A study of progression of Alzheimer's Disease using advanced graph theoretical analysis

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***Abstract*—Alzheimer's Disease is a neurodegenerative disease that affects millions of people. It impairs normal cognitive function. The hypothesis is that the degree of impairment of normal cognitive functions is directly proportional to the degree of degeneration caused due to Alzheimer's Disease. We have leveraged the Systems Neuroscience angle of Alzheimer's Disease to design a data-driven approach to understand and analyze brain networks with respect to certain network metrics. These metrics are then correlated with results of standardized tests designed to gauge cognitive function.**

***Index Terms*—fMRI, EEG, Graph Theory**

I. Introduction

Alzheimer's disease is a serious neurodegenerative disease affecting millions of people. It is especially detrimental to normal cognitive functions. Some of the symptoms of Alzheimer's disease include (but are not limited to) dementia, changes in mood and personality, decreased or poor judgement, difficulty completing familiar tasks, etc. Modelling the complex human brain as a functional network is an good way to simplify the complexity of the brain to study what is pertinent. Data recorded from EEG and fMRI can be used to extract functional brain networks. The corresponding graphs can be analyzed with respect to different subjects at different time points with corresponding psychometric test results to track the progression of AD.

II. Literature survey

Graph theoretical metrics have been used to identify biomarkers in Alzheimer's disease recently. [1] discuss various model-free and model-based methods for applying graph theory to identify such connectivity patterns. [2] showed that local connectivity is disrupted for left and right hippocampus regions of patients affected by Alzheimer's disease. This was observed due to a drop in clustering coefficients. Moreover, age-related changes in working memory (WM) ability appear to depend most strongly on the executive processes of updating and inhibition and [3] conducted experiments with WM cues and studied the connectivity patterns in cognitive control from FMRI data. [4] assessed the relationship between theta-gamma coupling and working memory deficits in Alzheimer's disease (AD) and Mild cognitive impairment (MCI). Previous attempts at not just identifying bio-markers but studying the progression of AD include work by [5]. They have observed that Randic index correlated with progression of AD.

III. Materials and Methods

We use "Working Memory" dataset with relevant psychometric tests for our EEG analysis. It consists of Question segment followed by Fixation segment followed by Response segment then again followed by a Fixation segment. We use a windowed mean filter to filter the EEG signals. Traditionally Pearson correlation coefficients were used for building the adjacency matrix from signals. We also explored and implemented graphs using Phase locking value which is a more faithful measure of synchronization. We also wish to include Spectral coherence to build graphs.

We use OASIS 3 as our fMRI dataset. We have retrieved it from the XNAT portal. It includes different types of scans such as T1/T2 weighted, T1/T2star, BOLD etc. We use T2star in our approaches as they have good temporal resolution. For parcellation, we use Ward's algorithm (a purely data driven approach). We heuristically set a the number of parcels and have varied over the range [50, 1000] in increments of 50 parcels. Another, a more well known method is anatomical parcellation, which we wish to implement in near future. Once we have parcelled data from fMRI, we encode it into a graph data structure. To do so, we find Pearson correlations between every pair of signals followed by a threshold of 0.75. All the edges with a correlation value greater than the threshold value are used to create a weighted graph.

$$e_{i_j} = \begin{cases} c_{i_j} & \text{for} \quad c_{i_j} \geq threshold \\ 0 & \text{for} \quad c_{i_j} < threshold \end{cases} \tag{1}$$

Once a graph is obtained, we use NetworkX, a Python package for the creation, manipulation, and study of the structure, dynamics, and functions of complex networks. NetworkX is used to compute the following graph metrics.

A. Graph metrics

1) **Edge betweenness centrality**: Betweenness centrality of an edge e is the sum of the fraction of all-pairs shortest paths that pass through e.
2) **Vertex betweenness centrality**: Betweenness centrality of a node v is the sum of the fraction of all-pairs shortest paths that pass through v.

$$c_B(v) = \sum_{s,t \in V} \frac{\sigma(s,t|v)}{\sigma(s,t)} \tag{2}$$

3) **Percolation centrality**: Percolation centrality of a node v, at a given time, is defined as the proportion of 'percolated paths' that go through that node.

$$PC^t = \frac{1}{N-2} \sum_{s \neq v \neq r} \frac{\sigma_{sr}(v)}{\sigma_{sr}} \frac{x_s^t}{\sum [x_i^t] - x_v^t} \quad (3)$$

where σ_{sr} is the total number of shortest paths from node s to node r and $\sigma_{sr}(v)$ is the number of those paths that pass through v. This measure quantifies relative impact of nodes based on their topological connectivity, as well as their percolation states.

