Functional EEG Network Analysis for Cognitive Diagnosis of Alzheimer's Disease

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Abstract

Electroencephalogram (EEG) is a test for electrical activity in the brain. Using Machine Learning approaches and adopting ideas from social network analysis (SNA), we construct a causality network to visually and mathematically analyze the cognitive function of EEG's of a group of 15 normal control (NC) subjects, 16 mild cognitive impairment (MCI) patients, and 17 Alzheimer's Disease (AD) patients. The functional EEG network for each subject is represented by a 30x30 matrix, where each element depicts a causal relation between two EEG channels. The network is visualized through a colored map of the matrix that illustrates the strength of causal relationship among the EEG channels. The cognitive state (NC, MCI, or AD) of a subject is classified using features of the functional EEG Network, including color maps and eigenvalues.

Keywords: Electroencephalogram (EEG), Social Network Analysis (SNA), Principal component analysis (PCA), Support Vector Machines (SVM), Leave-One-Out (LOO) Cross Validation

1 Introduction

1.1 Background

Alzheimer's Disease, one of the common forms of irreversible neurodegenerative dementia, is a progressive brain disorder which slowly destroys mentation, memory, and eventually, the ability to conduct the simplest tasks. The statistics from the World Alzheimer Report (2018) show that the number of people with dementia is estimated to be 50 million today. According to the U.S. department of health and human services (2019), Alzheimer's disease has been the sixth leading cause of death in the United States.

Although some factors, including increasing age and genetic inheritance, are well-known risks for Alzheimer's Disease, a combination of lifestyle and circumstantial factors plays a vital role as well.

According to the Alzheimer's Association (2018), 18% of the projects have been investigating the diagnosis, assessment and monitoring of Alzheimer's Disease. The rest of have been looking into the molecular pathogenesis, clinical intervention, health care enhancement, etc.

Unfortunately, there is no full-proof method for the diagnosis of Alzheimer's disease currently. Self-reporting about symptoms is still a key component of the diagnostic assessment. Other than that, diagnosis is based on fluid and imaging biomarkers. Currently, amyloid-specific PET ligands including florbetaben, flumetamol and florbetapir are in practice for the detection of AD (J. Weller and A. Budson, 2018), however, it has been limited owning to its unaffordable costs for the majority of patients, thus most patients who undergo such method are the participants of clinical trials.

Electroencephalography (EEG) was introduced as a tool of documenting human brain activity in 1929. Since EEG directly reflects cortical neural functioning (U. Hegerl, 1997) with high efficiency and considerably low cost, it remains a vital role in helping the detection of Alzheimer's Disease.

The EEG is a recording of the electrical activity of the brain used electrodes attached to scalp. During recent years, there have been extensive investigations of the potential use of EEG for the clinical diagnosis of Alzheimer's disease. Currently, accuracies up to 90% have been reported using methods such as neurological and medical records (Raymundo, 2018). However, depending on such approaches requires experienced clinicians, lengthy sessions and high expenses. An efficient, low-cost approach with EEG for AD detection is currently being studied. A common problem with this is that numerous factors lead to the loss of data, which yields inaccurate detection for AD.

Social Network Analysis, based on networks and graph theory, poses an advantage in revealing the insights in the intricate but organized network structures as well as relationships among the entities (Elisabeth, 2013). This technique has been exploited by various authors to study brain function. For example, previous research (Yongoh, 2017) has measured the brain effective connectivity from EEG data by network analysis. In this article, the team attempts to create a functional EEG network to investigate the inter-channel

causation of EEG data for each cognitive state and characterize corresponding features for classification and accurate diagnosis.

