DOI: http://dx.doi.org/10.26483/ijarcs.v9i2.5353

ISSN No. 0976-5697

Volume 9, No. 2, March-April 2018

International Journal of Advanced Research in Computer Science

SURVEY PAPER

Available Online at www.ijarcs.info

A COMPARATIVE SURVEY OF FEATURE EXTRACTION AND CLASSIFICATION TECHNIQUES FOR EARLY DIAGNOSIS OF ALZHIMER'S DISEASE

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***Abstract*:** Alzheimer's disease (AD) is a neurodegenerative disorder of the brain in the elderly population AD is most severe and common form of Dementia that affects memory and cognitive functions of the elder people with behavioral impairment. Various Computer-Aided Diagnosis (CAD) systems have been developed for early diagnosis of AD available in the literature. All CAD techniques select and extract some feature vectors such as Principal Component Analysis (PCA), Partial Least Square (PLS), random forest etc. for AD diagnosis. In this paper, various feature extraction and classification approaches using the three imaging modalities, MRI, SPECT and PET along with their merits and demerits are discussed. In particular, this paper mainly focuses on feature extraction and classification approaches for early diagnosis of AD. A tabular demonstration of all approaches is presented to facilitate the comparison. Some discussion about the future enhancement in this direction by identifying some open research problems is also presented.

***Keywords*:** Alzheimer's disease, CSF, EM algorithm, ICA, Multimodal classification and Non-negative matrix factorization.

I. INTRODUCTION

Alzheimer's disease (AD) is one of the most severe neurodegenerative disorders of the brain. It is a common cause of dementia and that leads to memory loss or other mental or cognitive impairments serious enough to disturb with daily life in elderly people worldwide. AD occurs in adults aged 60 and develops some of early symptoms of AD like memory loss, a lack of initiative, difficulty in retaining new information, difficulty in expressing thoughts, personality changes, changes in thinking and behaviour activities. The incidence and prevalence of this disorder various among many factors including genetics, age, education and co-morbidities [1]. Still AD is an incurable brain disorder and there is no better treatment available to delay the progression of AD. However, many new drugs and pills have been developed to slowdown the effect of this disease. If the disorder can be identified at an early stage, it is possible to repair some damages caused by AD and can assist the people to maintain daily life and stabilize the cognitive decline. This fact has emphasized the development of non-invasive techniques for early detection. Extensive progress has been reached to this end, but an efficient and accurate diagnosis of AD at an early stage is a challenging task [2].

Medical imaging practices can visualize the histological changes of the brain such as hypo-metabolism, atrophy and amyloid plaques introduced by neurodegenerative disorder. Therefore, extensive submissions of medical imaging practises have lead to the development in the early diagnosis of AD. The commonly used structural neuroimaging modalities in AD diagnosis like Computer Tomography (CT) or Magnetic Resonance Imaging (MRI). MRI uses radio wave and magnetic field to generate the image of the brain and tissues within the body. This modality offers some advantages, low cost, availability and better soft tissue contrast. However, structural changes may not be identified at visual examination until last stage of the disorder. Low sensitivity and specificity is the major limitation of conventional structural neuroimaging in AD diagnosis. They are mainly used for the routine evaluation of AD. To overcome the drawback of structural neuroimaging, several functional neuroimaging techniques have been developed including Positron Emission Tomography (PET), Single Photon Emission Computer Tomography (SPECT) and Functional Magnetic Resonance Imaging (fMRI) [3].

Finding suitable and sensitive methodologies for non-invasive modality observation and early diagnosis of AD is one of the primary steps to develop effective treatments that slow down the progression of AD. Brain autopsy is the only technique to diagnosis AD. However, some mental and behavioural assessment and physical tests enable the physicians to make an accurate diagnosis of AD in 90 percent of cases. Many recent research shows that pathological manifestations of AD start many years before the patient is symptomatic [4, 5]. Computer-Aided Diagnosis (CAD) system aid the general practitioner to recognise the AD in early stage and functional imaging has been proved to be effective and useful in this diagnosis. An accurate prediction of CAD system depends on the selected feature vectors. Therefore, the aim is to select the most important and essential feature vectors that they are able to distinguish between the normal and AD subjects.

