights. There are weights of two directions between every two layers except for the top layer. So actually the deep learning network is a graph model with a single layer neural network. We also can take the deep learning as a stack of encoding decoding layers. Here we can use RBM or auto encoder in each layer. Geoffrey E. Hinton promoted a framework of deep learning in [6]. In each single layer the learning process is greedily initialize the bias and weights between visible and hidden nodes. After the learning network is greedy initialized layer by layer, we need to fine-tune the network. Hinton promoted a supervised way called wake-sleep algorithm in [7]. It includes two parts called wake and sleep. In the wake stage, it recognizes the features and weights to produce the states of nodes in every layer. It will also adjust the weights in downward direction which are also called generated weights. In the sleep stage we use the note values from the top layer and generated weights which are learnt in wake stage to produce the lower layer's note values and adjust the upward weights which are also called recognize weights.

2.2 EEG Based Deep Learning Model of Alzheimer's Disease Analysis

The reason why we use deep learning network in the EEG analysis of Alzheimer's disease is that it can automatically generate helpful learning features which can make the analysis more efficient. The function of the EEG based deep learning model is like follows (Fig. 1):

The basic process of deep learning in EEG diagnosis of Alzheimer's disease includes two steps: the first step is the unsupervised training of a deep learning network with the EEG data of Alzheimer's disease patient and healthy people. The second step is to fine-tune the deep learning network with labels of the EEG data.

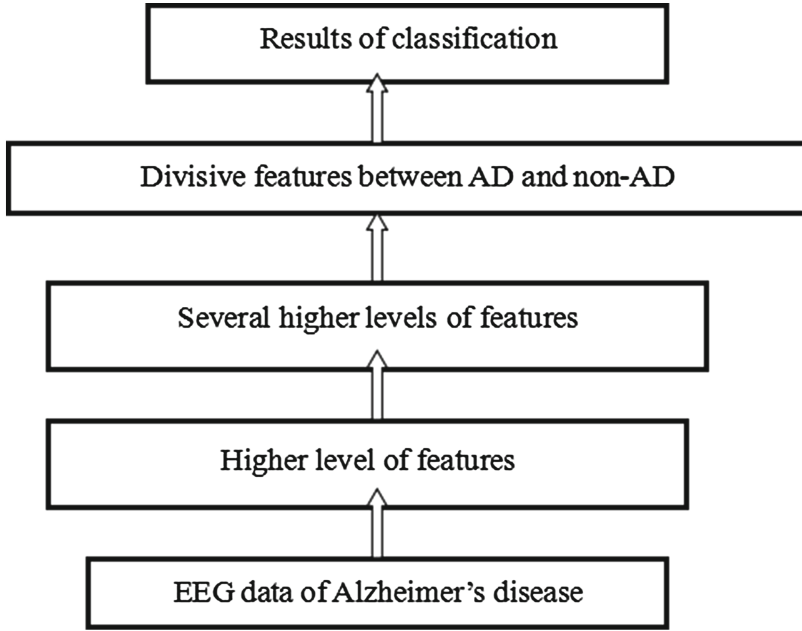


Fig. 1. EEG based deep learning network in the diagnosis of Alzheimer's disease. We use the several layer deep learning network to learn features that can distinguish Alzheimer's disease and healthy people. And then we use these features to do Alzheimers disease analysis.

The detailed learning process is as follows: We choose to use RBM as the basic structure in our work. By training a stack of n layers of RBM we model the deep learning network with weights generated from EEG data. We input the EEG data and train the first layer (bottom layer) of the DL network with random weight and biases, by minimizing the gap between decoded value and input value we can initialize the weight and bias and get the encoded value. We will carry on the learning process by taking the encoded data as the input of the next layer and repeat the first layer's initializing process. By doing the same layer by layer, we get the network with features which can represent the input better because of the restriction of the capacity and sparsity. Then we will use the parameters of every layer to initialize the whole network and then adjust the network in a supervised way with two kind of labels represent Alzheimer's disease or healthy people.

After we have got the data for training and testing from the raw EEG data, we start to input the data into the deep learning network. Firstly, we take the data units we have got earlier as the visible data of the first RBM layer. Take the node i from visible layer and the node j from the hidden layer for example.

$$p(h_j = 1|v) = \sigma(\sum_{i=1}^m w_{ij} \times v_i + c_j) \quad (1)$$

here, h_j is the value of node j , v_i is the value of node i , w_{ij} is the weight between i and j . c_j is the bias of hidden layer node j .

We can use the same way to reconstruct the value of the visible layer and get the biases of the nodes in the visible layer. By calculating the weights between nodes of two different layers we have got the connection between them.

