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A robust machine learning approach for multiclass Alzheimer's disease detection using 3D brain magnetic resonance images

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ABSTRACT

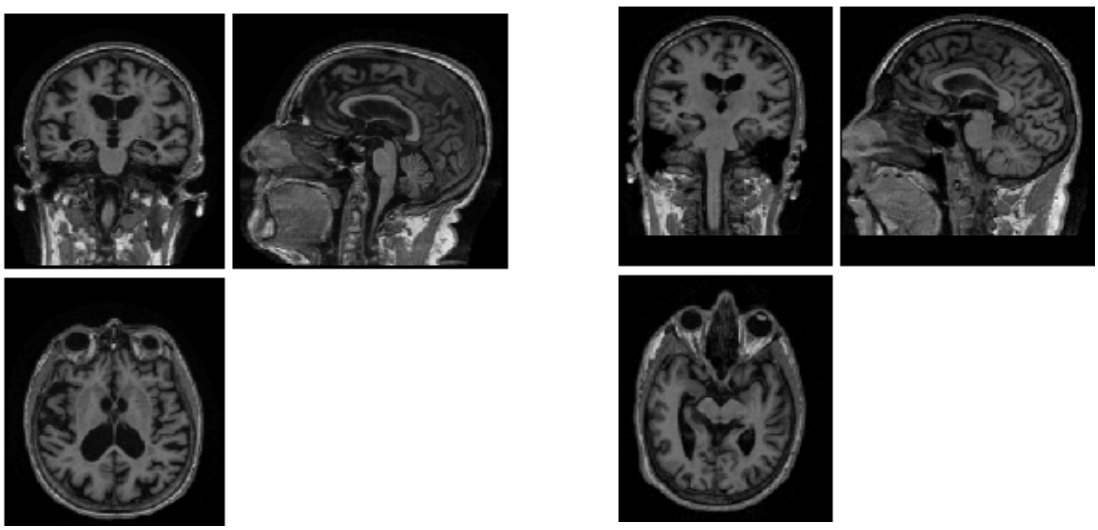
Alzheimer's disease (AD), a progressive dementia, is the neurodegenerative disorder that worsens memory and mental capabilities mostly in aged people. Currently, clinical and psychometric assessments are being used to diagnose the disease in patients. In clinical procedures, 3D Magnetic Resonance Image qualitative parameters are analyzed to identify the abnormality in brain shape, volume, texture, and cortical thickness. This paper presents a robust approach for categorizing 3D MR images into multiple stages of AD using hybrid features viz., Gray Level Cooccurrence Matrix (GLCM), 3D Scale and rotation Invariant Feature Transform (3D SIFT), Histogram of Oriented Gradients-Three Orthogonal Planes (HOG-TOP), and Complete Local Binary Pattern of Sign and Magnitude-Three Orthogonal Planes (CLBPSM-TOP). The proposed algorithm is validated using Open Access Series of Imaging Studies (OASIS) datasets to classify the subjects into AD, Mild Cognitive Impairment (MCI), and Cognitive Normal (CN) categories using various classifiers. Moreover, this approach is also evaluated and compared with the state-of-the-art approaches. 87.84% diagnosis accuracy is achieved with Ensemble classifier using hybrid features to diagnose the severity of AD. This approach also outperforms the majority of these techniques in key parameters, namely, accuracy, precision, recall, and F1-score.

Keywords: GLCM; 3D SIFT; HOG-TOP features; CLBPSM-TOP; Alzheimer's disease (AD); 3D magnetic resonance image (3D MRI).

