Computer-aided classification of Alzheimer's disease based on support vector machine with combination of cerebral image features in MRI

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Computer-aided classification of Alzheimer's disease based on support vector machine with combination of cerebral image features in MRI

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[*] Data used in preparation of this article were obtained from the ADNI database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report

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Abstract. Several studies have differentiated Alzheimer's disease (AD) using cerebral image features derived from MR brain images. In this study, we were interested in combining hippocampus and amygdala volumes and entorhinal cortex thickness to improve the performance of AD differentiation. Thus, our objective was to investigate the useful features obtained from MRI for classification of AD patients using support vector machine (SVM). T1-weighted MR brain images of 100 AD patients and 100 normal subjects were processed using FreeSurfer software to measure hippocampus and amygdala volumes and entorhinal cortex thicknesses in both brain hemispheres. Relative volumes of hippocampus and amygdala were calculated to correct variation in individual head size. SVM was employed with five combinations of features (H: hippocampus relative volumes, A: amygdala relative volumes, E: entorhinal cortex thicknesses, HA: hippocampus and amygdala relative volumes and ALL: all features). Receiver operating characteristic (ROC) analysis was used to evaluate the method. AUC values of five combinations were 0.8575 (H), 0.8374 (A), 0.8422 (E), 0.8631 (HA) and 0.8906 (ALL). Although "ALL" provided the highest AUC, there were no statistically significant differences among them except for "A" feature. Our results showed that all suggested features may be feasible for computer-aided classification of AD patients.

1. Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder, which is the most common type of dementia, causing confusion, memory decline, and loss of cognitive function [1]. The incidence of AD is strongly related with the age; therefore, AD becomes one of the major public health problems in countries with the longer life expectancy [1, 2]. To diagnose AD, magnetic resonance imaging (MRI) is one of imaging techniques which allows quantitative estimation of brain features for assessing AD in a non-invasive way [3]. Nevertheless, in routine clinical practice, subjective estimating the degree of AD by analyzing the morphological changes on MR images is very difficult and time-consuming [2], then various computer-aided diagnosis methods for AD have been developed to assist the radiologists in evaluating MR images. Many cerebral image features have been used to classify AD patients such as cortical thickness, volume and shape of gray matter, white matter, cerebrospinal fluid and hippocampus [4-6].

In this study, the classification of AD patients and normal subjects were performed by supplying the cerebral image features obtained from MRI including hippocampus volume, amygdala volume and entorhinal cortex thickness as input to the support vector machine (SVM).

2. Subjects and MR data

Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The ADNI was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. For up-to-date information, see www.adni-info.org. According to ADNI, T1-weighted (MPRAGE) sequence with 1.2 mm thickness were acquired from study volunteers using standard ADNI protocols (http://adni.loni.usc.edu). In this paper, T1-weighted MR brain images of 100 AD patients (47 females and 53 males, age range: 56-89 years, mean age: 74 years) and those of 100 normal subjects (53 females and 47 males, age range: 56-89 years, mean age: 74 years) were studied.

3. Methodology

Figure 1 represents an overall scheme of proposed method. First, T1-weighted MR brain images were processed using FreeSurfer software to measure cerebral image features including hippocampus and amygdala volumes and entorhinal cortex thicknesses in both brain hemispheres. Next, the relative volumes of hippocampus and amygdala were calculated by using total intracranial volume (TIV) to normalize the effect of individual head size. Then, cerebral image features were used as input into the SVM for classification of AD patients and normal subjects. Finally, we evaluated the performance of proposed method using receiver operating characteristic (ROC) analysis.

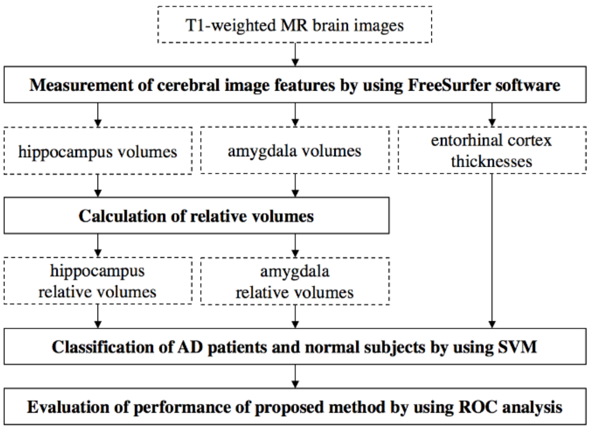


Figure 1. The overall scheme of proposed method.