1.2 Objectives

The goal of this research was to create a functional EEG Network that depicted the casual relationship between EEG channels. In order to find the relationships among the channels, the following objectives were established:

- Build reconstruction models that would predict lost data from EEG channels using the data from neighboring channels.
- Calculate the correlation coefficients among the original and reconstructed data to find the p-values explaining the greatest relationships between certain channels.
- Create a visual representation of the brain activity illustrating the causal relationship between EEG channels

2 Methods

2.1 Data

Raw EEG data was gathered from 48 subjects of various cognitive states: 15 NC, 16 MCI patients, and 17 AD patients. Each subject had numerous channels of data; however, 30 common channels were used for the purpose of this research. The physiological signals gathered from each EEG channel were sampled at 1-minute intervals with a sampling rate of 500 Hz, providing 30000 data points for each channel. The data was filtered for power-line noise at 60 Hz and artifacts due to blinking and muscle twitches prior to the start of the research.

2.2 Pre-processing

Before data processing and model training, subjects are split into three groups based on cognitive state: NC, MCI, or AD. For each training group, a leave-one-out cross validation training is applied where 1 subject is used for testing while the rest of the subjects are used for training. For every subject in each training set, all common EEG channels are compacted to form one continuous signal. Normalization is applied to the newly created signal to scale the data to unit variance.

2.3 Analysis

An adaption of social network analysis was adopted to create our functional EEG Network. Social Network Analysis (SNA) observes the relational link between individuals, groups, and other entities, similar to nodes in a graph. SNA can also provide a visual and mathematical representation of these nodes to better understand and measure the strength of these relationships. Using this approach, the functional EEG Network was built in the following steps:

1) Build a 30x30 matrix where each element m_{ij} in the matrix contains a reconstruction model for reconstruction of channel j using channel i.
2) Use reconstructed EEG data to make a 30x30 correlation matrix of the causal relationships between EEG channels i and j.
3) Create a color map using the values of the correlation matrix and perform image classification
4) Use PCA to reduce the dimensions of the matrix and classify using an SVM model

In Step 1, leave-one-out cross validation was not used. Instead, reconstruction was based on subject n's EEG data and applying a 75/25 split on the data. Essentially, 75%, or the first 45-seconds, of each channel's signal is used for training while the rest of the data is used for testing. **Fig. 1** shows the schematic creation of the models as well as the creation of the correlation matrix outlined in Step 2.

With the 45-seconds of training data, reconstruction models are created for each pair of EEG channels, which predict the physiological signal of a given channel j using EEG data only from channel i. Each model acts as an element in a 30x30 causality matrix representing an EEG Network for each subject. For each network, the models consist of three layers: an input layer, a hidden layer, and an output layer. The input layer takes data from each channel individually yet consists of 50 neurons. In order to pass in 50 input variables, each channel's signal is right-shifted 49 times. Each right-shifted signal truncates a data point off the right end of the signal and replaces the first data point with a 0 and is then stored in an array. The truncation and appending of data are to ensure that the size of each signal is the same after each right shift. The hidden layer contains 15 hidden neurons and uses a rectified linear unit activation function, and the output layer contains one neuron and uses a linear activation function. The initial weights for the reconstruction models are normally distributed.

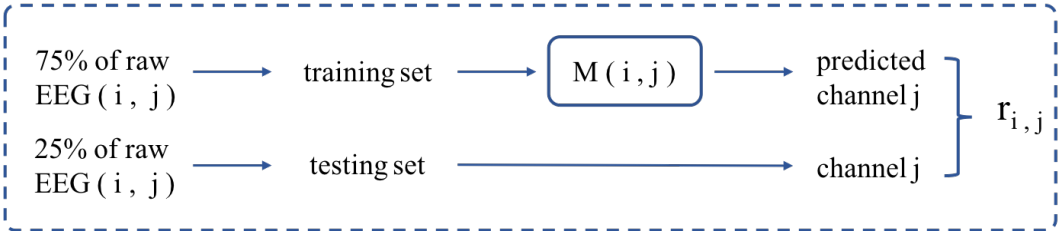

Fig. 1. Schematic for the creation of the EEG network depicting the causal relationship between channels i and j. M(i,j) represents the model for using channel i to reconstruct channel j. Each value of $r_{i,j}$ is treated as an element in a 30x30 causality matrix. This process is applied to each subject, resulting in 48 different matrices.