INTRODUCTION

Dementia is a word for the wide category of progressive brain disorders. According to World Alzheimer's Report 2018, 50 million patients were registered with dementia, where this number is expected to rise to 152 million by 2050 all over the world. Alzheimer disease (AD) is the most prevalent cause and can be diagnosed in 70–80% cases of age-related dementia. This disease is caused by development of β-Amyloid plaques and neurofibrillary tangles, which leads to demise of neurons in large count especially in neocortex and hippocampus parts of brain. Figure 1 shows the raw volumes of AD and Cognitive Normal (CN) subjects. The destruction of neuron synaptic function affects the cognitive skills of a patient. So, early identification of this disease helps provide essential future treatment.

Psychometric and Clinical procedures are jointly used to assess the disease progression. Under Clinical tests, Clinical Dementia Rating (CDR) is measured to describe the cognitive performance in terms of memory, orientation, judgment, problem solving, and personal care. Due to huge uncertainty in assessment of AD severity, it is essential to include an effective biomarker, which describes the characteristics of disease. Magnetic Resonance (MR) Image is used to quantify the atrophied portions of brain and also provide high spatial resolution morphological data, which is a critical biomarker to diagnose neurological disorders.



(a) (b)

Figure 1. Raw MR volumes a) AD b) CN.

Computer based techniques (Gad et al.) acquire the MR volumes from database, extract the effective discriminative features from atrophied hippocampus and subcortical regions of brain, and classify them into CN, MCI, and AD using classy algorithms. Many diagnosis studies focused on various qualitative features and classifiers used for labelling of MR volumes into stages of AD.

LITERATURE REVIEW

Khadim et al. had extracted GLCM features, which were used to discriminate between normality and abnormality in brain. An unsupervised learning, that is, K-Nearest Neighbors (KNN) approach, is trained to classify these features. Training and testing were carried out on 40 images, which include CN and AD. Experimental outcomes had shown that the classifier performs well in gray level feature spaces and achieved accuracy of 86.6%. The authors demonstrated that KNN and GLCM together produce this acceptable accuracy.

Daliri et al. had worked on 98 Normal and 100 AD subjects for an automatic diagnosis system for Alzheimer's disease from brain MR images using Scale-Invariant Feature Transform (SIFT). The characteristics extracted from 2D slices were combined to obtain 3D MRI features and classified with Support Vector Machine (SVM). The results of this technique used for AD diagnosis showed 86% accuracy for the subjects aged from 60 to 80 years old with mild AD.

Mondal et al. conferred a novel methodology for brain atlas generation based on dissimilar and repeatable consistent key-points in the brain volumes of population. 3D-SIFT is used to figure out the key-points within the volumes. Whole brain volume is considered in this approach to generate atlas. These invariant points are used for an early diagnosis of AD. Investigation outcomes illustrate an acceptable performance of the proposed approach.

Histogram of Oriented Gradients from Three Orthogonal Planes (HOG-TOP) features (Sarwinda et al.) can be used to generate dynamic textures from 270 MRI images of two labels, which include normal and abnormal brains. Using these features, the authors achieved 95% accuracy and 96% sensitivity, which outperforms state-of-the-art approaches.

Local binary patterns (LBP) (Ojala et al.) are a texture descriptor for contrast in an image. It is a very simple and efficient texture operator that generates a binary number obtained by tagging the pixels of an image by thresholding the neighborhood. Oppedal et al. used these features to discriminate the abnormality in brain MR images. An enhancement was proposed by Sarwinda et al. to achieve the best key evaluation parameters with the aid of Advanced LBP (ALBP) features.

A classification algorithm for diagnosis of Alzheimer's stages is presented by Altaf et al. using hybrid features. The proposed approach has used GLCM, grey matter proportion, and white matter volume to cerebrospinal volume ratio along with clinical features for classification. The investigations indicate that using clinical features (Sarwinda et al.) along with texture-based features can enhance classification accuracy in significant manner. This method achieves enhanced accuracy for binary categories and significant accuracy for multiclass classification.

These research articles present various procedures for feature extraction and classification for AD severity diagnosis. Even though the researchers proposed many techniques for detection of AD stages, there is a huge scope for more precise diagnostic mechanism to meet the demand of present health monitoring systems.

