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The Participation of Three Brain Tissues in Alzheimer's disease Diagnosis from Structural MRI

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Abstract

Alzheimer's disease (AD) is a progressive and irreversible disease which gradually makes patients unable to do their daily routines. Although the present treatments can not cure the disease completely, its early detection can reduce symptoms and enhance the patients' life quality. In the current literature, using the grey matter (GM) tissue which is known as an appropriate biomarker is highly common in AD diagnosis. However, two other brain tissues known as cerebrospinal fluid (CSF) and white matter (WM) seem to reveal beneficial information about the patients' brain changes. The aim of the present study is to develop an automatic system for the early diagnosis of Alzheimer's disease from structural MRI by simultaneously considering suitable features of all GM, CSF and WM tissues. A SVM-RBF classifier is trained and evaluated on the OASIS database to separate AD from healthy control (HC) subjects. The obtained results represent higher accuracy and sensitivity of the proposed algorithm in comparison with similar method.

Keywords: Alzheimer's disease; Biomarker; Classification; Feature extraction; Magnetic resonance imaging

I. Introduction

Alzheimer is a neurological disease which attacks the brain neurons and causes the brain neurodegeneration. Most of the time, its early symptom is the short term memory loss. However, Alzheimer's disease gradually causes some sever symptoms like changes in mood, speech, though and reasoning power. Human brain is made of nearly 100 billion neurons and scientists believe that any change in these neurons or their connections causes the Alzheimer's disease. Indeed, Alzheimer is the sixth death factor in the United States. It is apt to mention that increasing the age is the major risk factor in afflicting Alzheimer and may engage most of people who are above 65. However, people may be afflicted with AD during their forties or fifties [1]. Finding brain suitable biomarkers helps experts to AD detection by means of the computer aided diagnosis (CAD) systems. Besides, due to their high resolution and contrast, MRI images are considered as suitable means of finding these biomarkers [2].

The atrophy rate measurement in the grey matter (GM) tissue is highly applicable to diagnose Alzheimer' disease [3]. One of the first GM structures is Hippocampus which is entangled with atrophy in early stage of AD; thus, many studies have been focused on the volume measurement or the shape analysis of hippocampus [4-8]. Based on the research done by Colliot et al. [9], the hippocampus volume and the amygdala are 32% shrunk in comparison with healthy people. Although the GM changes of AD patients are proved, just a few concentrations are paid to the brain white matter (WM) changes. Like GM, the WM tissue undergoes changes along with the AD

progression and it can play a role as a good biomarker [10-13]. Stoub et al. [10] have extracted para-hippocampal WM manually and by measuring its volume, they have concluded that the WM atrophy can be a suitable biomarker in AD detection. When the brain tissue is damaged in AD patients and consequently GM and WM tissues are shrunk, the cerebrospinal fluid (CSF) volume is enlarged in the lateral ventricles and their surroundings to occupy the whole skull space [14]. Unlike hippocampus, lateral ventricle boundaries are clearly distinctive in the brain and they can easily be extracted by applying automatic methods [14]. Therefore, the ventricular measurements are known as a powerful property in some AD related studies [14-17]. Nestor et al. [15] in their study of investigating the ventricular enlargement in AD and healthy control (HC) have identified that the ventricular enlargement of AD patients is 4 times more than HC subjects.

In the present paper, an automatic system which is designed based on the participation of three brain tissues (GM, WM and CSF) is proposed to simultaneously take the advantages of these tissues in AD diagnosis.

The rest of this paper is organized as follows: in Section 2, the used database is explained. The proposed algorithm is presented in Section 3. Section 4 encompasses experimental results and discussion and finally, Section 5 concludes the paper.

2. Materials

T1-weighted MRI images needed for the algorithm evaluation are derived from the standard OASIS database [18]. This database includes cross-sectional collection of 416 individuals. Chosen individuals are divided into 49 AD and 49 HC subjects. To have a fair comparison, the number and the health condition of these individuals are selected the same with those who participated in [19]. In Table 1, these individuals' characteristics are listed.

–	Alzheimer's disease (AD)	Healthy control (HC)
number	49	49
age	78.06 (66-96)	77.77 (65-94)
CDR (0.5/1/2)	31/17/1	0
MMSE	24 (15-30)	28.9 (26-30)

Table 1: The used data derived from the OASIS database. The best CDR=0, and the worst CDR=2. The worst MMSE=15 and the best MMSE=30.

3. Methods

The blocked diagram of the proposed system to separate AD from HC subjects is shown in Figure 1. This system includes three steps: pre-processing, feature extraction and classification.

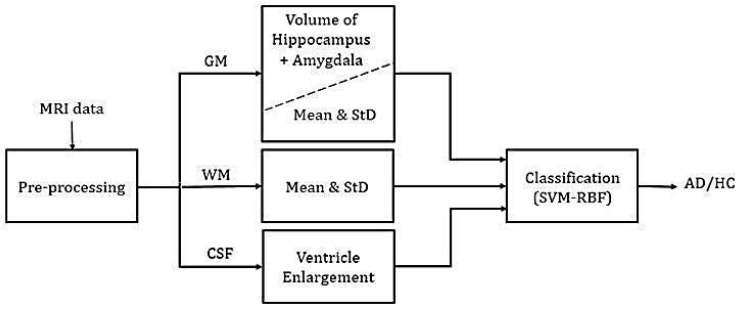

Figure 1: Block diagram of the proposed system to separate AD patients from HC subjects.

3.1. Pre-processing step

All pre-processing steps are done by the SPM software version 12 and the VBM software version 8. Before segmenting brain tissues, first all images are normalized. Each image is segmented into its three tissues known as GM, WM, and CSF. Furthermore, it must be noted that the inter-subject alignment is done by DARTEL. All GM images are modelled that help to preserve the total GM volume. In Figure 2, three segmented tissues of the brain are represented.