In Step 2, after constructing the causality matrix, the remaining 25% of the data extracted for testing and creating a similar matrix depicting the causal relationship for the EEG Network. **Fig. 2** illustrates the structure of the matrix for the EEG Network. Similar to training, the testing data is right shifted as well to ensure 50 input variables and similar sizes. Data from channel i is passed into the model and reconstructed data for channel j is produced.

The signal that is reconstructed for channel j is compared to the original signal of channel i to find a causality relationship. Comparison is done by calculating Pearson's correlation coefficient *r* between the two datasets shown in Eq. (1):

$$r = \frac{COV(X,Y)}{\sigma_X \sigma_Y} \tag{1}$$

where σ_X represents the standard deviation of the reconstructed EEG data for channel j, σ_Y represents the standard deviation of the raw EEG data for channel i, and *COV(X, Y)* represents the covariance of the reconstructed and raw EEG data.

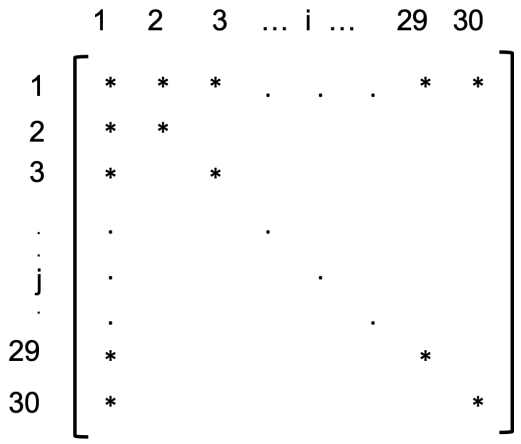

Fig. 2. Schematic for the structure of the 30x30 matrix for the EEG Network. The matrix structure is used for model creation as well as storing the correlation coefficients for channels i and j. Helps to illustrate the causal relationship for each channel and is later used for image classification.

Pearson's correlation coefficient measures the linear dependency between two datasets *X* and *Y*. Correlation coefficient values of r closer to 1 or -1 represent stronger correlations while values closer to 0 represent weaker correlations. The Pearson correlation coefficient is calculated using the scipt.stats.pearsonr function in Python, where the reconstructed and original data are the arguments passed into the function. Each coefficient value is saved in another 30x30 matrix structured similarly to the one mentioned above. In order to save time and avoid needless calculations, it is assumed that the correlation coefficient along the diagonal of the matrix is 1, i.e. if channel i and channel j are the same, their linear correlation should equal 1.

In Step 3, we use visualization techniques to illustrate the causal relationship between each channel in the EEG network. Since the EEG network is represented as a 30x30 matrix, we characterize each element in the matrix as a pixel in an image and the value of each element as the color index of the pixel. This means the EEG network can be visualized as a colored image of 900 pixels. By using each correlation coefficient as a value on a grey-scale color index, the causal relationship between EEG channel i and j is mapped out on a graph. After grey-scaled graphs have been created for the 48 subjects, they are separated into three

separate categories based on the subjects' cognitive states: NC, MCI, or AD. The Deep Neural Network Toolbox in MATLAB is then used to create and train a model for image classification.

Using the leave-one-out principle, a model is trained for each of the 48 subjects using the other 47 as training data. The accuracy and predicted labels obtained from testing are stored in a 1x48 array, where the first 17 elements represent AD subjects, the next 16 elements represent MCI subjects, and the last 15 elements represent the NC subjects. The accuracy scores are later counted to find the true accuracy of the model.