The motivation of this survey is to explore the existing feature extraction and classification approaches so that the researchers select the suitable and efficient approach for their works in this field and demerits of existing approaches can be surmount. This paper discusses various imaging modalities used for the diagnosis of AD. This paper also presents a survey of early diagnosis techniques in the literature. Similar to other classification problems, AD diagnosis methods has two important steps: feature vector selection and classification. Hence, this paper reviews the feature vector selection, extraction and classification methods used in those strategies

II. EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE

There exist enormous literatures which concentrate on developing CAD system for early diagnosis of AD. Recently, several pattern classification methods have been developed to automatically distinguish between patients with and without Alzheimer's disease using different imaging modalities including MRI, SPECT and PET. In the following section, this paper discusses various feature extraction and classification approaches for diagnosis of AD in early stage using medical images.

A. IMAGING TECHNIQUES

MRI

MRI imaging is a non-invasive technique for structural analysis. This is made with an MRI scanner. Structural brain imaging plays the most important role to identify the possible anatomical changes that occur in the brain related to AD. MRI scans shows the local perfusion of the brain that can be utilized for AD diagnosis as the perfusion pattern is affected by the disorder [7]. Making use of many image processing methods, automatic CAD systems have been developed, achieving better results separating AD patients from normal control patients.

SPECT

SPECT is non-invasive electronic tomography technique based on nuclear medicine that is commonly used to study the functional process in the brain. Several approaches have evaluated the predictive ability of neuro-imaging with respect to AD and other dementia can be found [5, 8-12]. Diagnosis of AD is still a stimulating task, especially in the early diagnosis of the brain disorder. This disease offers more opportunities to be treated during this early stage. This fact motivates developing new data extraction methods and early diagnosis by means of non-invasive methods.

PET

PET is a non-invasive, three dimensional functional neuroimaging technique that shows the glucose consumption rate of the brain. Glucose consumption depends on the brain activity. So, PET can be used as a promising tool for diagnosing brain disorder. In AD patients, PET scans are able to test the changes in neuro irritation, various neurotransmitter systems, cerebral glucose metabolism, and the protein aggregates that are characteristic of the disease, notably the amyloid deposits. These tests are supporting in further understanding the complex pathophysiological mechanisms that underlie AD disorder and helping the early diagnosis of the disease in the health centre [13].

It's a long standing challenge to develop an effective recovery model that can ease the users search by providing an optimal crawl of the Hidden Web resources. Certain proposals [2, 3, 4, 5, 6, 7] have been made to extract the content unseen behind the search forms. The work in [2] proposed HiWE, Hidden Web Exposer, a task-specific hidden-Web crawler, the main focus of this work is to learn Hidden-Web query boundaries. Their strategy aims to extract the labels of the form by rendering the pages. The crawler makes several filling attempts by testing various combinations of the values for HTML search forms available at the moment of crawl. Liddle et al. [3] performs a comprehensive study on obtaining valuable information from the web forms, but do not include a crawler to fetch them. Barbosa and Freire [4] experimentally evaluate methods for building multi-keyword queries that can return a large fraction of a document collection. Ntoulas et al. [5] differs from the previous studies, that, it provides a hypothetical framework for analyzing the process of generating queries for a database problem of Hidden Web crawling. Gravano [6] have developed an automatic query-based technique to retrieve documents for extracting user-defined relations from large text databases, which can be adapted to databases from various domains or types (multi-attribute databases) with minimal human effort.

Gupta and Bhatia [9] developed a domain Oriented Hidden Web crawler, HiCrawl targeted to crawl the sites in the 'Medical' domain. The system is based on the use of cataloguing hierarchies that might have either been manually or automatically constructed for decide on the right query term to be submitted to any search form interface that has been designed to accept keywords or terms as input to it. Whereas the work in [7] present a formal framework that regards the crawler as an agent that perceives its current state and the last performance action as input so as to output the next optimal action to be taken. It uses adaptive approach to reinforcement learning for deep web crawling where the action causes the agent (crawler) to transit from the current state to the next or successor state.