3.1. Measurement of cerebral image features by using FreeSurfer software

FreeSurfer is a set of software tools for analysis structural brain imaging data developed by the Laboratory for Computational Neuroimaging at Martinos Center (http://surfer.nmr.mgh.harvard.edu). FreeSurfer provides a fully automatic structural imaging stream for processing data in cortical and subcortical brain structure. In subcortical-based stream, FreeSurfer automatically assigned a neuroanatomical label to each voxel in MRI volume based on probabilistic information estimated from a manually labeled training set [7]. Figure 2(a) represents an example of hippocampus and amygdala regions labeled by using FreeSurfer. To measure entorhinal cortex thickness, FreeSurfer constructed models of boundary between gray matter and white matter as well as between gray matter and pia matter overlaid on original brain volume [8] as shown in figure 2(b). The distance between two surfaces was computed and considered as the thickness at each location of cortex. Therefore, applying this tool to T1-

weighted MR brain images, hippocampus and amygdala volumes and entorhinal cortex thicknesses in left and right brain hemispheres were obtained.

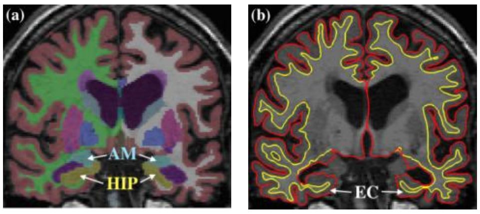


Figure 2. Hippocampus and amygdala regions (a) and entorhinal cortices (b) in left and right brain hemispheres obtained from an AD case by using FreeSurfer software.

3.2. Calculation of relative volumes of hippocampus and amygdala
To analyse the volume of brain structure, it should be realized that individual head sizes of each subject are markedly different. So some processes are required to account for head size variation. In this study, total intracranial volume (TIV) obtained by volume-based stream of FreeSurfer software was used to calculate the relative volumes of hippocampus and amygdala by using equation (1). Note that this correction is only useful for measurement of volume, not thickness because volume scales with head size which depends mostly on changes in surface area while thickness scales to much less degree.

$$\text{relative volume} = \frac{\text{hippocampus volume or amygdala volume}}{\text{TIV}} \quad (1)$$

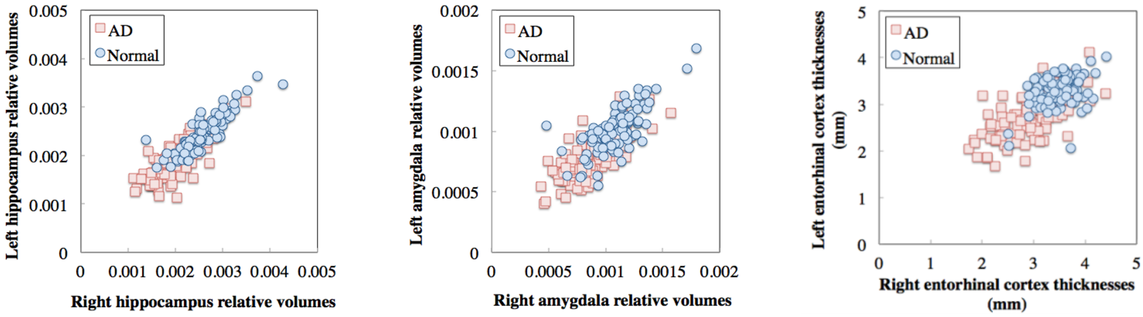
3.3. Classification of AD patients and normal subjects by using SVM
In classification step, support vector machine (SVM), discriminative classifier developed by Cortes and Vapnik in 1995, was used. In this case, we implemented SVM algorithm by using SVM light, open source software package (http://svmlight.joachims.org). Six cerebral image features, i.e., left and right hippocampus relative volumes, left and right amygdala relative volumes and left and right entorhinal cortex thicknesses, obtained from previous steps were normalized from 0 to 1 and then used as input features for classification. In this study, SVM with radial basis function (RBF) was trained with five combinations of those cerebral image features: H (left and right hippocampus relative volumes), A (left and right amygdala relative volumes), E (left and right entorhinal cortex thicknesses), HA (left and right hippocampus and amygdala relative volumes) and ALL (all features) as shown in table 1 to determine an SVM model which distinguished AD patients and normal subjects efficiently. For RBF kernel, parameter C and γ were estimated using a grid-search method [9]. Finally, SVM model obtained from training session was used to classify new unknown subjects into one of two groups (i.e. AD or normal).

3.4. Evaluation of proposed method
We evaluated the proposed method by using the receiver operating characteristic (ROC) analysis. The resulting data from SVM classifier were used to create an ROC curve and then analyzed to determine area under the curve (AUC) which represented as a measure of overall performance of classification. In this study, we applied SVM to 100 AD patients and 100 normal subjects using leave-one-out method, and ROC curves were obtained from ROCKIT, the software package for ROC analysis developed at the University of Chicago (http://metz-roc.uchicago.edu/MetzROC). Finally, the area under ROC curve (AUC) of each combination was calculated. The AUC differences between five different combinations were compared using a paired t-test with 95% confidence interval ($p < 0.05$).