In Step 4, a separate approach was taken for classification of subjects using the EEG Network. Instead of using image classification to classify subjects into their respective cognitive groups, principle component analysis (PCA) and support vector machines (SVM) were applied to the data. Since each subject had 900 correlation coefficient values, PCA was applied to reduce the dimensions of the data into two features. This was done in two ways: by calculating the eigenvalues for each row and by calculating column means for the data. Each method reduced the 30x30 matrix into a 30x1 matrix for each subject in which PCA was then directly applied to extract two features. The two features were then plotted against each other on a graph and then an SVM model was created based on the newly reduced data.

3 Results

1. Single-channel reconstruction

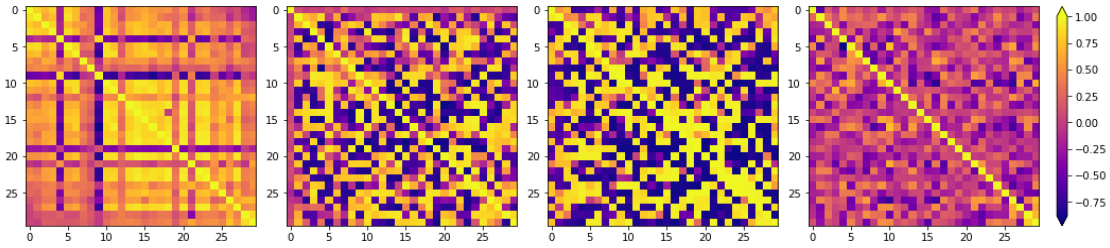

Fig. 3. Sample of colored-maps of correlation matrices for AD-subjects. The correlation matrices were created from the functional EEG Network.

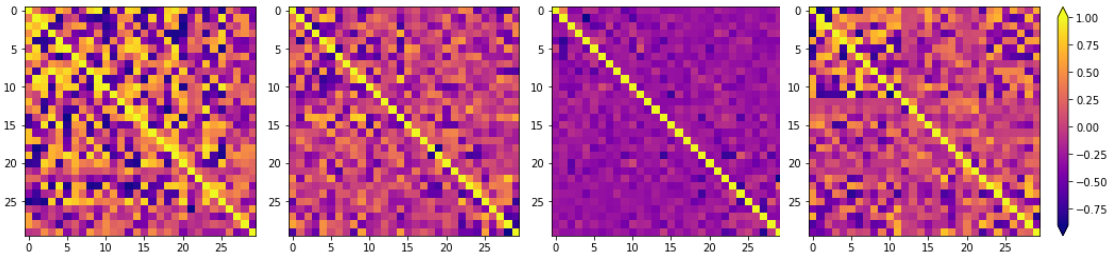

Fig. 4. Sample of colored-maps of correlation matrices for MCI-subjects. The correlation matrices were created from the functional EEG Network.

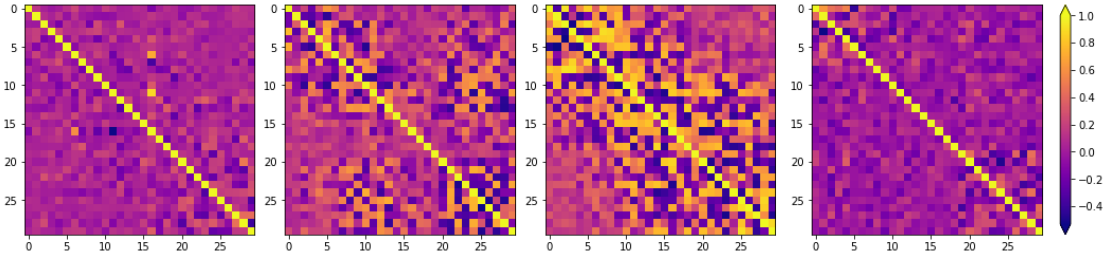

Fig. 5. Sample of colored-maps of correlation matrices for NC-subjects. The correlation matrices were created from the functional EEG Network.