Most of these methods generate candidate query keywords either by using a manually or semi automatically created database of values or by using only the frequency statistics derived from the records obtained by previously issued queries without considering the operational properties of the HTML documents. Our approach of crawling differs from other adaptive approaches (based on results obtained from previous queries) by taking into consideration the position as well as the distribution of the terms in the document space, unlike others. The measure proposed for use in our approach to weigh and rank terms has been termed as the Variable Document Frequency (Vardf) and is based on the fact that the vocabulary set changes and new structural properties of documents come up, as and by different documents are retrieved from the database. Thus, certain features should be re-estimated after any term has been selected and used as the query term.

B. FEATURE EXTRACTION AND CLASSIFICATION APPROACHES

In order to enhance the prediction accuracy in the early diagnosis of AD, CAD tools are preferred. The idea behind the development of CAD system is to reproduce the medical experts' knowledge in the form of complete database which is used to discriminate the AD subjects from normal controls. It is also used to prevent the errors which occur during single observer evaluation. Numerous approaches are found in the literature for CAD system to analyze the medical images especially in the early diagnosis of AD. Region of Interests (ROIs) analysis is the first basic approach for Computer aided AD diagnosis based on some discriminant function [14,15]. In 1999, Signorini et al.[16] have suggested that the Statistical Parameter Mapping(SPM) could be an appropriate method to describe the pattern of cerebral functional degeneration. Then, SPM and its numerous variants have been designed and widely used in neuroscience. SPM is a univariate statistical testing method and used for comparing the values of images. However, SPM application for AD analysis results in poor classification since t-test does not contain any pathology information [5, 15, 17].

Multivariate method such as Multivariate Analysis of Covariance (MANCOVA) [5, 18, 19] considers whole voxels in a single scan as one observation to make interferences about the effects due to activation. The significance of this method is that the confounding effects, activation effects and error effects are observed statistically in terms of effects of individual voxel and also interactions among voxels [5,20]. Voxel-As-Features (VAF) is one of the commonly used multivariate approaches for early diagnosis of AD. In this approach, Support Vector Machine (SVM) classifier is trained to separate the controls and AD subjects based on given threshold. It is the simplest approach but provides results similar to other sophisticated approaches. Voxel selection is one of the most important steps in classification. There are many techniques that have been introduced for voxel selection using t-student test ranking, including the commonly used SPM [21-23]. Voxels are selected and arranged from higher to lower following statistical test. Then, the first M voxels are chosen for further process. Diverse kind of algorithm PCA [24, 32], ICA [1, 25], FDA [26] and Factor analysis [27, 28] have been adopted for feature extraction.

Feature extraction based on Partial Least Square (PLS)

PLS is a promising tool for feature extraction that has shown enhanced results when compared to other feature extraction techniques like Principle Component Analysis (PCA),Independent Component Analysis (ICA),etc in classification problems **.**Random Forest (RF) based on ensemble of decision trees, majority voting and bagging outperforms a single decision tree classifier and achieves good accuracy than other traditional techniques in many applications [30,31]**.** Ramrez et al [15] in 2010 have presented a CAD system for early diagnosis of AD. This approach uses PLS for feature vector extraction and RF predictor. Experimental results have demonstrated that the error of the RF depends on the strength of each tree in the forest and connection between them. PLS-RF approaches provide better results than other existing approaches such as PCA-Bayesian classifier, PCA-SVM, GMM-SVM and VAF. However, this approach needs a method for selecting feature vector size and PLS decomposition procedure prone to attain biased results.

