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Identification of Brain Regions Related to Alzheimers' Diseases using MRI Images Based on Eigenbrain and K-means Clustering

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Abstract: *Early identification of Alzheimer's disease (AD) from the Ageing Movement Control (AC) is very important. However, the computer aided diagnosis (CAD) was not widely used, and the classification performance did not reach into practical use. Existing System has a novel CAD system for MRI brain images based on eigenbrains and machine learning with focus on two things: accurate detection of both AD subjects and AD related brain regions. The eigenbrain method was effective in AD subject prediction and discriminated brain region detection in MRI scanning. But, the results showed that existing method achieved 92.36% accuracy, which was competitive with state-of-the-art methods. We, Propose a system to improve the accuracy and easy computation of identification through MRI images based on K-Means Clustering.*

Keywords: *K-means Clustering, Region Detection, Support Vector Machine (SVM), Machine learning.*

INTRODUCTION

Alzheimer's disease (AD) is not a normal part of aging. It is a type of dementia that causes problems with memory, thinking, and behavior. Symptoms usually develop slowly and worsen over time. Symptoms may become severe enough to interfere with daily life, and lead to death (Hahn et al., 2013). There is no cure for this disease. In 2006, 26.6 million people worldwide suffered from this disease.

AD is predicted to affect 1 in 85 people globally by 2050, and at least 43% of prevalent cases need high level of care (Brookmeyer et al., 2007). as the world is evolving into an aging society, the burdens and impacts caused by AD on families and the society has also increased significantly. In the US, healthcare on people with AD currently costs roughly $100 billion per year and is predicted to cost $1 trillion per year by 2050 (Miller et al., 2012).

Early and accurate detection of AD is beneficial for the management of the disease (Han et al., 2011). Presently, a multitude of neurologists and medical researchers have been dedicating considerable time and energy toward this goal, and promising results have been continually springing up (Xinyun et al., 2011). Magnetic resonance imaging (MRI) is an imaging technique that produces high quality images of the anatomical structures of the human body, especially in the brain, and provides rich information for clinical diagnosis and biomedical research (Shamonin et al., 2014). The diagnostic values of MRI are greatly enhanced by the automated and accurate classification of the MR images (Goh et al., 2014; Zhang et al., 2015a,b). It already plays an important role in detecting AD subjects from normal elder controls (NC) (Angelini et al., 2012; Smal et al., 2012; Nambakhsh et al., 2013; Hamy et al., 2014; Jeurissen et al., 2014).

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The Eigenbrain was an excellent multivariate approach that solves both the curse of dimensionality and the problems in small sample size. It was proposed by Alvarez et al. (2009a) and Lopez et al. (2009), and was applied on Single Photon Emission Computed Tomography (SPECT) images. In their research, the eigenbrain approach was shown to efficiently reduce the feature space from ~5 × 10 to only ~10, and therefore, was able to achieve excellent classification accuracy. In this study, we make a tentative test of applying eigenbrains in MRI scans for AD detection.

Support vector machine (SVM) has been arguably regarded as one of the most excellent classification methods in machine learning (Zhang and Wu, 2012a). Original SVMs are linear classifiers, and do not perform well on nonlinear data. Hence, we introduced in the kernel SVMs (KSVMs), which extends original linear SVMs to nonlinear SVM classifiers by applying the kernel function to replace the dot product form in the original SVMs (Gomes et al., 2012).

Compared with the original plain SVM, the K-means Clustering allows one to fit the maximum-margin hyperplane in a transformed feature space (Garcia et al., 2010). The transformation may be nonlinear and the transformed space is high dimensional; Thus although the classifier is a hyperplane in the high-dimensional feature space, it may be nonlinear in the original input space (Hable, 2012).

The aim of our study was to develop a novel classification system based on eigenbrain and K-means Clustering, in order to grow a computer aided diagnosis (CAD) system for the early detection of AD subjects and AD related brain regions. Our goal was not to replace clinicians, but to provide an assisting tool. The rest of the paper was organized as follows: the next section reviewed relates literatures from two aspects: the extracted features and the classification methods. Section the Existing Method describes methodology of Classification of MRI images based on SVM. Section The Proposed Method describes the methodology of the proposed CAD. Section Experiments and Results contain the experiments and results. Finally, Section Conclusion and Future Research are devoted to conclusion and future research. For ease in reading, the acronyms and their meanings of this study are listed in Table 12 in the appendix.