The EEG Network was built using channel-to-channel reconstruction for each subject. For each network, a 30x30 matrix of correlation coefficients was constructed. Each correlation coefficient represents the causal relationship between channel i and channel j, and is used as a color index in a 30x30 graph to visualize the causal relationship. **Fig. 3**, **Fig. 4**, and **Fig. 5** show some samples of the visualized matrices for four random subjects from each cognitive group: NC, MCI, and AD. Based on observations, the matrices aren't fully symmetric, meaning the correlation coefficient for $r_{i,j}$ isn't the same as $r_{j,i}$. Also, subjects in the AD-category appeared to have strong channel relationships than those in the MCI- or NC-category.

Image classification was performed on the visuals using the Deep Neural Network Toolbox in MATLAB. The results of the classification model are presented in **Table 1**. Of the subjects classified, 5 were correctly identified as NC, 10 were correctly identified as MCI patients, and 7 were correctly identified for AD patients. Only for the MCI patients were the majority of the predictions accurate. Overall, the prediction accuracy of the classification model was 45.8%.

	Predicted classes				
		NC	MCI	AD	
True classes	NC	5	4	6	33.3%
	MCI	3	10	3	62.5%
	AD	2	8	7	41.2%
		50%	45.5%	43.8%	Overall Acc: 45.8%

Table 1. Confusion matrix of image classification using correlation matrices

Another classification approach we took was using PCA and SVM models in the hopes to improve or achieve the same accuracy rate of our model or those used in past research. Three different sets of features were used to perform PCA and SVM. The first set of features consisted of performing PCA on the eigenvalues of the correlation matrices. The top two features were plotted on the xy-axis in which it was concluded that using an SVM would be impossible to classify the data. As shown in **Fig. 6**, using an SVM model wouldn't have helped to distinguish the subjects by their features as the data mostly clusters around a similar area.

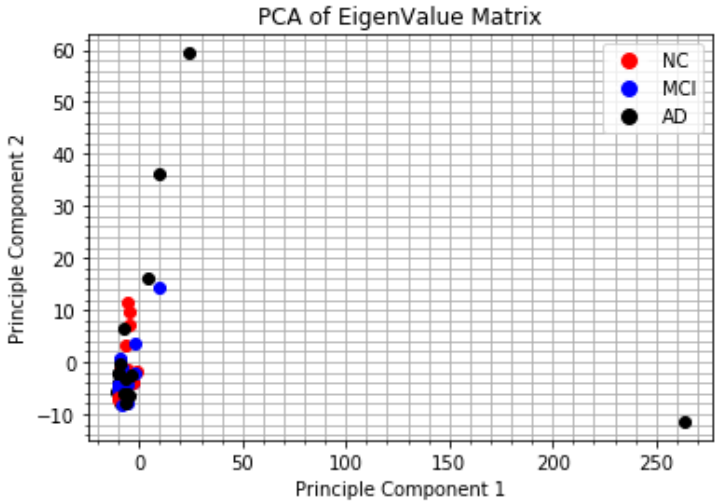

Fig. 6. Top two features of PCA on eigenvalues of correlation matrix

For the second set of features, column averages of the correlation matrices were used as features for our SVM model. This meant that our model would have to attempt to classify patients along a 30-dimensional plane of features. The results of the SVM model are shown in **Table 2**. For our model, 2 were correctly identified as NC, 5 were correctly identified as MCI-patients, and 14 were identified as AD-patients. The overall prediction accuracy was 43.75%. Although the accuracy rate of the model was not greater than the one used for image classification, the SVM model had a higher accuracy rate for correctly identifying patients in the AD-category.

	Predicted classes				
		NC	MCI	AD	
True classes	NC	2	1	12	13.33%
	MCI	0	5	11	31.25%
	AD	1	2	14	82.3%
		66.67%	62.5%	37.84%	Overall Acc: 43.75%

Table 2. Confusion matrix of classification using the column means of the correlation matrix

For the third set of features, eigenvalues were calculated for the correlation matrices. The linear algebra library in Python was used to calculate 30 eigenvalues for each correlation matrix; however,

each eigenvalue was returned as a complex number. In order to use SVM, the magnitude of each eigenvalue was calculated. Using the same method for the column averages, an SVM model was created in a 30-dimensional plane to classify each patient. According to **Table 3**, this approach had more significant results than the image classification and the column averages. Of all of the subjects, only 1 subject from each cognitive group was misclassified. The overall accuracy of the SVM model was 93.75%, nearly double of what was obtained during image classification.

