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ROI Analysis Using Harvard-Oxford Atlas in Alzheimer's Disease Diagnosis Based on PCA

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Abstract: Alzheimer's disease (AD) is characterized by impaired glucose metabolism and can be detected using Positron Emission Tomography (PET) neuroimaging. In this study, an automatic method for diagnosis of AD based on region of interest (ROI) is presented. First, subject's PET neuroimage is automatically parcellated into 48 predefined ROIs using Harvard-Oxford structural Atlas. The most discriminative regions are discovered using principal component analysis (PCA). Based on features extracted using PCA, support vector machines are adapted to discriminate normal control (NC) from AD. For classification of AD from NC, the proposed method achieves 89.14% of classification accuracy; while the accuracy of Automated Anatomical Labeling (AAL)-based approach is only 80.68%.

Key words: Alzheimer % Principal component analysis % Positron emission

INTRODUCTION

Alzheimer's disease (AD), the most common cause of dementia, is a progressive neurodegenerative disorder that impaired 5.3 million people worldwide. No cure has yet been found for Alzheimer's disease but early detection of AD is vital for early treatment [1]. Positron Emission Tomography (PET) has the capacity to distinguish mild common symptoms of AD such as amyloid plaques and impaired glucose metabolism. Therefore, extracting the features from brain using PET neuroimaging provides useful hallmarks to discriminate normal control (NC) from AD [2].

Voxel-wise based approaches, which are widely used in AD and use voxels as features, have a major problem namely the dimensionality [3]. In voxel-wise analysis, the number of features is very large compared to the number of available training samples. To overcome such problem, voxel grouping using regions of interest (ROIs) are performed [2]. ROIs are determined using some labeled Atlases, such as Harvard-Oxford Atlas and Automated Anatomical Labeling (AAL) Atlas. The Harvard-Oxford Atlas includes 48 cortical structural regions [4]. The AAL Atlas has been applied in AD [5] and in this study the potentiality of Harvard-Oxford Atlas is evaluated.

To the best of our knowledge, this is the first PET study using Harvard-Oxford Atlas in AD, demonstrating a better information compare to the AAL Atlas for automatic AD diagnosis. In this work, the features are extracted from predefined ROIs using Harvard-Oxford Atlas. In each individual ROI, the suitable feature is extracted by averaging the intensity of voxels within the ROI. After that, principle component analysis (PCA) is used to extract most discriminative regions (or features). Finally, support vector machine (SVM) classifier is used to evaluate the accuracy of proposed methods in AD diagnosis. The obtained results demonstrated high performance outcome in compare to traditional ROI-based method using AAL Atlas, which was previously reported in literature [4].

PCA and SVM Classifications: PCA is one of the most effective methods in pattern recognition. The aim of PCA is to reduce the dimension of the data and is used to omit redundant data for feature extraction. PCA depends on eigenvector method and is designed to model linear variations in large dimensional data. This technique projects the original n-dimensional data to k-dimensional (k<<n) linear subspace [6].

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SVM creates an optimal hyperplane using binary-labeled training data by maximizing the margin between two classes [4]. SVM maps linearly or nonlinearly the input data into a high-dimensional feature space through a suitable kernel function. The mapping is performed to alleviate the classification problem in the high dimension feature space. The SVM classification method has previously been applied in AD [7]. Because of high performance of SVM compared to other classifiers, this approach is widely used in AD diagnosis [8]. A detailed description of the PCA and the SVM algorithms are available in literature [6].

MATERIALS AND METHODS

In this study, 166 subjects, including 45 AD patients, 61 MCI patients and 60 normal controls (NC) were collected from the ADNI public database (LONI, University of California, http:// www.loni. ucla.edu/ADNI/Data). All PET images were preprocessed with SPM8 package (Welcome Department of Cognitive Neurology, Institute of Neurology, London, www.fil.ion.ucl.ac.uk/spm) in MATLAB 7.10.0.

Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.ucla.edu). ADNI was launched in 2003 by the National Institute on Aging (NIA), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the Food and Drug Administration (FDA), private pharmaceutical companies and non-profit organizations, as a 60 million Dollars, 5-year public- private partnership. The primary goal of ADNI has been tested whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD). Determination of sensitive and specific markers of very early AD progression is intended to aid researchers and clinicians to develop new treatments and monitor their effectiveness, as well as reduce the time and cost of clinical trials.

The Principal Investigator of this initiative is Michael W. Weiner, MD, VA Medical Center and University of California - San Francisco. ADNI is the result of efforts of many co-investigators from a broad range of academic institutions and private corporations. The subjects have been recruited from over 50 sites across the U.S. and Canada. The initial goal of ADNI was to recruit 800 adults,

ages 55 to 90 years, to participate in the research, approximately 200 cognitively normal old individuals followed for 3 years; 400 people with MCI followed for 3 years and a group of 200 people with early AD followed for 2 years.

Normalization into a standardized coordinate system was the first step on preprocessing. Normalization maps the voxels in different images into the same anatomical positions in the brains. Each individual PET image was automatically spatially normalized into the PET Montreal Neurological Imaging (MNI) template through 12-parameters affine model. After the spatial normalization, the dimensions of the images were resliced into a standard $91 \times 109 \times 91$ voxels and had a voxel size of 2 mm cubic. Then, images were smoothed using a Gaussian kernel with full- width of half-maximum (FWHM) of 8 mm.