In 2012 Rosa chaves et al.[29] have investigated the performance of kernel distance metric learning approaches for AD diagnosis. In this approach, t-test is applied on the brain image to select the ROI. Large Margin Nearest Neighbour based Rectangular Metric (LMNN-RECT) with PLS/PCA carry out feature reduction process. It also addresses the small sample size problem and dimensionality problem. Kernel SVM, LMNN using Euclidean, energy based metrics and Mahalanobis is used to separate the normal controls from AD. Results have shown that the PLS-LMNN-SVM gives promising result than other traditional methods like GMM, PCA and VAF.

Recent research has shown that pathological manifestations of AD may be identified by using functional images even before that the patients become symptomatic. This information emphasized the researchers to develop new approaches for analyzing functional images in order to get more accurate CAD systems for AD diagnosis. Segovia et al [5] in 2013 have proposed an effective method for feature extraction that enhance accuracy of CAD systems for AD. PLS method is used for feature score vector extraction and Out-Of-Bag error for feature selection.SVM classifier is used to distinguish between normal and AD subjects. Experimental results have shown that this method achieves accuracy rate 90 % and also provides better results than existing CAD systems for AD diagnosis such as VAF, GMM and PCA. It is also noticed that this method is more suitable for AD diagnosis.

Feature extraction based on PCA

L´opez1 et al [32] have presented a complete CAD system in 2009 for AD diagnosis based on multivariate analysis. This approach uses Fisher Discriminant Ratio (FDR) to obtain necessary information by applying PCA algorithm on the input image and also address the small sample size problem. Bayesian classifier which uses a posterior information for classification is used to discriminate between the normal and AD subjects. SPECT and PET images are used for analysis. This approach reduces the dimension of feature vector and categorizes the subjects with high accuracy. The results of a simulation show that this approach has shown better performance than VAF approach in terms of accuracy.

In 2011 illan et al.[1] have proposed automatic CAD tool for AD diagnosis which is based on eigenbrain decomposition. This approach has three stages: functional image dimension reduction with projection into a discriminative subspace, feature vectors are extracted by means of PCA/ICA techniques and classification task is managed by kernel SVM. Results have shown that this approach can identify the characteristic of AD in stable MCI patients and also able to discriminate between those MCI converters and normal one after 2 years.

Ben Ahmed et al. [33] in 2015 attempted to meet the challenges of small sample size problem by using visual features and pattern recognition method based on MRI scan image to separate three classes of patients: Normal Controls (NC), Mild Cognitive Impairment (MCI) and AD. Circular harmonic functions (CHFs) are adopted to extract local features from the hippocampus and Posterior Cingulated Cortex (PCC) in each slice. Bag-of-Visual-Words method carries out the quantization process.PCA algorithm is utilized to reduce the dimensionality of the features. Support vector machines classifiers are then applied to classify subjects. Results have shown that the use of PCC visual features description increases classification rate results by more than 5% compared to the use of hippocampus features only.

Multivariate approaches based CAD system for early diagnosis of AD from MRI images is proposed by Khedher et al. [34] in 2015.They have used PLS and PCA to extract the feature vectors. The subjects are classified into AD and normal by means of SVM- Radial Basis Function (RBF) classifier. Results show that the feature extraction method based on PLS and SVM-RBF classifier achieves good results than the PCA method and it is observed to be effective method for extracting necessary information from the data.

In 2016 Deepika et al. [35] have proposed feature based model for AD diagnosis. It is a multivariate model and uses PLS and PCA for future extraction. Texture features provide some useful information for identifying subjects at feature vector selection and classification stage. The authors combine Haralick texture parameters with the multivariate approach for feature extraction.SVM classifier is employed for distinguishing between normal and AD subjects. Haralick parameters with PLS gives better performance than PCA method.

Feature extraction based on ICA

Illán et al.[25] in 2010 have integrated Component Analysis (ICA) with SVM for developing CAD systems for AD diagnosis. ICA has been proven to be useful in many fields [36-39]. ICA is applied on the SPECT images to perform two important tasks, relevant feature extraction and dimension reduction.SVM classifier is adopted to discriminate between AD and normal subjects. This method provides promising results than VAF method.