	Predicted classes				
		NC	MCI	AD	
True classes	NC	14	0	1	93.33%
	MCI	0	15	1	93.75%
	AD	1	0	16	94.12%
		93.33%	100%	88.89%	Overall Acc: 93.75%

Table 3. Confusion matrix of classification using the magnitude of the eigenvalues of the correlation matrix

4 Conclusion and Discussion

In this research, we created a functional EEG Network to provide many ways into visualizing and classifying EEG data. Adopting the idea of SNA, our EEG Network maps out the causal relationships between all EEG channels and accurately reconstructs lost data. Based on the data gathered, our EEG Network seems to best classify patients when using the eigenvalues of the network as features for classification. Using image classification and column averages was less than half of the accuracy obtained from the eigenvalues. Results from principle component analysis on the eigenvalues of the correlation matrix show that the subjects didn't cluster and weren't easily distinguishable by the eye in **Fig. 6**. They clustered in a curvature making it difficult to create an SVM model that would easily group them into their respective cognitive groups. Yet, despite the results in **Fig. 6**, our EEG Network provides promising results as a novel approach to EEG analyzation for future research.

Even with the prediction accuracy from our SVM model in **Table 3**, there were many inaccuracies with some of the other models generated for the network. The SVM model used for the column means of the correlation matrix seemed to over-predict patients with Alzheimer's Disease. This could possibly explain why the prediction accuracy of that group was higher than others. With over-prediction, the model becomes biased in categorizing other subjects into the AD-category rather than the MCI-, or NC-category. The model used for image classification had the highest prediction accuracy when identifying MCI-patients; however, it did not over-predict any singular group like the column mean model. Because most of the colored-maps of the correlation matrices showed similar patterns across all subjects, it is possible that the model didn't obtain enough data of distinctive features to properly identify each subject into their respective cognitive group. The accuracy of the model could be purely due to random guessing, meaning that the prediction accuracy of the model would be extremely inconsistent if it were to be run again multiple times with the same dataset.

One drawback we had with this research was the small sample size used to train and test the models. LOO cross validation compensated for this. In the future, we wish to increase the sample size of patients to better train our models and yield higher prediction accuracies. We also wish to create separate networks for each cognitive group and compare the structure of the networks to the one created in this research. Conclusively, we would create an EEG network for the NC-, MCI-, and AD-patients and see if those networks would more precisely reconstruct the EEG data for their respective groups and provide a more accurate analysis of the causal relationships between the EEG channels.