Secondly we use the hidden layer data from the first RBM layer to be the visible layer of the second RBM. We can train as many RBM layers as we want by reusing the hidden layer from anterior layer as the posterior layer's visible layer.

Finally we have got the whole structure of the EEG based deep learning network. By layer wise RBM training we can have the weights and biases which are comparatively good. And then we can fine-tune the features to improve generation by back propagation. The learning model we used in our work is like follows (Fig. 2):

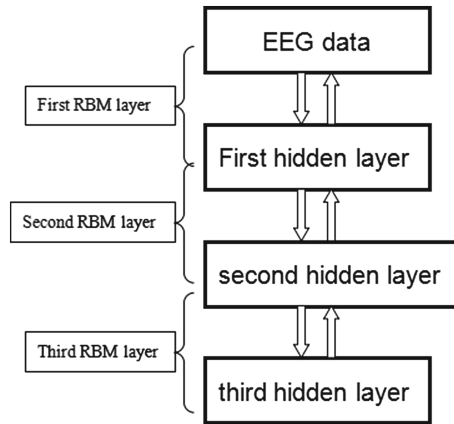


Fig. 2. The structure of the EEG based deep learning network. It's actually a stack of RBMs. We use the EEG data as the visible layer of the first RBM and then we use the hidden layer of the first RBM as the visible layer of the second RBM layer. We can set as many RBM layers as we want.

In our work, we explored the best structure of the EEG based deep learning network by experimenting with different amount of layers and different nodes in each layer. We finally find the layers and the nodes that can minimize the error of classify. We carried out the experiment on all sixteen electrodes with this optimal learning structure.

3 Experiment Design in Alzheimer's Disease (AD)

3.1 Experiment Data

In our work, we try to firstly build the EEG based auto-deep learning network and then evaluate it with 30 people's EEG data. We firstly collect the EEG data

from 15 Alzheimer's disease and 15 healthy people by qualified technicians under standard procedures and were recorded at rest state, with eyes closed. The data we used includes the EEG data in 16 electrodes. We can not use the raw data directly. We need to denoise the raw EEG data by setting thresholds and using filters.

Our data for training is the EEG data units we have got from the processed EEG data earlier. The EEG data of Alzheimer's disease is different from the image data. Compared to the two dimension data, the EEG data is one dimension data. So we should consider the data integrity of our input layer. Sixteen electrodes were fixed by collodium and placed over the scalp according to the 1020 International System (Fp1, Fp2, Fz, F3, F4, F7, F8, C3, C4, Pz, P3, P4, T5, T6, O1 and O2). Twenty minutes of EEG were collected with a band pass of 0.530 Hz and digitized at a sample. By cutting the collected EEG data into data units we can obtain more data for training and testing compared to using the data of a single person. Here we have got 30 people's EEG data with 16 electrodes per person. And by cutting each electrode data into 25 data units for training and 15 data units for testing we can have 30 batches of data with the training batch size being 25 and testing batch size 15. In each batch, we will input into the deep learning network one data unit at a time which means we have 750 training data units and 450 testing data units for 30 people on one electrode. The size of the data unit is also called the dim of the data. We will choose different dims of data such as 500, 1000, 1500, and 2000.

3.2 Experiment Structure of Learning Model

The structure of the net is represented by the amount of nodes in each layer like 2000-500-500-2000-2, here it means we put 2000 dim data into the visible layer and set the amount of three hidden layers' nodes as 500, 500, 2000 separately, and the last layer is the classify layer with two nodes representing Alzheimer's disease and healthy people. Firstly we should determine how many layers we will use as hidden layer in our deep learning net and then explore how many nodes we should use in each layer.

3.3 Incremental Learning for Updating Deep Learning Analysis Model in Alzheimer's Disease

The existing EEG data of Alzheimer's disease takes huge memory space and it's impossible for us to save all the EEG data after we have obtained the analysis model. But a static analysis will soon become outdated with the upcoming experimental data. So we use incremental learning in our experiment to update the analysis model. We make a rule on how to choose data to abandon and how to replace experimental data with new data to update the model. We make full use of the existing data by saving learning features in the deep learning network as parameters. Abandoning part of existing data saves a lot of memory space. When the amount of new data has reached to our experimental standard we will train the learning model again with data set which includes part of existing data and the new data.