METHODOLOGY

The proposed hybrid approach for AD diagnosis consists of data acquisition, preprocessing, feature extraction, and classification and evaluation phases. MR data sets were acquired from Open Access Series of Imaging Studies (OASIS) and normalized using SPM toolbox in MATLAB environment. Textural analysis is the key procedure to detect the abnormal features from human brain. The features that replicate the abnormality are extracted using various techniques. Once the four sets of features are extracted (Mathew et al.), they are combined together, and their dimensionality is reduced with feature dimensionality reduction process. The feature descriptors are then augmented and supplied to the classifier to diagnose the severity of AD.

After classifying, the performance of this technique is evaluated using well-established standards. The following subsections describe the inner details of all phases involved in the diagnosis approach. The workflow for this algorithm is presented in Figure 2.

Data Sets

The MRI volume data sets were acquired from OASIS (Daniel et al.) in a way that it contains all the subjects AD, CN, and MCI categories with mean age of 58 years. 144 AD, 120 CN, and

110 MCI subjects had been retrieved from database comprising MRI with T1-weighted scan generated from 1.5 Tesla system. MR volumetric data demographic characteristics are illustrated in Table 1.

Table 1. Characteristics of data set.

Attribute	CN	MCI	AD
Age	55	60	62
Sex	60% male	40% male	30% male
MMSE	29	24	21
CDR	0	0.5	0.5-1

Format: Mean details are presented

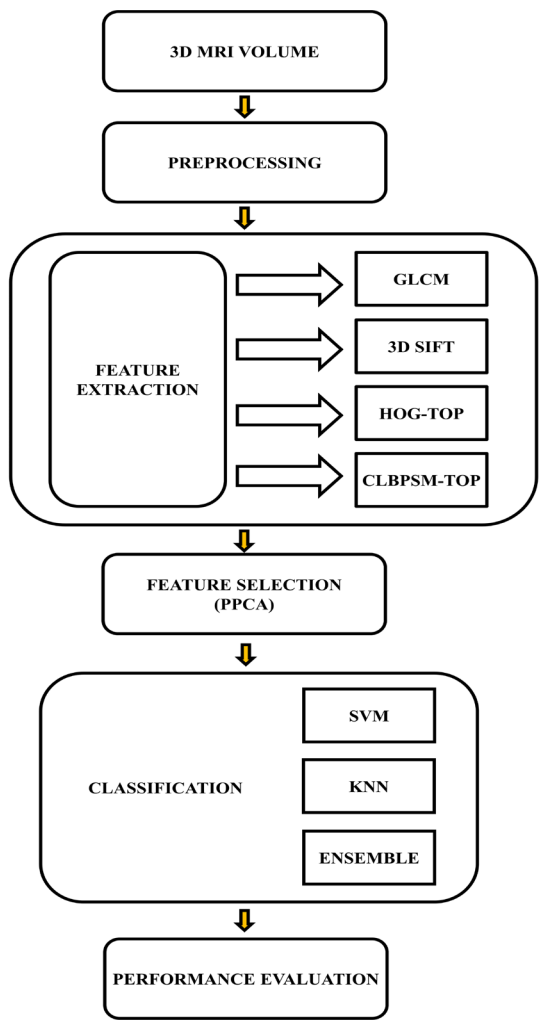
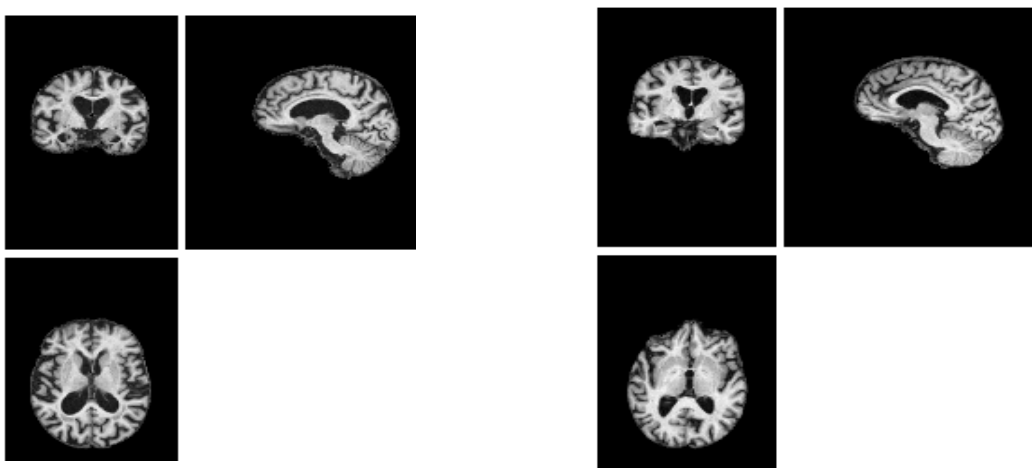