Literature Review: In common convention, the automatic classification consisted of two stages: feature extraction and classifier construction. We reviewed over ten literatures, and analyzed them through the two stages.

Feature of MR Image

Scholars have proposed numerous methods to extract various features. Chaplot et al. (2006) used the approximation coefficients obtained by discrete wavelet transform (DWT). Maitra and Chatterjee (2006) employed the Slantlet transform, which is an improved version of DWT. Their feature vector of each image was created by considering the magnitudes of Slantlet transform outputs corresponding to six spatial positions that were chosen according to a specific logic. From the literature used, the DWT based features were proven to be efficient. In this study, we suggested using a novel feature of eigenbrain, which was used for SPECT images but was never been used in MR images.

Classification Model in MRI

There are numerous classification models, but only a few of them are suitable for MR images. Chaplot et al. (2006) employed the self-organizing map (SOM) neural network, K-means Clustering and SVM. Maitra and Chatterjee (2006) used the common artificial neural network (ANN). ElDahshan et al. (2010) used ANN and K-nearest neighbor (KNN) classifiers. Plant et al. (2010) used SVM, Bayes statistics, and voting feature intervals (VFI) to derive the quantitative index of pattern matching. Zhang et al. (2011) suggested using ANN. Yang et al. (2015) used SVM as the classifier, and employed biogeography-based optimization (BBO) to train the classifier. Zhang et.al (2015) used SVM as the classifier based on eigenbrain. Suman Tatiraju proposed K-means clustering used for Image segmentation.

After reviewing the latest literatures that were related to classifiers, we found that SVM and K-means Clustering had significant advantages of high accuracy, elegant mathematical tractability, and direct geometric interpretation, compared with other classification methods (Collins and Pape, 2011). Here, we take K-means Clustering to classify the AD along with severity. In addition, it did not need a large number of training samples to avoid overfitting (Li et al., 2010).

The Existing Method

Eigenbrain

AD has different physical structures from NC. Revisit Figure 1 which indicated the AD subjects had severe atrophy of the cerebral cortex (region i), severely enlarged ventricles (region ii), and extreme shrinkage of hippocampus (region iii). Therefore, eigenbrain tried to capture those different characteristic changes of anatomical structures between AD and NC.

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Eigenbrain is carried out by PCA, which is a statistical procedure that uses an orthogonal transformation to convert a set of observations of possibly correlated variables into a set of values of linearly uncorrelated variables called principal components (PC). For 2D images the PCs are extended naturally to the 2D eigenbrains.

Suppose X is a given data matrix with size of $N \times A$, where N represents the number of samples and A number of attributes (For a 256 $\times$ 256 image, we need to vectorize it to a 1×65536 vector, hence $A = 65536$). First, we normalized the dataset matrix X, so that each sample in the normalized matrix Z was mean-centered and unit-variance scaled, by subtracting its mean value and dividing the difference by its standard deviation.

$$Z \leftarrow \frac{X-\mu(X)}{\sigma(X)} \qquad (2)$$

Next, we estimated the covariance matrix C with size of A $\times$ A by

$$C \leftarrow \frac{1}{N-1} Z^T Z \qquad (3)$$

Here we used N $-$ 1 instead of N in order to produce an unbiased estimator of the variance (See Bessel's correction (Russell and Cohn, 2012) for details).

Third, we perform the eigendecomposition of C:

C = U ^ U^{-1} (4)

Where U is an $A \times (N - 1)$ matrix, whose columns are the eigenvectors of covariance matrix C, matrix A is an $(N - 1) \times (N - 1)$ diagonal matrix whose diagonal elements are eigenvalues of C, each corresponding to an eigenvector of A. It is common to sort the eigenvalue matrix A and eigenvector matrix U in order of decreasing eigenvalue $u > u > \ldots > u_N$. To view the i^{th} eigenbrain $u(i)$, the i^{th} column of U was reshaped to an image.