Performance comparison of different classifiers is investigated by Ahsan Bin Tufail et al. [40] in 2012 on structural MRI images. ICA is used to extract the feature vectors. Three different classifiers namely Proximal SVM, Multilayer ANN and KNN classifier used to distinguish between the AD and normal subjects from MRI scans. Better results are achieved by KNN and PSVM in terms of both computational speed and accuracy.

Feature extraction based on NMF

An appropriate feature extraction and classification plays the most important role in the CAD system. For this purpose, in the year 1994, Paatero et al.[41] have applied Non-Negative Factor (NMF) analysis on the SPECT image database to extract necessary information. Then, the features are classified into normal and AD subjects using SVM classifier. This approach can reduce the slight sample size problem. Later in 2010, Padilla et al.[42] have used the NMF for feature extraction process. This approach uses Fisher discriminant ratio (FDR) for feature extraction and NMF for feature selection. Finally, reduced feature vectors are classified by means of SVM classifier. Results have shown that the NMF-SVM based approach capable of reducing the dimensionality problem with improved performance than other traditional approaches such as VAF-SVM and PCA-SVM.

Feature extraction based on GMM

Gorriz et al.[43] in 2011 have proposed a classification method for early diagnosis of AD based on Gaussian Mixture Model(GMM).GMM is mainly used for density estimation which selects the ROI. Expectation-Maximization (EM) algorithm is employed to construct the Gaussians based on maximum likelihood criterion.SVM classifier is used to differentiate the normal control and AD patients. Results have shown that the GMM method reduces the dimensionality problem and attains higher classification accuracy than other methods. This method also has the disadvantage mentioned in [15]. Moreover, this method does not depend on any pathological information about the disorder and it could be applied for other neurodegenerative disease as well as other biomarkers.

In order to develop more accurate system, two multivariate methods for feature extraction is presented by Segovia et al.[44] in2012.First method uses GMM to select the ROI. Feature vectors are extracted from the ROI by applying Expectation Maximization (EM) algorithm. Second method uses PLS for calculating score vectors. Experimental results have shown that the GMM method gives small number of features than PLS and outperforms with nonlinear classifier.

Work done by Segovia produces good results and reduces the dimension of feature vectors when compared to other traditional methods VAF and PCA.

Feature extraction based on Neuropsychological and functional measures

There exist several techniques to develop CAD system for AD diagnosis. Most of the proposed techniques analyze neurobiological brain images in order to detect the patterns that classify the AD and a few integrate several imaging modalities to improve the accuracy. In 2014 Fermın Segovia et al.[45] have combined neuro images with neuropsychological scores for CAD based AD diagnosis. Three different techniques like PLS, PCA and ICA are applied to reduce the dimension of the input. Subsequently, SVM classifier is used to discriminate the normal and AD subjects. Results have shown that combining neurophysiologic scores with functional image improves the classification accuracy considerably.

Other feature extraction techniques

In 2009, Salas-Gonezalez et al[47] have used skewness of SPECT image as feature for AD diagnosis. This approach selects the voxels that are present at very low or very high Welch's t-statistic between AD controls focusses. Some features are computed for selected voxels namely skewness, kurtosis, mean and standard deviation. The selected features are engaged as an input for three different classifiers: Multivariate normal model, Decision tree and SVM. This approach gives better performance in terms of accuracy.

Fung et al.[6] in 2007 have presented an approach for AD diagnosis using spatial information. This approach uses most relevant voxel and some areas as a feature vector for classification. Performance of this approach is compared with the Fisher Linear Discriminant and SPM.

SPECT image analysis using moments and SVM is done by Diego et al. [48] in 2009**.**Skewness is evaluated for each 3X3X3 sliding window of the SPECT images. Then, the central pixel is replaced and creates a new 3D image database consisting of skewness in each voxel. Mean and standard deviation of normal controls and AD images are calculated. Welch's t-statistic test is computed for each voxel. This test provides a value which is used to measure the difference between mean AD and mean normal images. Skewness, kurtosis, mean and standard deviation are estimated for chosen voxels. Finally, SVM classifier is used to discriminate between normal and AD subjects. This method yields high accuracy rate in classification task.

