Pattern Recognition Letters 34 (2013) 1725–1733

Contents lists available at SciVerse ScienceDirect

Pattern Recognition Letters

journal homepage: www.elsevier.com/locate/patrec

LVQ-SVM based CAD tool applied to structural MRI for the diagnosis of the Alzheimer's disease

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ARTICLE INFO

Article history:
Available online 28 April 2013

Communicated by Manuel Graña

Keywords:
Alzheimer's disease
Classification
MRI segmentation
Self-Organizing Maps
Feature reduction
Learning Vector Quantization

ABSTRACT

This paper presents a novel computer-aided diagnosis (CAD) tool for the diagnosis of the Alzheimer's disease (AD) using structural Magnetic Resonance Images (MRIs). The proposed method uses information learnt from the tissue distribution of Gray Matter (GM) and White Matter (WM) in the brain, which is previously obtained by an unsupervised segmentation method. The tissue distribution of *control* (normal) and AD images is modelled by means of Learning Vector Quantization (LVQ) algorithm, generating a set of representative prototypes of each class. The devised method projects new images onto the model vectors space for further classification using Support Vector Machine (SVM). The tool proposed here yields classification results over 90% (accuracy) for *controls* (normal) and Alzheimer's disease (AD) patients and sensitivity up to 95% to AD. Moreover, statistical significance tests have been also performed in order to validate the proposed approach.

1. Introduction

Nowadays, Alzheimer's disease (AD) is the most common cause of dementia which affects more than 30 million people worldwide. Due to the increasing life expectancy and the aging of the population on developed nations, it is expected AD to affect 60 million people worldwide over the next 50 years (Association, 2012; Education and Center, 2012). AD is a slow degenerative disease, with different evolution on every individual, but usually starting with mild memory problems and turning to severe brain damage in several years. AD patients start experimenting cognitive impairments but in a not long period of time they lose the spatio-temporal sense and are unable to recognize very familiar things or persons. Since currently there is no a known cure for the AD, the early diagnosis may help to slow down the rapid advance of the disease. Although the development of the disease depends on the individual, aging, etc. there are many common symptoms in addition to structural changes in the brain. These structural damages results on extreme shrinkage of the hippocampal volume or extreme reduction of cortical thickness, as well as severe enlargement of the internal ventricles. (Storey et al., 2002). However, AD diagnosis is actually performed when cognitive symptoms are present. At this point, the disease is at an advanced stage and there is no way to contain the disease. In order to deal with objective diagnosis of the AD, Brain Magnetic Resonance Images (MRI) (Cuingnet et al., 2010; Termenon and Graña, 2012; Chyzhyk et al., 2012) as well as functional images (Górriz et al., 2011; López et al., 2011; Segovia et al., 2012; Stoeckel and Fung, 2005) can be used to reveal common patterns in AD and healthy patients in order to diagnose the AD even before the manifestation of any cognitive symptoms. These approaches use different techniques to reduce the dimensionality of the feature space as well as to extract features from images. This way, Cuingnet et al. (2010) and Termenon and Graña (2012) compares the effect of different segmentation and registration methods in classification using SVM with different kernels. Moreover, Chyzhyk et al. (2012) make use of Lattice Independent Component Analysis (LICA) for feature extraction and dendritic computing (Graña et al., 2011) as classifier. Other works such as (Górriz et al., 2011; López et al., 2011; Segovia et al., 2012) use linear embedding techniques to reduce the feature space and the computational burden in the classification process. Specifically, Górriz et al. (2011) and López et al. (2011) present the use of *eigenbrains* to compress the information contained in the image and Gaussian Mixture Models (GMM) to quantize the space and to model the 3D intensity distribution

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[1] Data used in preparation of this article were obtained from the Alzheimers Disease Neuroimaging Initiative (ADNI) database (adni.loni.ucla.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. A complete listing of ADNI investigators can be found at: http://adni.loni.ucla.edu/wpcontent/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf.

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http://dx.doi.org/10.1016/j.patrec.2013.04.014

profile. On the other hand in Segovia et al. (2012), Partial Least Squares (PLS) is also used as a dimensionality reduction technique. In all of these works, SVM using different linear and nonlinear kernels are used for classification.

The classification method presented in this paper provides two main novelties. The first consist in a unsupervised technique to segment the structural MRI images, in order to delimitate the three main tissues present on a healthy brain: White Matter (WM), Gray Matter (GM) and Cerebrospinal Fluid (CSF). The second uses the prototypes computed from the segmented volumes using Learning Vector Quantization (LVQ) to derive a reduced set of features by projecting the most discriminative WM and GM voxels onto the prototype space. These features are proved to be discriminative enough for a Support Vector Machine classifier. Our algorithm has been tested using MRI from the Alzheimer's Disease Neuroimaging Initiative (ADNI) (2012) database.

