Abstract

The human brain can be viewed as a most complex network and understanding the human brain is a major issue of concern in biomedical signal processing. In our research work we have carried out the study and analysis of human brain by using MRI as imaging modality and graph theoretic tools as mathematical apparatus. The MRI is a non invasive Neuroimaging technique that provides structural information of brain and offers high spatial resolution, hence we have used MRI data in our work. The graph theory provides the platform to model the complex brain network mathematically. The research work is mainly focused on Alzheimer patients because Alzheimer is the most disabling global health problem and therefore understanding the structural connectivity of brain has long been the central goal of neuroscience.

In order to explore the possibility of finding the biomarkers of Alzheimer's disease, we have carried out the graph theoretical analysis of whole brain using MRI data, corresponding to three classes of Normal controls, MCI and Alzheimer's and compute various graph theoretic measures or brain measures. Since it is well known that Alzheimer causes various brain regions to shrink, it is natural to expect that it would lead to changes in the structural connectivity. Since the graph theoretic tools are best suited to capture this information, they were the natural choice, as mathematical tool, for our study. The structural connectivity matrix for each category of normal control, MCI and Alzheimer's is built, the graph theoretical measures are calculated and the brain graphs are obtained. These brain graphs describe the pattern of connectivity in each category of normal controls, MCI and Alzheimer's. These graph theoretical measures and alterations in network topology may act as quantitative biomarker of Alzheimer disease. Further to analyze the deep down networks of brain, we have carried out the graph theoretical analysis of sub cortical regions of brain and also sub field regions of Hippocampus as Hippocampus is the first and foremost region affected by Alzheimer disease. Through our analysis we have tried to establish the link between the connectivity strength and stages of degradation of brain due to Alzheimer's.

As a first step, we carried out the group analysis, so in order to analyze the structural connectivity of single subject, we propose a novel approach to define structural connectivity matrix of single subject in terms of weighted adjacency matrix, to form graphs and carried out associated analysis. We use two different structural features, namely cortical thickness and cortical volume to compute the weighted adjacency matrix. In single subject analysis, we

have computed connectivity measures, namely, connectivity strength and Algebraic connectivity and also carried out comparative analysis of connectivity measures for each category of Normal controls, MCI and Alzheimer's. These connectivity measures and their comparative analysis provide clear differentiation between Alzheimer's and Normal controls and between Alzheimer's and MCI.

Recently, it is observed that the eigenvectors, corresponding to lower eigenvalues, provide class specific information, that is the information that does not change much within a class. The space spanned by these eigenvectors is termed as invariant eigenspace, as it does not vary much from realization to realization. Motivated, by this, for deeper understanding of the disease progression, we have carried out the invariant eigen space analysis, corresponding to three classes of interest, namely, normal controls, MCI and Alzheimer's. Since, in our work the main aim is to quantify the structural changes, suitable modifications are done. In particular the analysis is performed with graph Laplacian matrices instead of covariance matrices. Near invariance of intra subjects is clearly observed. . Our experiments show that changes from normal to MCI to Alzheimer's are gradual and hence can play vital role in diagnosis of Alzheimer disease.

In our work, we propose two approaches for finding graph distances in order to classify the diseased state from healthy state i.e. Alzheimer's from Normal controls and Alzheimer's from MCI. In our first approach, we calculate eigenvalues and eigenvectors of averaged graph Laplacian matrices of three categories namely Normal controls, MCI and Alzheimer's separately. In our work, we tried to classify Alzheimer's from Normal controls and Alzheimer's from MCI by examining the distance between Eigen spaces spanned by invariant eigenvectors. In order to find the distances between invariant Eigen spaces, we have used a distance measure, where the angle between two spaces is computed and is termed as "Principal angle". We found that the principal angle between subspaces provides good classification between Alzheimer's and Normal controls and between Alzheimer's and MCI.

To capture the progression of disease from normal to MCI to Alzheimer's, it is natural to have representation which captures differential information. For this purpose our motivation comes from a recently proposed, matrix pencil based approach which quantifies differential information in different classes. We use that result and specialize it to graph theoretic setting to quantify differential information for the three classes of our interest, namely, normal controls, MCI and Alzheimer's. Using matrix pencil method we are able to classify the

diseased state from the healthy state and also define a matrix which is normalized graph Laplacian matrix to quantify differential information in terms of distance measure, called as ‘Principal angle’. All the results and the findings suggests that the distance measure i.e. Principal Angle may act as quantitative tool to classify the diseased state from healthy state.