Martinz et al.[22] in 2012 have presented Mann-Whitney-Wilcoxon U-test based CAD tool for early diagnosis of AD. This approach has three phases namely voxel selection, feature vector extraction and classification. Mann-Whitney-Wilcoxon U-test is utilized for voxel selection task. Feature vector are selected and extracted by factor analysis. Linear SVM is adopted to classify the images. To evaluate the performance of the approach, the authors have conducted several experiments on two different functional images, viz., SPECT and PET. Results have shown that the proposed method achieves accuracy 92.9% and 93.7% for PET and SPECT images respectively.

In 2013 Andres Ortiz et al.[68] have presented a classification system for normal and AD structural MRI images. Voxels are selected based on their discriminative capabilities by means of FDR. Learning Vector Quantization (LVQ) is used to derive a reduced set of features by projecting the most discriminative WM and GM voxels onto the prototype space. Subsequently, SVM classifier is used to distinguish between normal and AD subjects.

Complete automated CAD tool for diagnosis of AD in early stage from MRI scans using structural features is proposed by Saima farhan et al.[46] in 2014.Volume of GM,WM,CSF and hippocampus size are selected as feature vectors. Four different classifiers namely SVM, Multilayer Perceptron (MLP)[48] and ensemble of classifier based on majority voting is adopted discriminate the normal control and AD patterns. When an integration of all features is considered, SVM and J48 outperform than MLP. Higher classification accuracy is obtained with all classifiers by using left hippocampus as a feature vector alone.

For an accurate classification, feature selection plays the most important role. In 2015 Imène Garali et al [49] have proposed a new feature selection method for AD diagnosis from PET scan. The authors have introduced Separation Power Factor (SPF) to extract the most important features from the image. Then, the selected features are used an input for the SVM to classify the subjects.SPF based approach yields high accuracy than VAF and other region based approaches.

In order to improve the performance of AD diagnosis, in 2013 Ramrez et al.[26] have developed a method based on some image parameters. This method uses first and second order characteristics of coronal, sagittal and transverse section of the brain for AD diagnosis.FDR is applied on the selected features to reduce their dimension. Then, the issues are classified by means of SVM classifier. Experimental results have evidenced that coronal standard deviation and sagittal correlation are the most discriminant image parameters of the AD. This method gives better classification rate than VAF method.

Feature extraction from multi-modality images

AD related to pathlogical amyloid, depositions, structural atrophy metabolic changes in the brain .Recently, multiple biomarkers have been proven to be sensitive to an early diagnosis of AD and MCI [50, 51]. Hypometabolism measurement in the brain is obtained from fluorodeoxyglucose (FDG)-PET used for [55, 56],brain atropy is measured from structural MRI[52-54] and specific proteins can be quantified from CSF measures [54,57,58].Many classification techniques use only one modality for diagnosis of AD and MCI. Recent research has shown that different biomarkers give complementary information for AD and MCI diagnosis [54,59]. For example, MRI and cognitive testing have been used in [60,61], PET and cognitive testing have been used in [62], MRI and CSF have been used in [63,64], FDG-PET, PET and CSF have been used in [65] and MRI, FDG-PET and CSF have been used in [66].

For an accurate and effective diagnosis of AD and MCI, multimodal classification methodology have been proposed by daoqiang zhang et al.[67] in 2011.This approach integrates the MRI, FDG-PET and CSF modality of biomarkers. This methodology uses volumetric features of MRI and FDG-PET images and original values of CSF biomarker as a feature vector. Linear SVM classifier carries out the classification. Results have shown that the multimodal method achieves high classification accuracy than single modality.

In 2011 Chris Hinrichs et al.[69] have presented a multimodality framework for AD diagnosis. They have used Multi-Kernel Learning (MKL) for classification purpose. MKL is designed to deal with multiple data sources while controlling model complexity. SVM classifier is used to distinguish between normal and AD subjects. This approach provides better results than single imaging system in terms of accuracy.