4 Experiment in Alzheimer’s Disease (AD)

4.1 Experiment to Find the Best Amount of Layers

Firstly, we trained the AD patients data and normal people’s data on 16 different electrodes in time domain. We set a deep auto-encoder network which has several hidden layers besides the input layer and output layer. By setting the input visible layer data as 500, we explore how many hidden layers we should use in the EEG based deep learning network by changing the amount of layers. The amount of hidden layer changing from 3 to 7. The experiment sample is with 10 people including 5 healthy people and 5 AD patients. The accuracy of each experiment is the average accuracy of 16 electrodes on the test data set with 150 data of 10 people. The results of the different networks is as follows (Table 1).

Table 1. The accuracy of EEG based deep learning network with different amount of layers.

Layer amount	Accuracy
3	86 %
4	83.6 %
5	78.1 %
6	80.4 %
7	75.33 %

Considering the different performance of different hidden layers in a deep learning network, we choose the amount of layers which has the best performance as our default amount of layers in the followed experiments. So we will continue our experiment with three hidden layers.

Secondly, we will do experiment to find the best amount of nodes in each layer.

We carry out the experiment on the influence of the amount of nodes in each layer and decide how many nodes we should set for each hidden layer. We will fix two of the three hidden layers and change one layer to see the difference. Here is the accuracy according to our experiment design on the same data set.

We will set the first two layers as 500 and 500 nodes. And change the third layer. The accuracy of each experiment is the average accuracy of 16 electrodes on the test data set with 450 data of 30 people. The results are shown as follows (Figs. 3, 4 and 5 and Tables 2, 3 and 4):

Secondly, we change the amount of the second layer and fix the first layer as 500 and the third layer as 2000 nodes.

Finally, we will change the first layer’s nodes and fix the rest and fix the second layer as 500, the third as 2000.

With the results from the above experiments, we choose the best model of deep learning network in the analysis of Alzheimer’s disease. We set the amount

Table 2. The accuracy of EEG based deep learning network with different amount of nodes in 3rd hidden layer.

Nodes	Accuracy	Nodes	Accuracy
500	80 %	2500	82 %
1000	82.9 %	3000	83.7 %
1500	78.2 %	3500	81.2 %
2000	85 %	4000	84 %

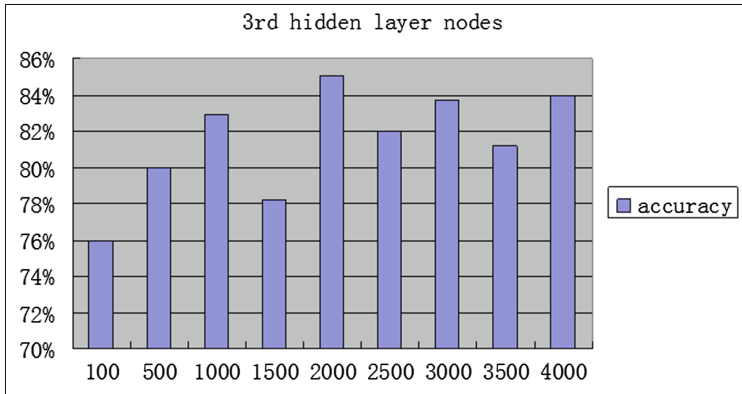


Fig. 3. The accuracy of the EEG based deep learning network with the node amount changing in the third layer.

Table 3. The accuracy of EEG based deep learning network with different amount of nodes in 2nd hidden layers.

Nodes	Accuracy	Nodes	Accuracy
100	77 %	500	82 %
200	79 %	1000	84.9 %
300	76 %	2000	80.33 %
400	80.7 %	3000	76 %

Table 4. The accuracy of EEG based deep learning network with different amount of nodes in 1st hidden layer.

Nodes	Accuracy	Nodes	Accuracy
100	75.1 %	500	85.1 %
200	80.5 %	1000	83.9 %
300	79.8 %	2000	82.3 %
400	83.4 %	3000	77 %

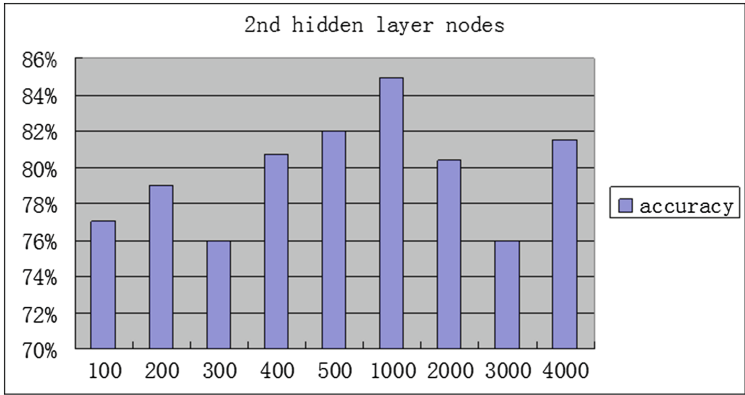


Fig. 4. The accuracy of the EEG based deep learning network with the node amount changing in the second layer.