Figure 2. Workflow of AD diagnosis.

Preprocessing

Once the MR volumes are acquired from database, they are subjected to experience through preprocessing phase to make them ready for further processing since noise and wrong alignment of MR slices may lead to inaccurate assessment. Preprocessing of MR image primarily includes several phases, like Realignment, Normalization, Segmentation, and Smoothing. The first three tasks were employed using Statistical Parameter Mapping (SPM12) toolbox in MATLAB 2018b.

Finally, preprocessing can be completed by removal of speckle noise in skull stripped MR volumes using 3D median filters. The skull stripped and smoothed MR brain volumes of Figure 1 are shown in Figure 3. Volumetric information is now enriched and set for classification.



(a) (b)

Figure 3. Preprocessed volumes a) AD b) CN

Feature Extraction

The strategy of feature extraction phase is to derive more effective and discriminative textural feature descriptors from preprocessed data. Since the performance of any classifier depends on features extracted during training, they should replicate the features of disease to be diagnosed. The hybrid features are formed with four sets of powerful features presented in the following subsections.

Gray Level Cooccurrence Matrix

Texture is one of the most discernible appearances of an image. It is distinguished by the spatial allocation of gray levels in a community. GLCM is one of the best statistical techniques (Haralick et al.) that explores gray level spatial dependence of texture. In this research work, five features are extracted from axial views of MRI volume, namely, energy, contrast, entropy, correlation, and homogeneity. Using the normalized GLCM matrix P(x,y), the textural features are computed with the following mathematical formulae:

$$Energy = \sum_{x,y}(P(x,y))^2 \quad (1)$$

$$Contrast = \sum_{x,y}(x-y)^2 \log P(x,y) \quad (2)$$

$$Entropy = -\sum_{x,y} P(x,y) \log P(x,y) \quad (3)$$

$$Correlation = \sum_{x,y} \frac{(x-\mu_x)(y-\mu_y)\,P(x,y)}{\sigma_x \sigma_y} \quad (4)$$

$$Homogeneity = \sum_{x,y} \frac{P(x,y)}{1+(x-y)^2} \quad (5)$$

Since all these parameters replicate the characteristics, namely, homogeneousness, complexity, and local variations in gray levels of 2D slice of brain 3D MR volume, they could be used as discriminative features for AD diagnosis. So, by using equations 1, 2, 3, 4, and 5, these statistical parameters are extracted and merged to form a vector.

3D SIFT based features

It is necessary to extract the features from the training data set to detect AD even under image scale variations. 3D SIFT is an optimal transform (Lowe et al.) developed for detecting and describing the features to detect abnormality of brain. This algorithm works by detecting 128 key points from MRI volume at which local gradient direction intensities statistics were collected to produce summarized description of local structures around each key point in a local neighborhood. Each key-point calculated using 3D SIFT is characterized by a 128-dimensional descriptor that includes its 3D coordinate position. Due to the huge number of key points in 3D, this method is computationally rigorous to match key points of any two MR volumes. To facilitate this, a Model Based MRI Alignment (MBMRIA) is proposed by Mondal et al.