C. Summary and feature comparison

The table 1 shows summarized form of feature extraction and classification methods used for AD diagnosis discussed above. Table 2 presents the list of evaluation metrics used to evaluate each author's method.

Five major and most popular feature extraction techniques are found: PCA, PLS, ICA, GMM and Structural feature. Feature extraction and classification techniques are evaluated based on widely used performance measures such as accuracy, specificity and sensitivity. Any feature extraction technique tries to improve one or more of the measures mentioned above. Most of the proposed techniques try to increase the classification accuracy rate in order to improve the performance. Some techniques also attempt to reduce the dimensionality problem.

It is observed from this literature survey that most of the classification methods compare the results with the very basic models such as VAF, PCA and GMM. The authors do not compare the proposed work with the existing model which are already better than very basic models. Therefore, lot of experimentation is needed to test new approaches with the known better ones instead of simple VAF, PCA and GMM.

III. CONCLUSION

This paper presents a comparative survey of feature extraction, selection and classification strategies for automated identification AD using medical images. Different feature extraction, dimension reduction and classification methodologies are proposed by researchers.

It has been observed that there exist no standard or specific feature vectors that address all issues involved in the diagnosis of AD. For example, some strategies consider sample size problem, sensitivity, accuracy and specificity while some partially or totally ignoring these. Some strategies consider that prediction accuracy is the most important factor while some strategies have used

It is also noted from this survey that most of the strategies compare the experimental results with the very basic methods including VAF, PCA-SVM, GMM-SVM.A variety of them do not compare the proposed methods with the existing methods which are far better than the basic methods.

Table 1. Comparison of feature extraction and classification techniques

Authors	Year	Datasets	Modality	Feature extraction/selection methods	Classifier	Targets
Fung et aal.[6]	2007	ADNI	SPECT	Spatial information	SVM	NC versus AD
Lo´pez et al.[32]	2009	ADNI	PET and SPECT	PCA	Bayesian	NC versus AD
Salas et al.[47]	2009	ADNI	SPECT	Skewess	SVM, Decision tree and multivariate model	NC versus AD
Diego salas et al.[48]	2009	ADNI	SPECT	Mean, standard deviation, skewness and kurtosis	Linear SVM	NC versus AD
Lo´pez et a.[70]	2009	ADNI	SPECT and PET	PCA	Bayesian classifier	NC versus AD
Ramírez et al.[15]	2010	ADNI	SPECT	PLS	Random Forest	NC versus AD
Padilla et al.[42]	2010	ADNI	SPECT	NMF	SVM	NC versus AD
Illán et al.[25]	2010	ADNI	SPECT	ICA	Kernel SVM	NC versus AD
Illán et al.[1]	2011	ADNI	PET	PCA and ICA	Kernel SVM	NC versus AD
Górriz et al.[43]	2011	ADNI	SPECT	GMM-EM	SVM	NC versus AD
Daoquiang et al.[67]	2011	ADNI	MRI, FDG-PET,CSF	Volumetric feature-MRI and FG-PET, Original intensity-CSF	Linear SVM	NC versus AD
Hinrich et al.[69]	2011	ADNI	MRI+ PET	MKL	SVM	NC versus AD
Segovia et al.[44]	2012	ADNI	PET	GMM and SIMLS	SVM	NC versus AD
Ahsan et al.[40]	2012	OASIS	MRI	ICA	PSVM,KNN and ANN	NC versus AD MCI versus AD NC versus MCI
Martinez et al.[22]	2012	ADNI	SPECT and PET	Factor analysis	Linear SVM	NC versus AD
Rosa Chaves et al.[29]	2012	ADNI	SPECT and PET	NMSE-PLS-LMN	SVM,LMNN using Euclidean	NC versus AD
Segovia et al.[5]	2013	ADNI	SPECT	PLS and out-of – Bag error	SVM	NC versus AD
Ramírez et al.[26]	2013	ADNI	SPECT	coronal standard deviation , the sagittal correlation and FDR	SVM-RBF	NC versus AD
Andres Ortiz et al.[68]	2013	ADNI	MRI	LDR	LVQ-SVM	NC versus AD
Saima Farha et al.[46]	2014	OASIS	MRI	GM,WM,CSF and hippocampus size	SVM,MLP,J48 and ensemble of classifier	NC versus AD
Fermı´n Segovia et al.[45]	2014	ADNI	PET Images and Neuropsychologic	PLS,PCA and ICA	SVM	NC versus AD