The flowchart of calculating eigenbrain is shown in Figure 2.

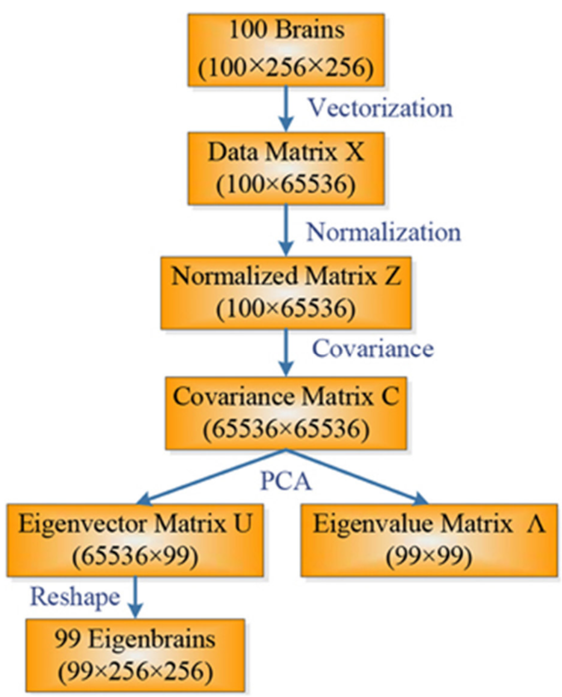

Figure 2: Flowchart of Calculating Eigenbrain

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Region Detection

In existing method, a visual interpretation method of Eigenbrain to detect regions that can distinguish AD and NC, which is not reported in literatures of Alvarez et al. (2009a) and Lopez et al. (2009). The interpretation in a four-stage process is listed in Table 1.

Measure	Definition
Accuracy	$(TP+TN)/(TP+TN+FP+FN)$
Sensitivity (Recall)	$TP/(TP+FN)$
Specificity	$TN/(TN+FP)$
Precision	$TP/(TP+FP)$

Table 1: Four Stage region detection Method

Classifier

SVM was used as the classifier. In addition, sequential minimal optimization (SMO) is chosen to train SVM due to simple and fast speed (Zhang and Wu, 2012b). Traditional linear SVMs cannot separate intricately distributed data. In order to generalize SVMs to create nonlinear hyperplane, the kernel trick is applied. The KSVMs allows us to fit the maximum-margin hyper-plane in a transformed feature space (Liu et al., 2014). The transformation may be nonlinear and the transformed space is a higher dimensional space. Though the classifier is a hyper-plane in the higher-dimensional feature space, it may be nonlinear in the original input space.

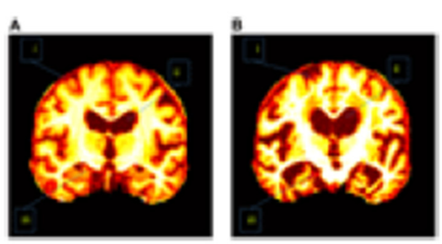
The Proposed Method

Pre-processing on Volumetric Data

For each individual, all available 3 or 4 volumetric 3D MR brain images were motion-corrected, and co-registered to form an averaged 3D image. Then, those 3D images were spatially normalized to the Talairach coordinate space and brain-masked. CDR was interpreted as the target (label). It is a numeric scale quantifying the severity of symptoms of dementia (Williams et al., 2013). The patient's cognitive and functional performances were assessed in six areas: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. In this study, we chose two types of CDR, i.e., the subjects with CDR of 0 were considered as NC and subjects with CDR of 1 were considered as AD (Marcus et al., 2007). Calculating eigenbrains on the entire brain was difficult. Instead, we proposed a simplified method that selected several key slices that capture structures indicative of AD from NC. The procedure was as follows: we established the ICV v as

$$v(k) = \|\mu_{AD}(Slice = k) - \mu_{NC}(Slice = k)\|^2 \qquad (1)$$

Where k was the index of key slice, μ_{AD} and μ_{AC} represented the mean of gray-level values of the k^{th} slice of AD subjects and NC subjects, respectively, $||.||^2$ represented the l_2 norm. Then, we selected the key-slices of ICV larger than 50% of maximum ICV, with 10× under-sampling factor (i.e., every 10 slices).



