A Regularized LDA Approach for AD, MCI and Normal Subjects Classification Using Resting-State fMRI Data

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***Abstract*— This paper conducts the Alzheimer's Disease (AD), mild cognitive impairment (MCI) and normal control (NC) subject classification, by exploiting brain network connectivity pattern analysis. More specifically, we propose a regularized linear discriminant analysis (LDA) approach to reduce the noise effect (including both biological variability and measurement errors) under size limited functional magnetic resonance imaging (fMRI) data samples. The proposed approach is shown to be effective in increasing the classification accuracy significantly.**

I. Introduction

Alzheimer's Disease (AD) is the most common form of dementia, and causes problems with memory, thinking and behavior. Mild Cognitive Impairment (MCI) is a condition in which people show a slight, but noticeable and measurable decline in cognitive capabilities. Recently, functional magnetic resonance imaging (fMRI), which maps brain activities to metabolic changes in cerebral blood flow, has been used to classify AD, MCI and normal control (NC) subjects. fMRI data can display active brain areas more directly, and has much better spatial resolution. However, the size of fMRI data samples is generally quite limited, which has become a major bottleneck. Motivated by this observation, we develop a reliable method for AD, MCI and NC classification that is robust with respect to size limited fMRI data samples. We propose a regularized linear discriminant analysis (LDA) approach to reduce the noise effect under size limited fMRI data samples.

II. Methods

We conduct the AD, MCI and NC subject classification by applying the regularized LDA and AdaBoost classifier based approach. *First*, the hippocampus and the isthmus of the cingulate cortex (ICC) are selected as regions of interest (ROIs) to formulate a sub-network. The Pearson correlation coefficients are calculated between all possible ROI pairs in the sub-network to form a feature vector for each subject. *Second*, we propose a regularized linear discriminant analysis approach, where we take shrinkage based regularization procedures to reduce the noise effect due to limited sample size. The first shrinkage method moves the estimated means of each category towards the overall mean; while the second shrinkage method moves the estimated covariance matrices towards the identity matrix. The feature vectors are then projected onto a one-dimensional axis using the proposed regularized LDA, where the differences between AD, MCI and NC subjects are maximized. *Finally*, a decision tree based multi-class AdaBoost classifier, is applied to the projected one-dimensional vectors to carry out the classification task.

III. Results and Discussions

In our data collection process, 10 patients with mild-to-moderate probable AD, 11 patients with MCI and 12 age- and education-matched healthy NC subjects were recruited [1]. The performance of the classifier is evaluated by the Leave-One-Out (LOO) cross-validation.

TABLE I: Comparison of Classification Results

Algorithm	Accuracy
LDA+Bayesian	44%
LDA+AdaBoost	69%
Regularized LDA+AdaBoost	75%

Table I shows the performance of three classifiers. In the first one, a naive Bayesian classifier is employed after the original LDA transform. Its accuracy is only 44%. The main reason of such an unsatisfying performance is that: when the number of data samples is small, the estimation of class means and covariance matrices in LDA suffers from severe noise effect, leading to overfitting. In the second one, the original LDA is combined with the AdaBoost classifier. The accuracy is increased to 69% by AdaBoost. The third one is what we proposed, the regularized LDA is combined with the AdaBoost classifier. *The regularized LDA can reduce the noise effect and further improve the accuracy to* 75%.

References

[1] D. C. Zhu *et al.*, "Alzheimer's disease and amnestic mild cognitive impairment weaken connections within the default-mode network: a multi-modal imaging study," *Journal of Alzheimer's Disease*, vol. 34, no. 4, pp. 969–984, 2013.