4. Results
Figures 3(a), (b) and (c) show relationships between relative volumes of left and right hippocampus, relative volumes of left and right amygdala, and left and right entorhinal cortex thicknesses obtained from AD patients and normal subjects, respectively. Figure 4 shows ROC curves and AUC values which represented the performance of proposed method using SVM with five combinations of cerebral image features for classification of AD patients and normal subjects. The AUC values for five combinations including H, A, E, HA and ALL were 0.8575, 0.8374, 0.8422, 0.8631 and 0.8906, respectively. Table 2 shows statistically significant differences among AUC values of five combinations.

Table 1. Five combinations (Codes) of cerebral image features.

	Hippocampus relative volume		Amygdala relative volume		Entorhinal cortex thickness	
Code	Left	Right	Left	Right	Left	Right
H	✔	✔				
A			✔	✔		
E					✔	✔
HA	✔	✔	✔	✔		
ALL	✔	✔	✔	✔	✔	✔



(a) (b) (c)

Figure 3. Relationships between cerebral image features of AD patients and normal subjects including left and right hippocampus relative volumes (a), left and right amygdala relative volumes (b) and left and right entorhinal cortex thicknesses (c).

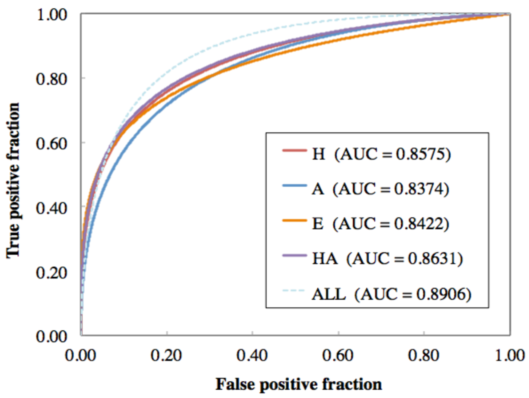


Figure 4. ROC curves and AUC values representing the performance of proposed method for classification of AD patients and normal subjects by using SVM with five combinations of cerebral image features.

Table 2. Comparison of AUC of five combinations.

	P-value				
Code	H	A	E	HA	ALL
H	-	0.2905	0.6151	0.4152	0.1441
A	-	-	0.7655	**0.0328**	**0.0199**
E	-	-	-	0.4305	0.0602
HA	-	-	-	-	0.2220
ALL	-	-	-	-	-

5. Discussion

The results of our study showed that all of five combinations (H, A, E, HA and ALL) provided high AUC values indicating good classification of AD. Although, using "ALL" feature yielded the highest

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classification with AUC of 0.8906, there were no statistically significant differences among the rest, except for "A" feature as shown in table 2.

The advantage of the proposed method is its achievably high discriminant ability. The overall process includes feature extraction and classification which can be performed automatically using open source software together with T1-weighted MR brain images. However, the limitation of this study is the relatively small number of subjects used in the classification training step. The larger number of subjects may be included for the training process in the future studies. Other machine learning techniques should be investigated in order to improve the performance of AD classification process.

6. Conclusion

This study proposed a computer-aided method for classification of AD patients and normal subjects based on SVM with cerebral image features derived from T1-weighted MR brain images including hippocampus and amygdala relative volumes and entorhinal cortex thicknesses. Our preliminary results suggested that using "ALL" features provided good differentiation of AD.

References

[1] Reynolds A 2013 *Radiologic Technology* **85** 187CT-211CT
[2] Arimura H, Magome T, Yamashita Y and Yamamoto D 2009 *Algorithms* **2** 925-52
[3] Luccichenti G, ́Ran P P, Cherubini A, Giugni E, Scarabino T, Hagberg G E and Sabatini U 2006 High-field 3 T imaging of Alzheimer disease *High-Field Brain MRI* (Germany: Springer Berlin Heidelberg) chapter 17 p 201
[4] Arimura H, Yoshiura T, Kumazawa S, Tanaka K, Koga H, Mihara F, Honda H, Sakai S, Toyofuku F and Higashida Y 2008 *Academic Radiology* **15** 274-84
[5] Magnin B, Mesrob L, Kinkingnehun S, Pellegrini-Issac M, Colliot O, Sarazin M, Dubois B, Lehericy S and Benali H 2009 *Neuroradiology* **51** 73-83
[6] Gerardin E *et al*. 2009 *Neuroimage* **47** 1476-86
[7] Fischl B, Salat D H, van der Kouwe A J, Makris N, Segonne F, Quinn B T and Dale A M 2004 *Neuroimage* **23** S69-84
[8] Desikan R S *et al*. 2006 *Neuroimage* **31** 968-80
[9] Hsu C W, Chang C C and Lin C J 2010 A Practical Guide to Support Vector Classification http://csie.ntu.edu.tw/~cjlin/papers/guide/guide.pdf

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