Histogram of Oriented Gradients-Three Orthogonal of Planes (HOG-TOP)

Histograms of oriented gradients (HOGs) were initially suggested for human detection. HOGs can retrieve and describe object deformations effectively due to their high sensitivity. In this work, HOGs are extended to compute oriented gradients (Nisha et al.) on three orthogonal planes of MR volumes. Feature vector will be generated for each plane (Coronal, Sagittal, and Axial) that represents the histogram. Once the histograms are generated for three planes, these three feature vectors are generated for all three planes; histograms are merged into one to represent a new feature vector for MR volume, which consists of 243 feature bins for the whole MR volume.

Complete Local Binary Pattern of Sign Magnitude-Three Orthogonal Planes (CLBPSM-TOP)

Local Binary Patterns are visual descriptors in the computer vision. Since these features are used to obtain the feature extraction on 2D brain slice, an advanced approach is needed to be implemented

on MR brain volumes. As an advanced Local Binary Pattern, Complete Local Binary Pattern of Sign and Magnitude Three Orthogonal of Planes (CLBPSM-TOP) was projected Sarwinda et al. These features are acquired

from the combination of the Complete Local Binary Pattern of Sign value (CLBPS) and Complete Local Binary Pattern of Magnitude value (CLBPSM). Moreover, CLBPSM is obtained for all 2D slices of brain volume in each plane (Coronal, Sagittal, and Axial). In order to obtain the whole CLBPSM histogram, histograms of the three planes are pooled into one and are considered as the input feature vector, and this approach is recognized as CLBPSM-TOP. 300 feature bins are extracted using this approach for entire MR volume.

The augmentation of all these 676 features yields an efficient representation of discriminative features for AD diagnosis. Because the feature dimensionality is the critical issue in classification, some features are carefully chosen with feature selection approach.

Feature Selection

The extracted features should be augmented (Nanni et al.) since these features are not appropriate for classification. The main aim of feature selection (Yang et al.) is to optimize the feature vectors that replicate more impact on AD diagnosis. For that, Probabilistic Principal Component Analysis (PPCA) is used to reduce the dimensionality (Tipping et al.) of feature vectors and analyze data through a lower dimensional latent space. The PPCA approach considers that each sample is derived from the following model. Eq. 6 is useful in mapping a feature vector from a high-dimensional space into low-dimensional space.

$$X = Wy + \varepsilon \tag{6}$$

where y is a low dimensional hidden space vector, W is a weight matrix, and ε is the noise term. Here, the generated samples X are alike principal components, which can be retrieved from maximum likelihood estimation. In our case, the augmentation of all features including GLCM, 3D-SIFT, HOG-TOP, and CLBPSM-TOP yields 676-dimensional features for each feature vector.

Using PPCA approach, the top 90 discriminative features are selected per each feature vector for classification purpose.

Multistage Classification

After selection of features from MR brain volumes using PPCA technique, proper training must be given to a classifier to diagnose the severity of AD. Support Vector Machine (SVM), K-Nearest Neighbors (KNNs), and Ensemble algorithms are used for robust AD diagnosis.

Support Vector Machine (SVM)

SVMs are successful approaches for binary classification, proposed by Vapnik, to provide good generalization ability. Training should be given to SVM with appropriate kernel function to fit the best hyperplane for robust classification of subjects into AD, MCI, and CN. Unlabeled MR volumes could be classified with the support of hyper plane fitted during training.