Table 1 summarizes all approaches tested in this study. To find the role of Atlas choice on ROI methods, experiments were performed on AAL and Harvard-Oxford Atlases. Therefore, three different experiments were performed. First and second approaches were based on AAL Atlas and Harvard-Oxford Atlas without any feature extraction. The last approach listed in Table 1 is the proposed method based on Harvard-Oxford Atlas with PCA feature extraction. To evaluate the performance of different classification experiments, 10-fold cross-validation was performed. Since subjects were randomly divided into 10 subsets in 10-fold cross-validation, 100 random 10-folds were calculated. Finally, the classification experiments were evaluated based on all those 10-folds.

RESULTS

Table 1 shows the classification accuracy of the proposed method, the method previously applied on Atlas by other researchers [5] and the method Harvard-Oxford Atlas was used. In addition, Figure 1 plots the corresponding ROC curves of different classification methods. From Table 1 and Figure 1, the proposed method based on Harvard-Oxford Atlas consistently achieved highly accurate discrimination between AD patients and NC. For classifying AD from NC, the proposed method achieves 89.1% of classification accuracy, while the accuracy of "AAL" method (Table 1), which features extracted from AAL Atlas without any feature selection, is only 80.7%. Also, the area under the ROC curve (AUC) is 0.928 for the proposed method (Figure 1), while 'AAL' and 'Harvard-Oxford' methods are 0.909 and 0.910, respectively.

Table 1: Comparison between different classification experiments

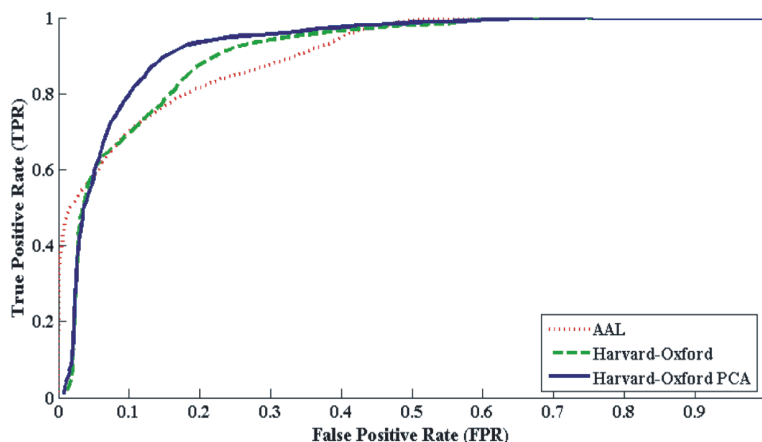| Method's Name	Atlas	Feature Extraction	Accuracy	AUC
AAL	AAL	No	80.6762	0.9092
Harvard-Oxford	Harvard-Oxford	No	84.4381	0.9103
Harvard-Oxford PCA	Harvard-Oxford	PCA	89.1429	0.9280

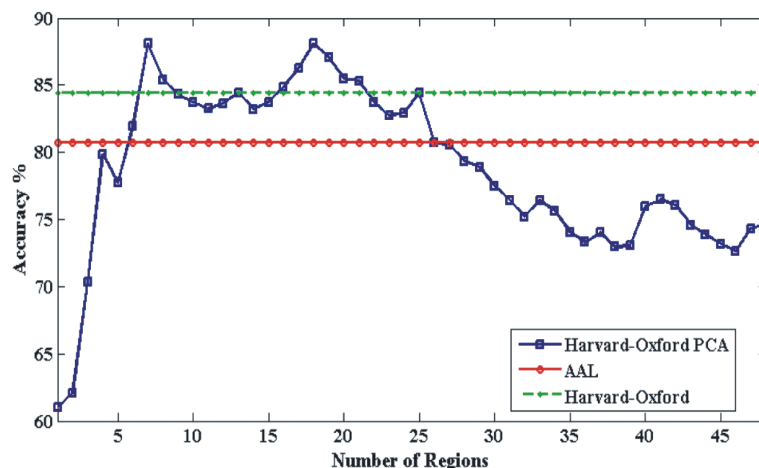Fig. 1: ROC curves of different methods for AD classification

Fig. 2: Classification accuracy of classification experiments, with respect to different number of regions

Figure 2 shows the accuracy of the proposed method considering different number of regions selected from Harvard-Oxford Atlas and accuracy of the first and second classification experiments.

CONCLUSION

In this research, a reliable method for diagnosis of AD is presented. The aim of this study was to reduce the dimension of the voxel-wise features, which after the preprocessing step are more than 900000 voxels. Because of the small number of subjects compared to large dimensionality of voxel-wise features, the method was not able directly use feature selection/extraction approaches, e.g. PCA. Therefore, the preprocessed images were parcellated into ROIs. The main goal of this study was (1) to adapt the Atlas-based approaches by using Harvard-Oxford Atlas for PET neuroimages (2) to use PCA feature extraction for discovering more discriminative region of brain in AD.

As it was demonstrated in this paper about the usefulness of extraction discriminative regions of Harvard-Oxford Atlas using PCA, the proposed method can be applied to diagnose similar diseases.

ACKNOWLEDGEMENTS

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