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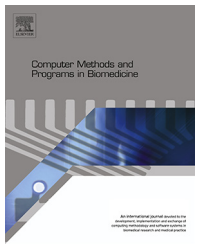

Structural MRI-based detection of Alzheimer's disease using feature ranking and classification error

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ABSTRACT

Background and objective: This paper presents an automatic computer-aided diagnosis (CAD) system based on feature ranking for detection of Alzheimer's disease (AD) using structural magnetic resonance imaging (sMRI) data.
Methods: The proposed CAD system is composed of four systematic stages. First, global and local differences in the gray matter (GM) of AD patients compared to the GM of healthy controls (HCs) are analyzed using a voxel-based morphometry technique. The aim is to identify significant local differences in the volume of GM as volumes of interests (VOIs). Second, the voxel intensity values of the VOIs are extracted as raw features. Third, the raw features are ranked using a seven-feature ranking method, namely, statistical dependency (SD), mutual information (MI), information gain (IG), Pearson's correlation coefficient (PCC), t-test score (TS), Fisher's criterion (FC), and the Gini index (GI). The features with higher scores are more discriminative. To determine the number of top features, the estimated classification error based on training set made up of the AD and HC groups is calculated, with the vector size that minimized this error selected as the top discriminative feature. Fourth, the classification is performed using a support vector machine (SVM). In addition, a data fusion approach among feature ranking methods is introduced to improve the classification performance.
Results: The proposed method is evaluated using a data-set from ADNI (130 AD and 130 HC) with 10-fold cross-validation. The classification accuracy of the proposed automatic system for the diagnosis of AD is up to 92.48% using the sMRI data.
Conclusions: An automatic CAD system for the classification of AD based on feature-ranking method and classification errors is proposed. In this regard, seven-feature ranking methods (i.e., SD, MI, IG, PCC, TS, FC, and GI) are evaluated. The optimal size of top discriminative features is determined by the classification error estimation in the training phase. The experimental results indicate that the performance of the proposed system is comparative to that of state-of-the-art classification models.

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1. Introduction

Alzheimer's disease (AD), a progressive irreversible neurodegenerative disorder, occurs most frequently in older adults and gradually destroys regions of the brain that are responsible for memory, thinking, learning, and behavior [1]. It is estimated that 5.3 million Americans of all ages suffer from AD in 2015 [2]. Among the top 10 causes of death among Americans, AD is the only disease that cannot be cured, prevented, or slowed [2]. Although there is no cure for AD, early detection may shed light on AD mechanisms and improve the responses of AD patients to drug therapy and their quality of life. In recent years, the analysis of neuroimaging data, such as structural magnetic resonance imaging (sMRI) [3–12], functional MRI [13–15], and diffusion tensor imaging [16–18], in addition to positron emission tomography (PET) and single photon emission computed tomography (SPECT) [19–24], has attracted much interest, with recent improvements in accurate detection of AD. In this paper, we focus only on the use of sMRI data in the classification of AD. Recently, sMRI brain data have been widely used to design computer-aided diagnosis (CAD) systems for the classification of AD [4,9,25,26], because of the noninvasiveness, excellent spatial resolution, and good tissue contrast of sMRI, in addition to the absence of radioactive pharmaceutical injection, as occurs with PET and SPECT [19–22]. Many researchers studied advanced pattern analysis and classification approaches for extracting complex spatial patterns of brain structure [14,27–30]. This paper describes the application of an automatic CAD system, which uses statistical feature-ranking methods as part of a novel feature-selection process, followed by estimation of the classification error in AD and healthy control (HC) groups to determine the optimum number of highest-ranking features to be selected. In the training set, resubstitution and cross-validation error estimators were used as classification errors to measure the quality of a classifier. We used these classification error metrics as stopping criteria among the ranked features to estimate the optimal number of features with the most discriminative information in the classification process. We evaluated seven feature-ranking methods, namely, statistical dependency (SD), mutual information (MI), information gain(IG), Pearson's correlation coefficient (PCC), the *t*-test score (TS), Fisher's criterion (FC), and the Gini index (GI) in the proposed CAD system. In the proposed approach, high-dimensional feature space was reduced into lower dimensional space by employing the minimized classification error as the dimensionality selection criterion in an iterative process of incrementing the number of ranked features. The proposed feature-selection method was applied to gray matter (GM) atrophy clusters of voxels, which corresponded to the volume of interests (VOIs) of the sMRI data obtained through the voxel-based morphometry (VBM) analysis during preprocessing. VBM is an advanced method used to assess the whole-brain structure using voxel-by-voxel comparisons [8,31–36]. It is one of the best methods for feature extraction from sMRI in AD [9]. In the proposed system, we used only sMRI data. The proposed CAD system was applied in four stages in a systematic manner. In the first stage, the VBM technique was employed, in addition to diffeomorphic anatomical registration using the exponentiated Lie algebra (DARTEL) [33]. This approach was used to analyze group-wise comparisons between cross-sectional structural MRI scans to detect the MRI voxels that were best discriminated between the AD group versus HCs [8,31–33]. Based on the VBM and DARTEL approach on a global brain scale, and regional structural GM alterations, regions with significant atrophy of GM were investigated and specified in the patients who suffer from AD. In the second stage, specified VOIs were used as 3D masks for extracting voxel intensity values from GM atrophy regions to generate raw feature vectors. These feature vectors were subjected to further data-selection processes before they were used by the classifier. In the third stage, the extracted features were ranked based on the statistical scores (i.e., SD, MI, IG, PCC, TS, FC, and GI) of the AD and HC groups in the training set. The ranking scores can be considered an indicator of the level of separation/discrimination between the AD and HC groups in the training set. Feature ranking has been used successfully in a number of pattern-recognition studies [37–42]. In addition, an automatic approach based on classification error estimation was used to determine the number of top features using the AD and HC groups in the training set. This approach adaptively determines the optimum number of top features and identifies a discriminative subset of high-performance features based on the training data in each fold instead of using a fixed number of features. In the fourth stage, the performance of the proposed feature-selection technique was evaluated using a support vector machine (SVM) classifier. In this work, the SVM classifier with a linear kernel was trained to discriminate between the classes. In addition, instead of using a single feature ranking method, the results of multiple individual feature ranking methods were combined through the proposed data fusion technique for improved classification performance.

In summary, the aim of this study was to design an automatic CAD system based on statistical feature ranking and classification errors as part of a novel feature-selection method. The proposed system utilizes feature ranking based on statistical scores, followed by the determination of resubstitution and cross-validation error estimators to identify the number of ranked features that minimizes the error in the training set. This process helps to identify a selected discriminative subset of high-performance features into a lower-dimensional feature vector space representing sMRI images. In addition, a data fusion technique was proposed to improve the AD classification performance among different feature ranking methods. The performance of the proposed system was assessed using a data set from the Alzheimer's Disease Neuroimaging Initiative (ADNI) containing 260 subjects (130 AD patients and 130 HCs) using 10-fold cross-validation. The experimental results showed that the accuracy (ACC) (92.48%), sensitivity (SEN) (91.07%), specificity (SPE) (93.89%), and area under the curve (AUC) (0.963) of the proposed system were well comparatively to results obtained with state-of-the-art techniques in terms of AD classification.

The rest of the paper is organized as follows: Section 2 details the statistical data in the study. Section 3 describes the proposed methodology to design an automatic CAD system based on feature ranking and classification error. Section 4 presents the experimental results, discussion, and analysis of the proposed system. Finally, Section 5 presents the conclusions.