K-Nearest Neighbors (KNN)

KNN algorithm is a well-known and efficient classifier to classify MR volumes samples in unsupervised style. It finds the test sample class by determining its 'k' neighbor features in terms of Euclidean distance (Gayathri et al.). This distance is defined below with equation (7).

$$d_E(x, x_i) = \sum|x - x_i| \tag{7}$$

Here, $x\ and\ x_i$ are test and training data samples, respectively. Testing sample class is determined based on the minimum distance K samples.

Ensemble

In order to increase the clustering and classification performance, a combination of classifiers is proposed in various research studies. Ensemble classifiers (Dietterich et al.) use several models rather than one model to classify the samples. Due to their flexibility and classification performance, these classifiers got wide popularity. In the presented approach, an advanced ensemble method, that is, boosting, is used to enhance the accuracy of both SVM and KNN classifiers.

RESULTS AND DISCUSSION

This proposed model was implemented in MATLAB 2018b environment in a computer with i3 processor with 1.7 GHz speed, 4GB RAM, and Windows 8.1 pro-operating system. The above discussed approaches were validated using standard cross validation for reliable performance.

To evaluate the performance of the classifiers, the data sets were primarily divided into 80% and 20% for training and testing purposes. Among the MR volumes acquired from OASIS, 116 AD subjects, 96 CN subjects, and 88 MCI subjects were used for training purpose. SVM, KNN, and ensemble classifiers were carefully trained to validate the effectiveness of feature extraction. 28 AD, 24 CN, and 22 MCI subjects were utilized for testing purpose. All these classifiers were cross-validated using fivefold, where complete data set is partitioned equally into groups with five samples, algorithm was trained for fourfold, and testing is implemented on fivefold.

Even though SVM is trained with several kernel functions like linear, quadratic, cubic, and Gaussian, the linear kernel had produced optimal results. KNN classifier was trained for k=4 neighbors using Euclidean distance as a significant metric. Ensemble technique was accomplished using boosting technique, that is, AdaBoost controller. Once the SVM classifier is trained with linear kernel with proposed features, the following confusion matrix presented in Table 2 is obtained for AD diagnosis. By applying the testing data set, 22 were classified accurately among 28 AD subjects. Within 24 CN subjects, 19 were classified accurately, and 20 subjects were diagnosed properly among 22 MCI subjects.

Table 2. Confusion Matrix for SVM classifier.

	AD	MCI	CN
AD	22	4	2
MCI	1	20	1
CN	1	4	19

Table 3. Confusion Matrix for KNN classifier.

	AD	MCI	CN
AD	23	4	1
MCI	2	20	0
CN	1	4	19

The KNN classifier with k=4 neighbors yielded the confusion matrix specified in Table 3 for AD diagnosis. Among 28 AD test subjects, 23 were classified accurately. Within 24 CN test

subjects, 19 were categorized correctly, and 20 subjects were diagnosed appropriately among 22 MCI subjects. The confusion matrix obtained for AD diagnosis using hybrid features along with Ensemble approach is described in Table 4. In testing, among 28 AD subjects, 25 were classified correctly. Within 24 CN subjects, 20 were categorized perfectly, and 20 subjects were diagnosed among 22 MCI subjects.

Table 4. Confusion Matrix for Ensemble approach.

	AD	MCI	CN
AD	25	2	1
MCI	1	20	1
CN	1	3	20

Performance measures were evaluated for all classifiers in terms of Accuracy, Precision, Recall, and F1-Score using equations 8, 9, 10, and 11. By studying the performance of these models, it is observed that ensemble technique classifies the MR volume subjects effectively and produces robust performance in multiclass AD diagnosis. The final accuracy is determined by averaging the accuracies of all predictions made over the population.

$$Accuracy = \frac{TP+TN}{TP+FP+TN+FN} \quad (8)$$

$$Precision = \frac{TP}{TP+FP} \quad (9)$$

$$Recall = \frac{TP}{TP+FN} \quad (10)$$

$$F1-Score = \frac{2*TP}{2*TP+FP+FN} \quad (11)$$

Here, TP, TN, FP, and FN are true positive, true negative, false positive, and false negative estimations. The above metrics for this approach are compared with the results of Altaf et al. and Mondal et al., where GLCM and 3D SIFT individual features are employed for AD diagnosis, respectively. The hybrid features with SVM classifier

achieved the accuracy of 82.43%. With KNN classifier, accuracy is enhanced to 83.78%. Accuracy is also boosted to 87.84% by implementing ensemble approach. Detailed comparison of results is given in Table 5.

