



Multi-class Alzheimer's disease classification using image and clinical features

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ABSTRACT

Alzheimer's disease (AD) is the most common form of dementia, which results in memory related issues in subjects. An accurate detection and classification of AD alongside its prodromal stage i.e., mild cognitive impairment (MCI) is of great clinical importance. In this paper, an Alzheimer detection and classification algorithm is presented. The bag of visual word approach is used to improve the effectiveness of texture based features, such as gray level co-occurrence matrix (GLCM), scale invariant feature transform, local binary pattern and histogram of gradient. The importance of clinical data provided alongside the imaging data is highlighted by incorporating clinical features with texture based features to generate a hybrid feature vector. The features are extracted from whole as well as segmented regions of magnetic resonance (MR) brain images representing grey matter, white matter and cerebrospinal fluid. The proposed algorithm is validated using the Alzheimer's disease neuro-imaging initiative dataset (ADNI), where images are classified into one of the three classes namely, AD, normal, and MCI. The proposed algorithm outperforms state-of-the-art techniques in key evaluation parameters including accuracy, sensitivity, and specificity. An accuracy of 98.4% is achieved for binary classification of AD and normal class. For multi-class classification of AD, normal and MCI, an accuracy of 79.8% is achieved.

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1. Introduction

Alzheimer's disease (AD) is a neurological brain disorder, which damages the brain cells, and eventually a patient loses the ability to carry out simple day to day tasks [1]. According to an estimate, about 5.3 million Americans are suffering from AD in 2015. This number is likely to go as high as 16 million by 2050 [2]. The cause of AD is inadequately understood and still no proper treatment has been discovered to stop the progression of this disease [3,4]. An early diagnosis of AD can help in determining its progression and also improve the quality of life of AD patients. Recently, the analysis of neuro-imaging data has drawn attention because it helps in

early and accurate detection of AD. The prodromal stage of AD is known as the mild cognitive impairment (MCI), which has a 10% conversion rate to AD [5]. Magnetic resonance imaging (MRI) has been used in studies related to AD due to its exceptional spatial resolution, high accessibility, and good contrast [6,7]. Structural MRI has been used in various studies for feature extraction and classification of AD using volume of interest (VOI) and region of interest (ROI) [8–10], grey matter (GM) voxels in the segmented images [11], measurement of hippocampus, the medial temporal lobe (MTL) and morphometric methods [12–14]. In spite of the improvements in early diagnosis of AD, the prediction of progression of disease using structural MRI remains a challenging task and needs further investigation.

For the diagnosis of AD, a careful medical assessment is required, which include patient history, mini-mental state examination (MMSE), clinical dementia rate (CDR), physical and neuro-biological exams. Additionally, non-invasive methods like structural MRI and resting-state functional MRI (rs-fMRI) have also been used to study the structural and functional changes in the brain [15,16]. The hippocampus and the cerebral cortex shrinks, whereas, the ventricles enlarge in the brain due to the AD. These

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changes in cerebrum and hippocampus regions effect tasks including memory, planning, thinking, and judgement. The magnitude of change in different brain areas depends on the phase of disease progression. A severe reduction in volume of the hippocampus and cerebral cortex and a significantly enlarged ventricles are easy to detect using MR images.

The development of an algorithm, which can differentiate between brain disorder and healthy subjects is of great importance to the clinicians [17]. As of now, contributions in the field of AD classification and detection are growing and medical community is already achieving promising results [18]. A broad knowledge and experience is required to distinguish between AD and normal ageing by looking at the visible changes in brain areas on an MR image, where a diagnosis remains subjective. Therefore, the imaging data should be combined with other clinical outcomes such as MMSE for a more accurate data classification.

In this work, a texture based feature analysis is performed where MR images are segmented into three regions namely, grey matter, white matter (WM), and cerebrospinal fluid (CSF). Texture based features are extracted from MR images without segmentation as well as from the segmented regions using techniques including gray-level co-occurrence matrix (GLCM), scale invariant feature transform (SIFT), histogram of oriented gradient (HOG) and local binary pattern (LBP). The feature descriptors are then optimized using the bag-of-words (BOW) method [19]. Features are also used from the related clinical data for subjects. These optimized feature vectors are given as input to classifiers, which perform binary class or multi-class classification for the detection of AD. Our contributions in this work comprise of the following key points:

- A hybrid feature based classification method is proposed incorporating texture based features along with clinical data.
- The effect of using complete as well as segmented MR images for feature extraction and classification is explored, where it produces improved results on binary and multi-class classification.
- The proposed method classifies Alzheimer subjects using multi-class classification, in contrast to most state-of-the-art methods, which rely on expensive binary classification.