5 Appendix

5.1 Appendix I: Fig. 7

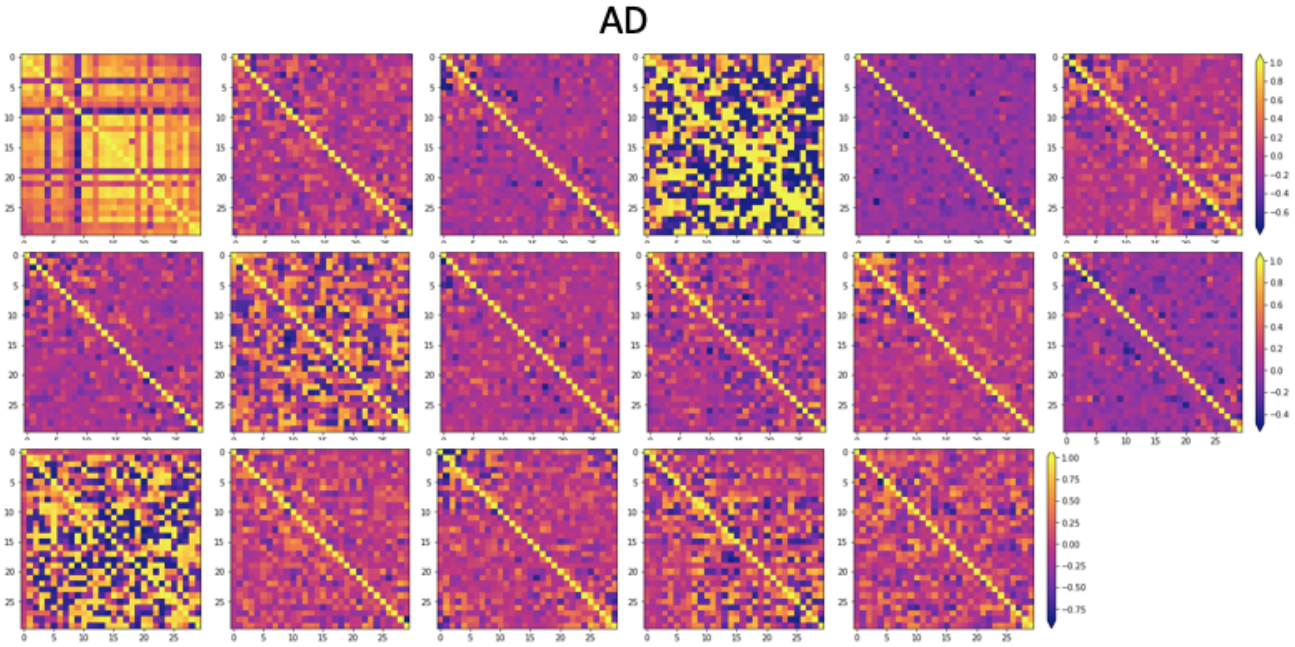

Fig. 7. Visual representation of the EEG Network for all AD-patients.