2. Material and methods

2.1. Database

The source of images we used in this paper were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) (2012). This database was created to study the advance of the Alzheimer disease, collecting a vast amount of MRI and Positron Emission Tomography (PET) images as well as blood biomarkers and cerebrospinal fluid analyses. The mail goal of this database is to provide a way to the early diagnose of the Alzheimer disease. ADNI database provides data for three groups of patients: healthy patients (normal), Alzheimer disease patients (AD) and patients with cognitive symptoms (MCI). In this work, we use 50 T1-weighted MRI images (25 Normal and 25 AD) to asses the performance of our classification method.

Fig. 1 shows the proposed method to classify images between NORMAL and AD. The training phase shown in Fig. 1 consists of four stages. First, NORMAL and AD images are used to compute the most discriminative voxels by means of Fisher Discriminant Ratio (FDR) (Theodoridis and Koutroumbas, 2009). Then, the images are segmented in an unsupervised way using the method described further, and the most discriminative WM and GM voxels (previously computed by FDR) of these segmented images are used to generate model vectors using Learning Vector Quantization (LVQ) algorithm (Kohonen, 2001). The images used to train the LVQ are projected onto the prototypes to generate a reduced number of features to train a Support Vector Machine (SVM) (Vapnik, 1998). In the testing stage, the image under test is first segmented. Then, the most discriminative voxels computed during the training phase are selected, and these WM and GM voxels are projected onto the prototypes to obtain the features. Thus, the generated features are used to classify the image by means of the previously trained SVM.

2.2. Image preprocessing

Features extracted from each image are used to train the classifier. Therefore, each image voxel should correspond to the same anatomical position. This is addressed by co-registering all the images on the ADNI database using the SPM (London Institute of Neurology (UCL), 2012) software and the built-in templates. After image registration, all the images from ADNI database were resized to $91 \times 109 \times 91$ voxels with voxel-sizes of 1.5 mm (Sagittal) $\times$ 1.5 mm (coronal) $\times$ 1.5 mm (axial). Furthermore, non-brain structures were removed using the BET 2.0 tool (FMRIB Centre. Nuffield Department of Clinical Neurosciences. University of Oxford, 2012a) from FSL package (FMRIB Centre. Nuffield Department of Clinical Neurosciences. University of Oxford, 2012b), running two iterations on every subject. We run BET twice on each subject since non-brain material remains on the MRI after one iteration and three iterations tend to remove some parts of the brain. This way, running BET twice was determined to be optimum. Additionally, the images are intensity normalized. In order to avoid the effect of noisy voxels in the normalization, we followed the method presented in Padilla et al. (2012) for PET (Positron Emmision Tomography) images, where the 0.1% of the voxels in

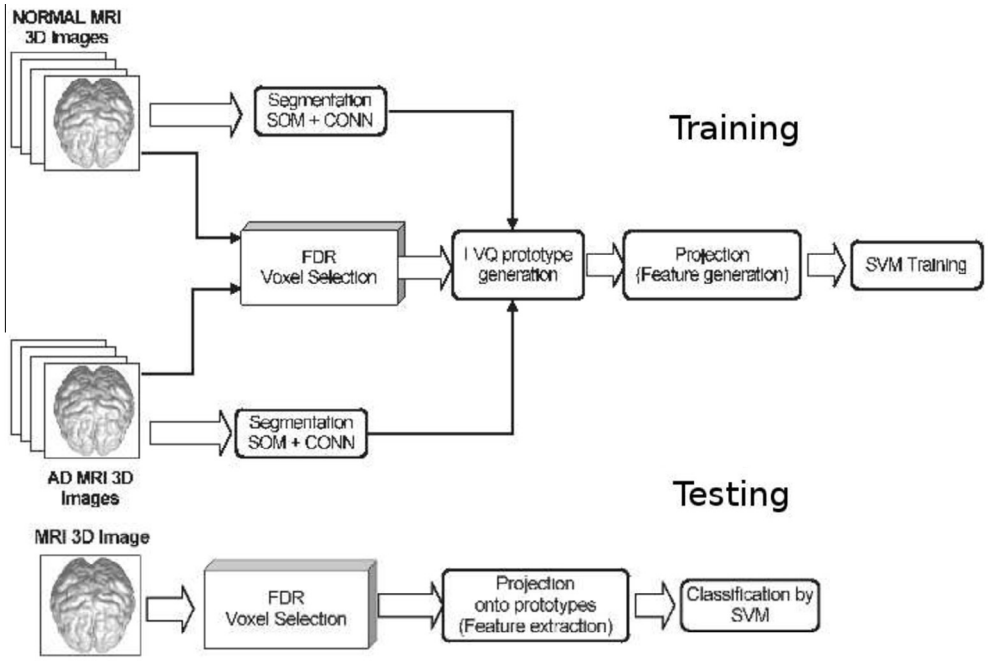

Fig. 1. Block diagram of the proposed classification method.