The remainder of this paper presents related work in Section 2, proposed methodology in Section 3, experimental result and discussion in Section 4, and conclusion in Section 5.

2. Related work

In [1], five stages were used, where images were pre-processed and segmented into GM, WM and CSF in the first stage. The GM segmented ROIs were used to build similarity matrices in the second stage whereas, statistical features were extracted in the third stage. In the final two stages, statistical features were combined with clinical data i.e., functional activities questionnaire (FAQ) and support vector machine (SVM) classifier was used to classify data in AD vs normal group. In [4], a 3D displacement-field estimation was used for classification of AD and normal subjects. Feature selection was performed using three methods including Bhattacharyya distance, student *t*-test and Welch's *t*-test. The data was classified using SVM classifier and achieved a classification accuracy of 93.05%. Local and global GM atrophy in AD patients against healthy controls was found using voxel based morphometry (VBM) [20]. The VOIs were segmented from regions having significant GM volume reduction. A feature vector was extracted from these voxel values and ranked using *t*-test scores and genetic algorithm, to select an optimal subset of features. The classification was performed using SVM with a 10-fold cross validation and achieved an accuracy of 84.17% and 70.38% for AD vs normal and MCI vs normal class respectively.

In [21], GM volume was detected using VBM for AD patients and healthy controls, and regions with significant GM atrophy change were selected as VOIs. The voxel values from these regions were treated as raw features, which were then evaluated using seven different feature ranking techniques i.e., mutual information (MI), information gain, statistical dependency, Fisher's criterion, *t*-test score, Pearson's correlation coefficient, and the gini-index. The classification of subjects was performed using SVM with an accuracy of 92.48%. In [22], a Laplace Beltrami eigenvalue shape descriptor was used to classify the AD. The shape changes of corpus callosum were analyzed by segmenting T1-weighted MRI scans using reaction diffusion level set approach. Information gain ranking was used to select the significant features, which were classified using *K*-nearest neighbour (KNN) and SVM. A maximum classification accuracy of 93.37% was achieved using the KNN classifier. However, quantifying variations in the micro structure of corpus callosum is difficult, which makes the method less useful in practice.

A framework for feature extraction from low-dimensional subspaces that signify inter-subject variability was proposed in [23]. Data-driven ROIs were used to build the manifold subspace. A sparse regression with MMSE score was used to learn these regions. The sampling bias was reduced along with a re-sampling scheme using sparse regression for performing variable selection. A classification accuracy of 71% was achieved. In [24], a sulcal medial surface for AD and cognitively normal (CN) classification method was proposed. Brain-VISA sulcal identification pipeline was used on subjects to extract 24 distinct sulci for each subject and SVM was used to classify AD and CN along with the computation of sulcal medial surface features. A classification accuracy of 87.9% was achieved. In [25], various measurements like cortical thickness, hippocampus texture and shape, were combined to make a bio-marker that used information from MRI data. The method was trained on MR scans from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database using linear discriminant analysis (LDA). The results showed that the combination of these MRI bio-markers achieves 62.7% multi-class classification accuracy. In [26], local features were extracted using the circular harmonic functions (CHFs) from hippocampus and posterior cingulate cortex. The classification accuracy for AD vs MCI task was 62.07%.

A deep learning algorithm was presented to classify AD subjects in [27]. Auto-encoders were used alongside convolutional neural networks to predict the output classes as AD and normal, with a classification accuracy of 98.4%. Other classes and multi-class classification was not considered. Convolution neural network was used to extract discriminative features for classification of AD and normal subjects [28,29]. Although, deep learning based methods have achieved significant results in big data analysis, but harvesting useful information from large collections of unstructured data require a lot of training, and computational power [30]. The selection of optimal hyper-parameters and best architecture is also a difficult task.

The binary classification of AD and MCI, as well as multi-class classification including AD, normal and MCI is a challenging task. Most methods reported in literature focused solely on features directly extracted from the brain images, which limited their effectiveness in classification. In this study, clinical information was used along with features extracted from whole as well as segmented brain images, which significantly improved the binary and multi-class classification performance.

3. Proposed methodology

The proposed system has three main modules namely pre-processing, feature extraction, and disease classification. A detailed

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