Table 5. Comparison of evaluation metrics for proposed technique with preexisting method

	Features		Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)
Altaf et al.	GLCM		79.8	-	-	-
Mondal et al.	3D SIFT		70	-	-	-
Proposed	**Hybrid features**	**SVM**	**82.43**	**83.00**	**83.00**	**82.67**
		KNN	**83.78**	**84.00**	**84.66**	**83.67**
		Ensemble	**87.84**	**87.66**	**88.00**	**87.66**

Graphical representations of the above comparison are illustrated in Figure 4 and Figure 5. Visually, it is observed that hybrid features with ensemble technique produced optimal results in comparison with individual features. Figure 4 demonstrates that the hybrid features produce good accuracy than individual features.

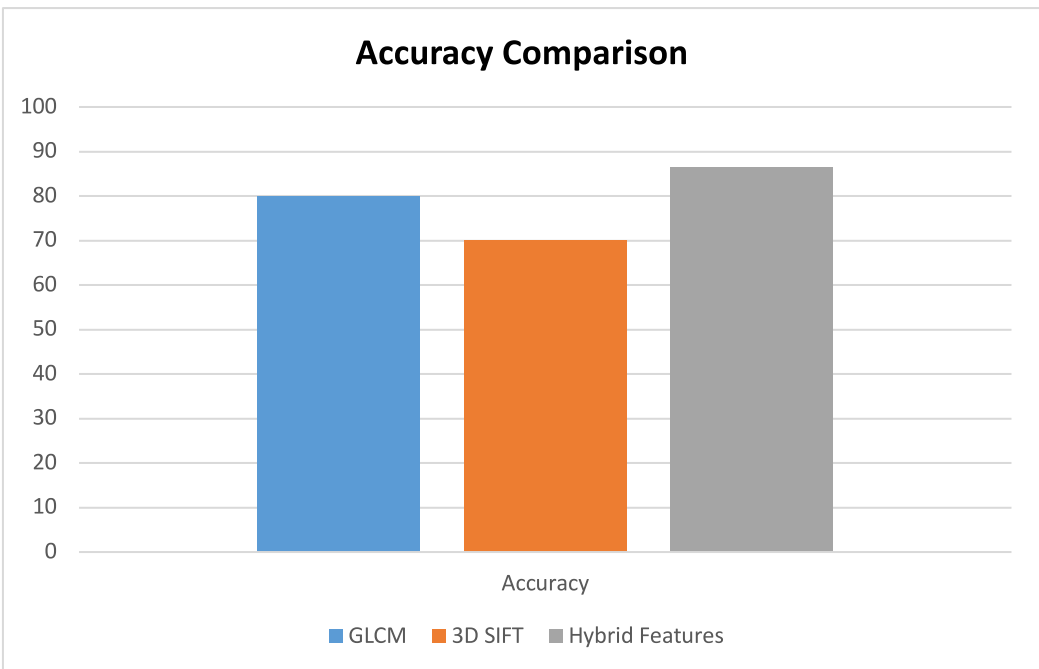


Figure 4. Comparison of features.