Other metrics under consideration are Shortest path of Epicenter, Nodal Hazard, Edge current flow betweeness centrality, Local efficiency, Closeness centrality, Wighted participation coefficient, Eigen vector centrality. We are also considering Randic index (measure of assortivity), Fiedler and Normalized Fiedler value, Characteristic path length, Clustering coefficient as they were used in analyzing Alzheimer's disease affected brain networks in [5]

IV. Results and Discussions

Currently for EEG analysis we have only taken one subject under consideration. For FMRI study, we are considering 3 age groups: 42-47 years, 62-67 years, 82-87 years.

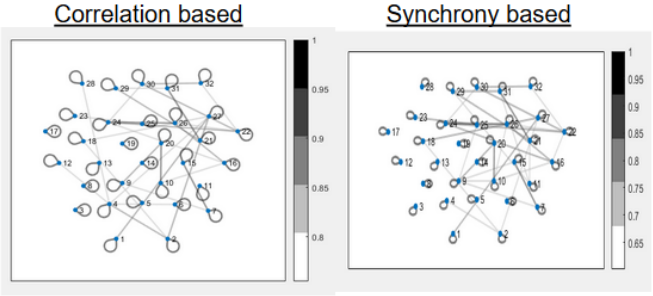

Fig. 1. Comparison of networks built from EEG data using Correlation and Phase locking value measures.

In Fig.2 we plot a circos plot of the network similar to how [1] utilized to identify and viualize small world and random characteristics.

V. Future scope and conclusions

Next we need to calculate the centrality measures for both the networks and once the pipeline is working we can try Hyper alignment and Network alignment. We can also implement Graph Neural Networks to understand these feature rich networks better.

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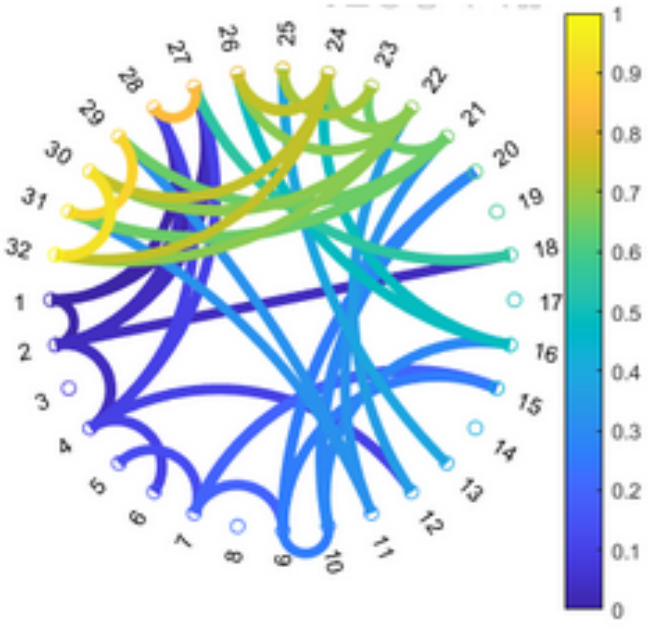

Fig. 2. Circos plots of the network in Fig.1

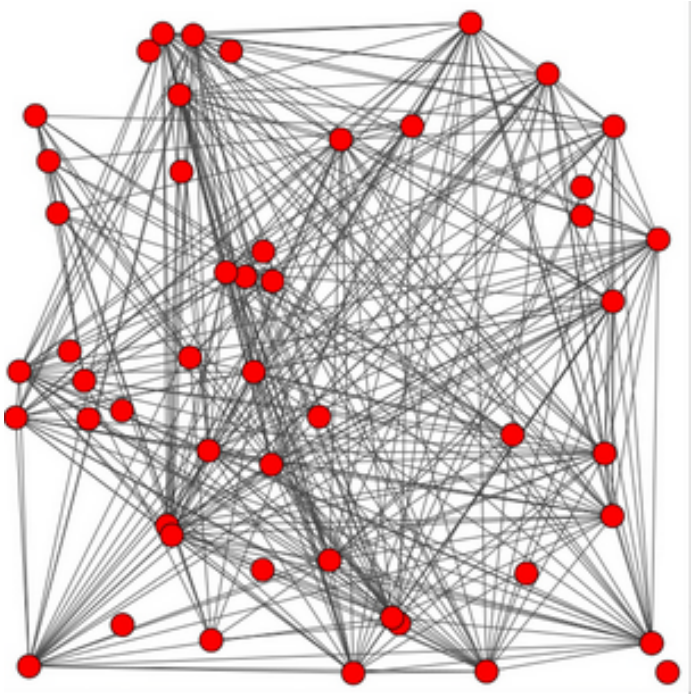

Fig. 3. Sample network of 50 nodes built from FMRI data for illustration purposes.

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