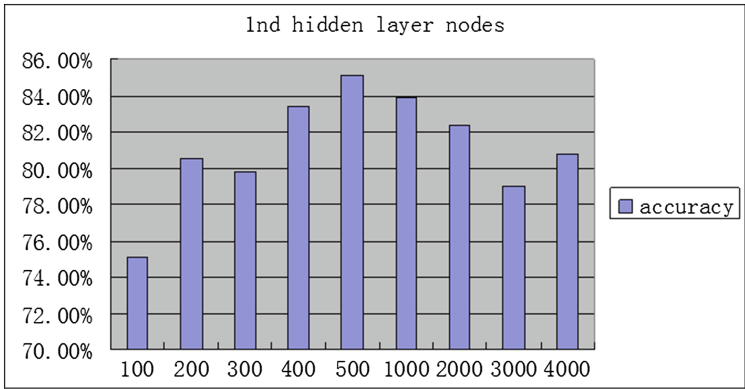


Fig. 5. The accuracy of the EEG based deep learning network with the node amount changing in the first layer.

of layers as 3 and the amount of nodes in each layer as 500, 1000, 2000 separately. Now we work on exploring the relation between the change of training data size and accuracy of classification. According the sampling frequency, the smallest experimental data size is 500, which is sampled in a complete period. We also tried different data sizes which are in integral multiple of 500. Based on the former learning model we choose. We have experimented with the input data size from 500 to 10000, when the data size is 500, the accuracy is under 50 %, but with the increasing of the data size, the accuracy also increased to be around 90 %, when the data size become 2000, the accuracy also reach the peak which is 92.5 %, then we got the decrease of the accuracy from 2000 to 10000. So we choose the training data size as 2000.

4.2 Experiment to Update Analysis Model with Incremental Learning

There are two steps in the incremental learning of the analysis model. Firstly, we define a rule on how to abandon useless data after the deep learning model on EEG data has been built. Secondly, we use the saved data and model to train with new data for updating the model. According to the different analysing result on different data, we calculate the average error rate of each data in the train set. Because the data which has a lower classification error can be better represented by the feature in the analysis model, we choose to abandon them. The data with low classification accuracy will be kept until the next round of training. By replacing 250 of 750 existing data with new data, we update the analysis model by making full use of the features in the deep learning model. The amount of misclassified data of 750 testing data in each electrode changes differently. But in 12 of the total 16 electrodes, we got less misclassified data than updating the model. The combination accuracy of 16 electrodes after incremental learning is 0.5% higher than it was before incremental learning.

4.3 Comparison of Deep Learning Analysis with Other EEG Analysis Method on Alzheimer's Disease

There have been a lot of research in the EEG analysis of Alzheimer's disease. But the problem is that different methods are studied on different datasets. So it's a little bit hard for us to compare our method to others in a general dataset. Here are some methods we mentioned in the introduction and the different accuracies they have got. SampEn have got 72.3% by testing 11 AD patient and 11 healthy people. Graph theory/SVM has got the result as 93.8 with 17 AD patients and 15 healthy people. Wavelets-chaos has the result 99.3% with the sample 20&7(AD&HC). Since the analysis of Alzheimer's disease is a complicated process, we should consider both the accuracy of analysis and the practicability of the method. Using deep learning in the analysis of Alzheimer's disease can have both the high accuracy and the low cost of time and expenses.

5 Conclusions

In our study we applied the deep learning network into the EEG diagnosis of Alzheimer's disease. We modify the structure of deep learning network to adapt to the feature of EEG data and get the suitable structure of the deep learning network by changing the layers and the amount of nodes on each layer. We conducted experiment on 30 people with 15 Alzheimer's disease and 15 healthy people by imputing 16 electrodes' data of each people separately into the deep learning network. After all the deep learning on the 16 isolated electrodes, we combine them to get a final result with the help of SVM and finally get the accuracy of 92%. Here we combine the advantages of the EEG analysis and deep learning network by analyzing the Alzheimer's disease in an early stage

with flexible size of data. We have the possibility to do early stage analysis of Alzheimer's disease more commonly since we only need the machine to collect EEG data and can use deep learning network to analyze the data collected as long as the data size is larger than a period's data size. We also applied incremental learning in the update of the existing analysis model and have improved the analysis result with 0.5 % higher accuracy. In our future work, we will try to improve the deep learning network on EEG data of Alzheimer's disease by applying the algorithms of transfer learning to make full use of the existing features in other well studied deep learning models.

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