A B

Figure 1: Difference between healthy brain (A) and AD brain (B)

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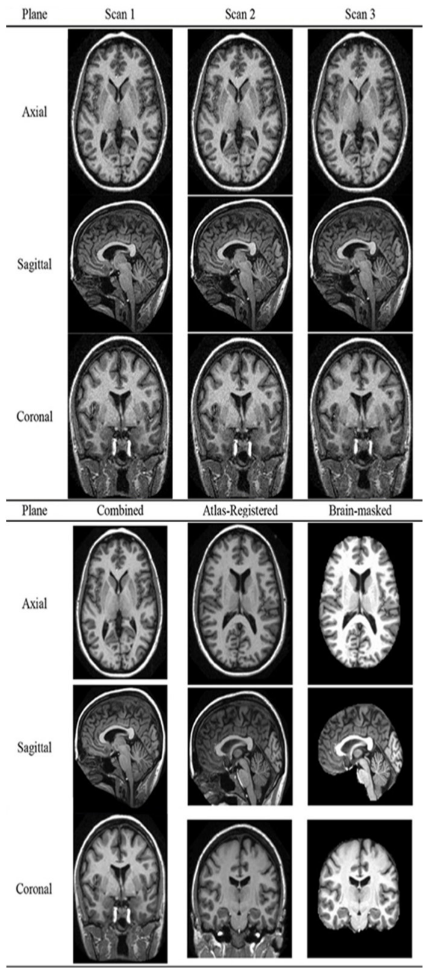
Table 2 shows an example of the combination of 3 individual scans of a subject. The resolution is 1 × 1 × 1.25 mm. The preprocessing performed motion-correction on the 3D MR images, registered them to form a combined image in the native acquisition space, and re-sampled to 1 × 1 × 1 mm. afterwards, the combined image was spatially normalized to the Talairach coordinate space, and brain-extracted (Table 2).



The null hypothesis is that the eigenvalues of AD and NC have equal means, without assuming they have equal variances. The alternative hypothesis is they have unequal means. WTT was carried out at the 95% confidence interval. The eigenvalues of the selected most important eigenbrain (MIE) were used as input features for following classification.

Classification by K-means Clustering

K-Means algorithm is an unsupervised clustering algorithm that classifies the input data points into multiple classes based on their inherent distance from each other. The algorithm assumes that the data features form a vector space and tries to find natural clustering in them. The points are clustered around centroids μ_i *for* $i = 1,2,\ldots.k$ which are obtained by minimizing the objective

$$V = \sum_{i=1}^{k} \sum_{x_j \in S_i} (x_j - \mu_i)^2 \qquad (5)$$

Where there are k clusters S_i, i = 1,2….. k and μ_i is the centroid or mean point of all the points x_j € S_i

As a part of this project, an iterative version of the algorithm was implemented. The algorithm takes a 2 dimensional image as input. Various steps in the algorithm are as follows:

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1. Compute the intensity distribution (also called the histogram) of the intensities.
2. Initialize the centroids with k random intensities.
3. Repeat the following steps until the cluster a label of the image does not change anymore.
4. Cluster the points based on distance of their intensities from the centroid intensities.

$$c^{(i)} := \arg\min_j ||x^{(i)} - \mu_j||^2 \tag{6}$$

5. Compute the new centroid for each of the clusters.

$$\mu_i := \frac{\sum_{i=1}^{m} 1\{c_{(i)} = j\} x^{(i)}}{\sum_{i=1}^{m} 1\{c_{(i)} = j\}} \tag{7}$$

Where k is a parameter of the algorithm (the number of clusters to be found), i iterates over the all the intensities, j iterates over all the centroids and μ_i are the centroid intensities.