5.2 Appendix II: Fig. 8

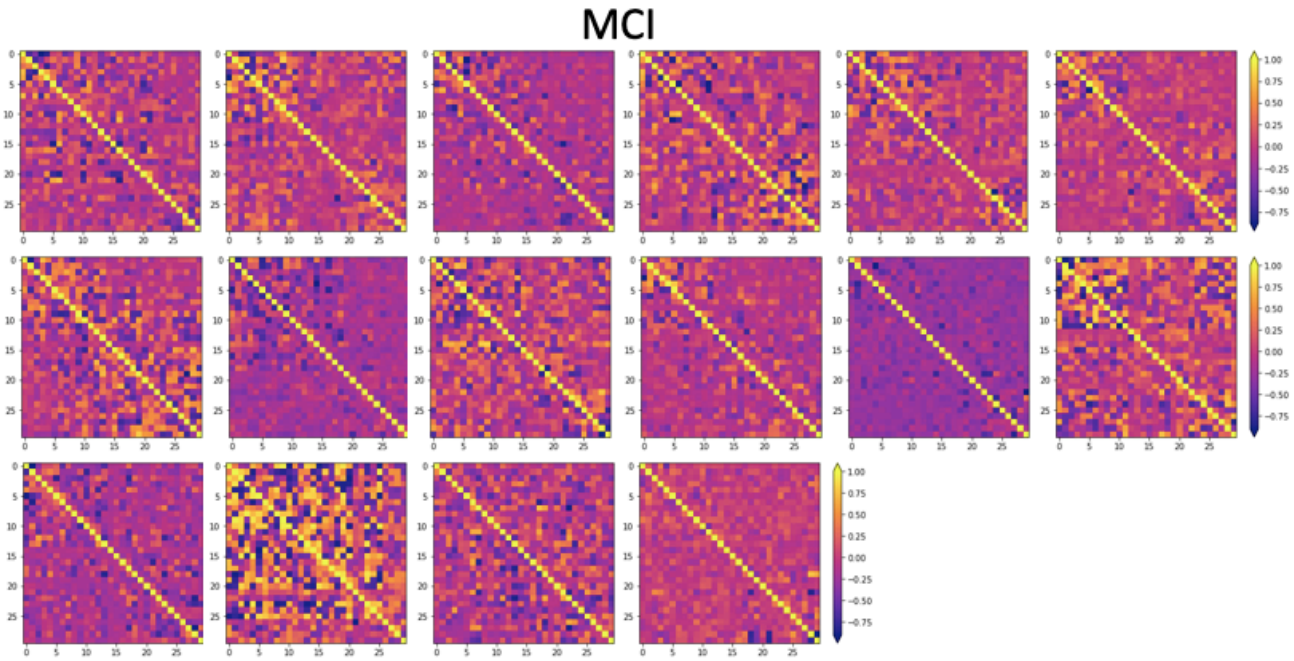

Fig. 8. Visual representation of the EEG Network for all MCI-patients.

5.3 Appendix III: Fig. 9

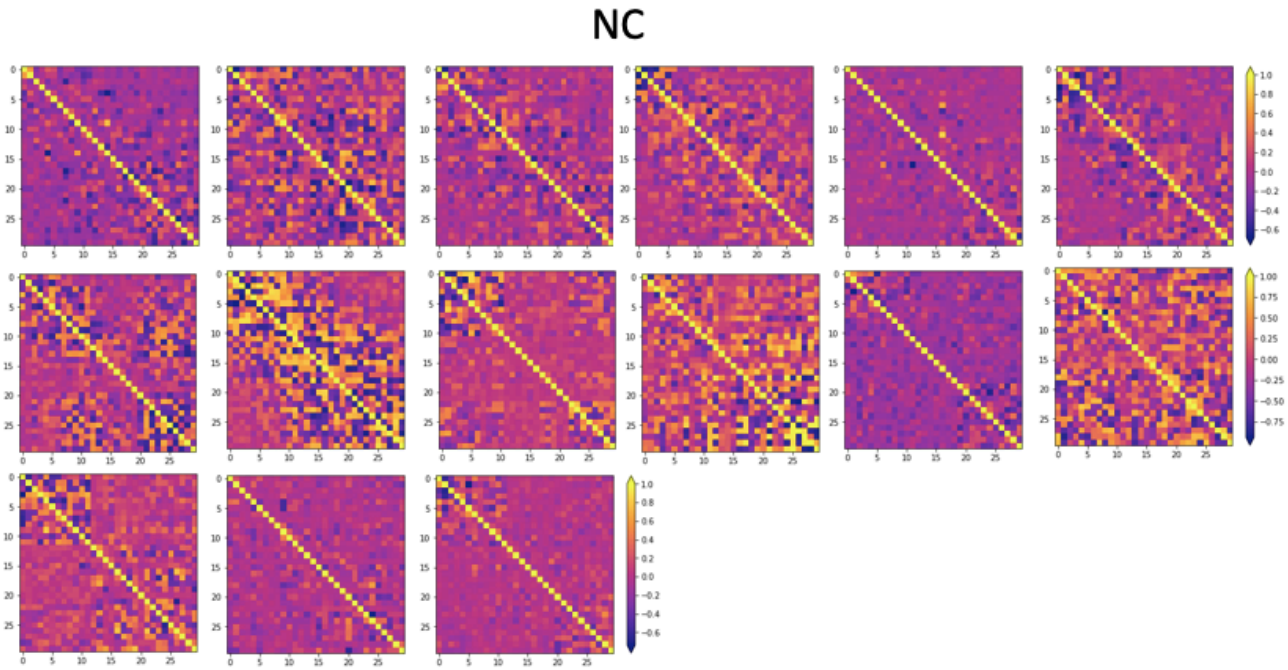

Fig. 9. Visual representation of the EEG Network for all NC-patients.

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