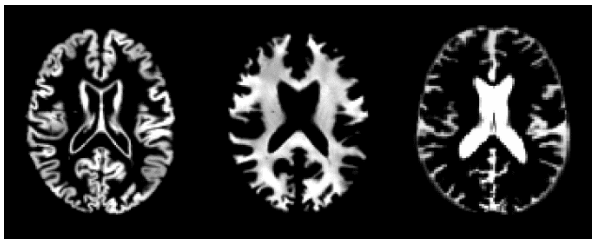

Figure 2: Segmenting of an AD patient into its three tissues: respectively from the right side there are GM, WM, and CSF.

3.2. Feature extraction step

As mentioned, hippocampus is prone to be afflicted with atrophy at the early stages of the Alzheimer's disease; thus, this structure feature extraction is highly helpful and beneficial. Although the manual segmentation of the hippocampus is the most precise method [20], it is highly time consuming. Therefore, in the present article an automatic atlas-based method is used. Additionally, the Automatic Anatomic Labelling (AAL) atlas is utilized for segmenting the hippocampus [21].

Lateral ventricle is clearly visible from the brain CSF tissue. Noticeably, the ventricle volume is bigger in AD patients in relation to HC subjects. This incident is occurred as a result of shrinking of two other tissues of GM and WM. To segment this structure, the ALVIN toolbox is used. This algorithm is completely automatic, run under SPM software and can segment the lateral ventricle from MRI images. Figure 3 shows the lateral ventricle enlargement in AD and HC subjects.

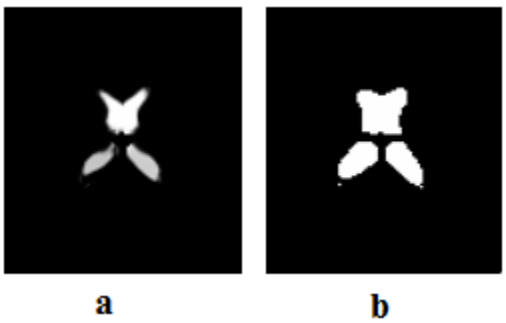

Figure 3: Sample of brain lateral ventricle. a) HC subject, b) mild AD patient.

Totally, the applied features are as follows:

- Features extracted from the GM include: a) the hippocampus + the ventricle volume b) the mean and the standard deviation of the GM
- Features extracted from the WM tissue which include the WM mean and standard deviation
- Features extracted from the CSF which include the lateral ventricle enlargement

Using these features, efficient biomarkers are extracted from the most regions of the brain and the participation process of three brain tissues is fulfilled. This task can improve the performance of the proposed system.

3.3. Classification step

In the proposed system a support vector machine (SVM) classifier is employed. SVM occupies an elegant role in the literature and could accurately separate AD from HC subjects. The considerable fact regarding the SVM classifier operation is its structural risk minimization strategy which is handled to arrive at a hyper plane and consequently maximize the distance between training classes. The produced feature vector is given to this classifier as an input. The RBF kernel is used in the present study.

4. Experimental results and discussions

Cross validation (CV) is known as a statistical method to evaluate and compare classifiers. In CV, a part of database is chosen to train and another part is selected to test the classifier. Elaborately, k-fold CV is a common method to evaluate the performance of the classifier. This task reduces the evaluation variance. In the present study, samples are divided into 10 parts and then they are trained and evaluated for 10 times. Finally, their output results are averaged. It should be mentioned that the number of AD patients and HC subjects are considered equal. To evaluate the algorithm performance, some

criteria have been considered like accuracy (ACC) and sensitivity (SEN).

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$$ACC = \frac{(TP + TN)}{(TN + FN + TP + FP)} \quad (1)$$

$$SEN = \frac{TP}{(TP + FN)} \quad (2)$$

Table 2 shows the results of investigating the effect of each brain tissue in separating AD from HC subjects. For this purpose, features related to each tissue are separately given to the SVM-RBF classifier to determine the effects of each tissue in classification. As expected, the GM tissue has the greatest participation in AD diagnosis. However, two other tissues also have effective roles in separating patients; therefore, three tissues' participation could improve the ACC and SEN of the proposed system.

Tissues	AD/HC	ACC (%)	SEN (%)
GM	49/49	81.7	75.6
WM	49/49	62.3	71.5
CSF	49/49	63.3	51.1
All tissues	49/49	86.8	85.8

Table 2: Proposed system performance on GM, WM, and CSF tissues

In Table 3 a comparison result of the proposed algorithm performance with similar method which is presented in [19] is shown. To have a fair comparison, all features of the used database are same with this work. Papakostas et al. [19] have used a new k-NN classifier named Lattice Computing (LC) to reduce the dimension of features and to classify AD and HC subjects. As the results show, the proposed system overcomes the method in [19] in both ACC and SEN.

Methods	Database	AD/HC	ACC (%)	SEN (%)
Papakostas et al. [19]	OASIS	49/49	85	78
Proposed method	OASIS	49/49	86.8	85.8

Table 3: The comparison of the classification results in separating AD from HC subjects on MRI images.

5. Conclusions

Early diagnosis of Alzheimer's disease can increase the life quality of AD patients. In the present article, an automatic system was proposed to diagnose the Alzheimer's disease. In this system, the participation of three brain tissues known as GM, WM, and CSF was considered since all these three tissues are prone to be affected by changes in Alzheimer's disease; therefore, each tissue can play a role of a good biomarker. The proposed method is tested on 98 MRI images derived from the OASIS database. Results have shown that the proposed system has an accepted performance in classifying AD from HC subjects and can successfully reach at 86.8% accuracy.

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