Table 3 shows the ranges for AD and classification as follows:

Slice	λ_1 NC	λ_1 AD	p
60	−3.36 ± 20.01	11.75 ± 27.91	**0.01**
70	−6.84 ± 25.60	23.92 ± 28.33	**0.00**
80	−7.48 ± 29.05	26.18 ± 27.04	**0.00**
90	6.79 ± 32.04	−23.75 ± 24.86	**0.00**
100	−6.93 ± 34.25	24.27 ± 30.89	**0.00**
110	−6.95 ± 31.89	24.31 ± 24.10	**0.00**
120	−5.93 ± 31.60	20.74 ± 23.14	**0.00**
130	5.02 ± 28.13	−17.56 ± 28.09	**0.00**
140	4.27 ± 25.02	−14.94 ± 22.06	**0.00**
150	5.51 ± 18.50	−19.30 ± 30.21	**0.00**

P-values less than 0.05 are in bold.

From the ranges the K-means clustering happens for each slice.

Experimental Result

The contributions of the paper fall within the following five aspects: (i) we generalize the Eigenbrain to MR images, and prove its effectiveness; (ii) We propose a hybrid eigenbrain based CAD system that can not only detect AD from NC, but also detect brain regions that related to AD. (iii) We prove the proposed method has classification accuracy comparable to SVM methods, and the detected brain regions are in line with 17 existing literatures. (iv) We use ICV and WTT to reduce redundant data; (v) we find POL kernel is better than linear and RBF kernel for this study.

Conclusion

We presented an automated and accurate classification method that was based on eigenbrains and K-means Clustering, in order to detect AD subjects and AD related brain regions using 3D MR images. The results showed the proposed K-means Clustering method achieved 96% accuracy, which was competitive with SVM methods.

In the future, we will focus our research in the Eigenbrain can be used in combination with DWT based features and others, and an increase in classification accuracy is expected.

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References

1. Yudong Zhang, Zhengchao Dong, Preetha Phillips, Shuihua Wang, Genlin Ji, Jiquan Yang and Ti-Fei Yuan, Detection of subjects and brain regions related to Alzheimer's disease using 3D MRI scans based on eigenbrain and machine learning
2. Suman Taitraju, and Avi Mehta., Image Segmentation using k-means clustering, EM and Normalized Cuts
3. Aich, U., and Banerjee, S. (2014). Modeling of EDM responses by support vector machine regression with parameters selected by particle swarm optimization. Appl. Math. Model. 38, 2800–2818. doi: 10.1016/j.apm.2013.10.073
4. Alvarez, I., Gorriz, J. M., Ramirez, J., SalasGonzalez, D., Lopez, M., Puntonet, C. G., et al. (2009a). Alzheimer's diagnosis using eigenbrains and support vector machines. *Electron. Lett*. 45, 342–343. doi: 10.1049/el.2009.3415
5. Álvarez, I., Górriz, J. M., Ramírez, J., SalasGonzalez, D., López, M., Segovia, F., et al. (2009b). Alzheimer's diagnosis using eigenbrains and support vector machines in *BioInspired Systems: Computational and Ambient Intelligence*, Vol. 5517, eds J. Cabestany, F. Sandoval, A. Prieto, and J. Corchado (Berlin: Springer), 973–980.
6. Anagnostopoulos, C. N., Giannoukos, I., Spenger, C., Simmons, A., Mecocci, P., Soininen, H., et al. (2013). "Classification models for Alzheimer's disease Detection," in *Engineering Applications of Neural Networks*, Vol. 384(Pt II), eds L. Iliadis, H. Papadopoulos, and C. Jayne (Berlin; Heidelberg: Springer), 193–202. doi: 10.1007/9783642410161_21
7. Angelini, E. D., Delon, J., Bah, A. B., Capelle, L., and Mandonnet, E. (2012). Differential MRI analysis for quantification of low grade glioma growth. *Med.Image Anal*. 16, 114–126. doi: 10.1016/j.media.2011.05.014
8. Arbizu, J., Prieto, E., MartinezLage, P., MartiCliment, J. M., GarciaGranero, M., Lamet, I., et al. (2013). Automated analysis of FDG PET as a tool for single-subject probabilistic prediction and detection of Alzheimer's disease dementia. *Eur. J. Nucl. Med. Mol. Imaging* 40, 1394–1405. doi: 10.1007/s002590132458z

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