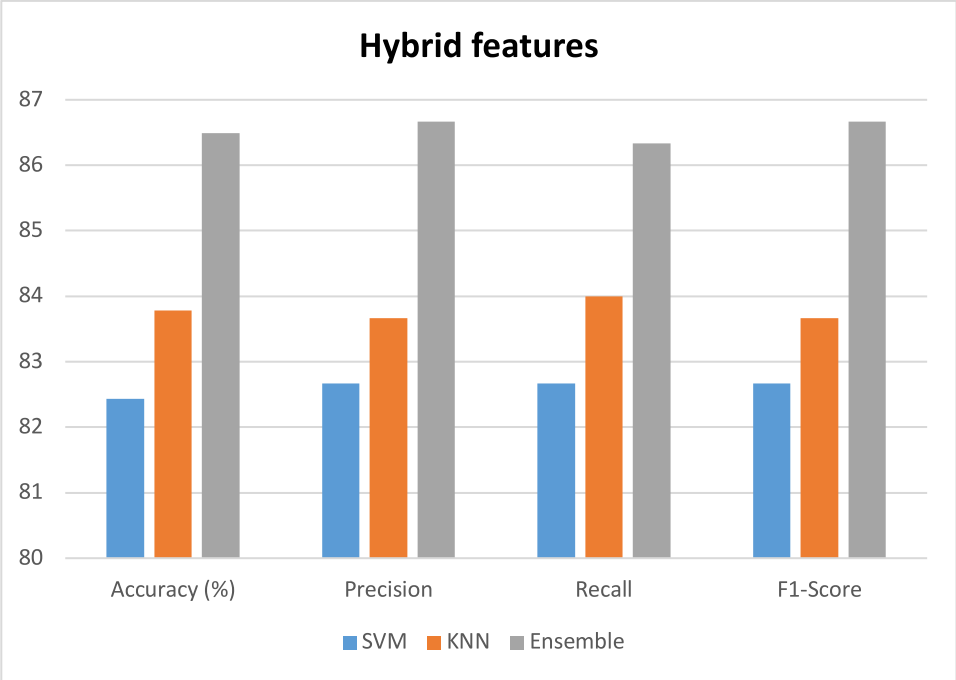


Figure 5. Graphical representation of evaluation metrics.

The hybrid features are very powerful features because they could retrieve and describe object deformations effectively due to the high sensitivity of HOG vectors and CLBPSM over three orthogonal planes.

Figure 5 illustrates the performance metrics of three different classifiers over hybrid features. Among three classifiers, the ensemble approach using boosting technique along with augmented features yields outstanding results than individual SVM and KNN models in multiclass AD diagnosis. Diagnosing accuracy can be further improved with rigorous training of classifiers over a huge number of MR volumes along with supplementary clinical features.

CONCLUSION

3D MR volume texture features based Alzheimer's disease diagnosis is a challenging and everlasting issue in healthcare especially for multiclass diagnosis. 3D texture feature extraction is an important step in discriminating well in machine learning systems when the images are three-dimensional like many MR volumes. This research article presents a hybrid approach for multiclass AD diagnosis using MR volumes retrieved from OASIS database. The visual features are extracted from structural 3D MR brain volumes with GLCM, HOG-TOP, SIFT, and CLBPSM-TOP approaches in an effective manner. Since the dimensionality of features is the main issue in classification, PPCA approach is employed to select top quality features from the collection for classification. The combination of these features with SVM, KNN, and ensemble classifiers produced auspicious results over the preexisting state-of-the-art techniques, which used the individual features. The achieved accuracy was 87.84%, and the computational speed of the proposed hybrid features with SVM, KNN, and ensemble classifiers is reasonably acceptable and can offer the worthy classification results with good performance for multiclass in detecting Alzheimer's disease. Despite the fact that this approach is classifying several stages of AD, it cannot efficiently diagnose the transitional phases between CN and MCI, that is, progressive MCI and stable MCI, to enable the early detection of Alzheimer's disease.

FUTURE WORK

For more accurate future diagnosis, an efficient optimization technique along with more data sets with additional clinical features can be used for training the diagnosing system for multiclass AD diagnosis. In addition, correlation analysis can be performed between texture features and cognition because that can improve the clinical work.

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