			al Test			
Ben ahmed et al.[33]	2015	ADNI and Bordeaux -3City	MRI	Circular harmonic functions and PCA	SVM	NC versus AD MCI versus AD NC versus MCI
Khedher et al.[34]	2015	ADNI	MRI	PLS and PCA	SVM-RBF	NC versus AD MCI versus AD NC versus MCI
Imène Garali et al [49]	2015	NaN	PET	Separation Power Factor	SVM	NC versus AD
Deepika et al.[35]	2016	NaN	MRI	PLS,PCA and Haralick texture	SVM	NC versus AD

Table 2. Performance measures

Authors	Year	Accuracy	Specificity	Sensitivity	Performance
Fung et aal.[6]	2007	NaN	90.9	84.4	This method is better than FLD and SPM
Lo´pez et al.[32]	2009	88.6-SPECT 98.3-PET	NaN	NaN	For getting good classification this method is best
Salas et al.[47]	2009	98	NaN	NaN	Reduced dimensionality problem
Diego salas et al.[48]	2009	99	NaN	NaN	Improved performance than FDR and PCA-SVM.
Lo´pez et a.[70]	2009	91.21-SPECT 98.33-PET	NaN	NaN	It reduces drastically the feature space dimension
Ramírez et al.[15]	2010	96.9	92.7	100	Better than PCA-Bayesian classifier, PCA-SVM,GMM-SVM and VAF
Padilla et al.[42]	2010	94.9	92.8	96.4	This strategy yields better accuracy than VAF and PCA-SVM
Illán et al.[25]	2010	91.14	92.68	89.47	Improved performance than VAF
Illán et al.[1]	2011	88.24	88.64	87.70	It is able to identify the characteristic of AD in MCI subjects
Górriz et al.[43]	2011	89.69	90.24	89.24	It is able to reduce the dimensionality problem
Daoquiang et al.[67]	2011	93.2	93.3	93	This method gives best result than single modality
Hinrich et al.[69]	2011	87.6	93.8	78.9	It achieves high accuracy
Segovia et al.[44]	2012	90	92.98	90.50	GMM based method yields higher accuracy
Ahsan et al.[40]	2012	68-KNN,53-ANN,60.65-PSVM	NaN	NaN	KNN performs well than PSVM and KNN
Martinez et al.[22]	2012	93.7-SPECT, 92.9-PET	95.1-SPECT, 91.1-PET	92.9-SPECT, 94.7-PET	This method reduce the dimensionality problem and better performance than VAF
Rosa Chaves et al.[29]	2012	92.78-SPECT, 90.67-PET	95.12-SPECT, 93.33-PET	91.07-SPECT, 88-PET	Stable and robust approach
Segovia et al.[5]	2013	91.6	91.1	92.7	This strategy provides best results than VAF,PCA,GMM
Ramírez et al.[26]	2013	90.38	86.96	93.10	This strategy is effective than VAF
Andres Ortiz et al.[68]	2013	91	88	90	This approach provides better result.
Saima Farha et al.[46]	2014	93.75	100	87.5	It reduces computation time
Fermı´n Segovia et	2014	89	85	92.31	Improved accuracy rate

al.[45]					
Ben ahmed et al.[33]	2015	83.77	88.2	79.09	This approach does not require the intervention of the clinician and low computation time
Khedher et al.[34]	2015	88.49	91.27	85.11	PLS algorithm is effective than PCA
Imène Garali et al [49]	2015	95.07	NaN	NaN	Less computation time and reduced feature vector
Deepika et al.[35]	2016	88.49	NaN	NaN	Improved classification accuracy rate

IV. REFERENCES

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