Towards the identification of Parkinsons Disease using T1 MR Images

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Abstract. Parkinsons Disease (PD) is one of the most common type of neurological disease which is caused by progressive degeneration of dopaminergic neurons in the brain. Even Though there is no fixed cure for this neurodegenerative disease but the earlier diagnosis result the earlier treatment which could help to the patients to have better life quality. Neuroimaging has been remarkably used for diagnosing the neuro disease which Magnetic Resonance Imaging (MRI) is one of the most popular one because it is a non-invasiveness method that gives the high resolution Images. In this paper, the goal is using MR Images for automatically diagnosing the PD. Basically, the proposed method has three main steps : 1) Preprocessing 2) Feature Extraction 3) Classification. The Fressurfer library is used for the first and second step. In the classification part, three main types of the classifier including Logistic Regression (LR), Random Forest (RF) and Support Vector Machine (SVM) are applied and their classification ability is compared. The Parkinsons Progression Markers Initiative (PPMI) data set is used for evaluation of the proposed method. The proposed CAD system prove promising ability for assisting to diagnose the PD.

1 Introduction

Parkinson's Disease (PD) is the second important neurodegenerative disease after Alzheimer's Disease (AD) which expose to middle age and elderly people. The statistical information presented by Parkinsons News Today [1] showing that an estimated seven million to 10 million people worldwide have Parkinsons disease. PD is provoked by progressive loss of dopamine generating neurons in the brain which causes to two types of symptoms including motor and non-motor. The motor symptoms are bradykinesia, muscles rigidity, tremor and abnormal gait [2] whereas non-motor symptoms show mental disorders, sleep problems and sensory disturbance [3]. Even Though, there are some medical methods for diagnosing and progress determination of PD but the results from these experiments are subjective and is highly depend on the expertise of the clinicians. On the other hand, most of them are expensive and is time consuming for the patients [4]. Neuroimaging techniques has remarkably improved the diagnosis of neurodegenerative disease. There are different types of neuro imaging techniques which Magnetic Resonance Imaging is one of the most popular one because it's

a cheap and non-invasiveness method which has the ability to present high resolution images. The people with PD show their symptoms when they lose almost 80% of their brain dopamine [5]. All of these facts prove the urgent need of having a Computer aided diagnosis (CAD) system for automatically detection of this type of disease which is a challenging process. These decades, machine learning has shown remarkable results in the medical image analysis field. The proposed CAD system in neuro disease diagnosis use different types of imaging data including Single-photon emission computed tomography (SPECT) (prashanth et al [6]), DTI, positron emission tomography (PET)(Loane and Politis [7]) and MRI. In this study, the goal is to utilize structural MRI (sMRI) for developing automated CAD for early diagnosis of PD. Focke et al [8] propose a method for PD classification using MR Images. The proposed method in [8] is used Gray Matter (GM) and White Matter (WM) individually with SVM classifier. The voxel-based morphometry (VBM) has been used for preprocessing and feature extraction. The reported results show poor performance 39.53% for GM and 41.86% for WM. In [9] Babu et al, propose a CAD system for diagnosing of PD. Their method have three general steps : feature extraction, feature selection and classification. In the first part the Voxel Based Morphometric (VBM) is used over GM to construct feature data. For the feature selection, recursive feature elimination (RFE) has been used to select the most discriminative features. In the last step, projection based learning and meta-cognitive radial basis function has been used for classification which resulted 87.21% accuracy. The potential biomarker for PD is identified as superior temporal gyrus. The limitation in this work is that VBM is univariate and RFE is computationally expensive. Salvatore et al [9], propose a method that is used PCA for feature extraction. The PCA has been applied on normalized skull stripped MRI data. Then SVM is used as the classifier which gives 85.8% accuracy. Rana et al [10] have done feature extraction over the three main tissues of the brain consist of WM, GM and CSF. Then they have used t-test for feature selection and in the next step SVM for classification which result 86.67% accuracy for GM and WM and 83.33% accuracy for CSF. In their other work [11], graph-theory-based spectral feature selection method is applied to select a set of discriminating features from whole brain volume. A decision model is built using SVM as a classifier with leave-one-out cross-validation scheme which result 86.67% accuracy. The proposed method in paper [4], is not focused on just individual tissues (GM,WM and CSF) but it considers the relationship between these areas because the morphometric change in one tissue might affect the other tissues. Thus, in this paper a CAD system is designed based on the fused feature descriptor (FFD) which consider the tissues features and the features related to their relationship. $3D$ LBP has been used as a feature extraction tool which could produce structural and statistical information. After that, minimum redundancy and maximum relevance with t-test are used as feature selection methods to get the most discriminative and non-redundant features. At the end, the SVM is used for classification which give 89.67% accuracy. In [13], the low level features (GM, cortical volume, ..) and the high level features (region of interest (ROI) connectivity) are combine to

do multilevel ROI feature extraction. Then filter and wrapper feature selection method is followed up with multi kernel SVM to achieve 85.78% accuracy for differentiation of PD and healthy control (HC) data. Adeli et al [14] propose a new joint feature-sample selection (JFSS) procedure, which jointly selects the best subset of most discriminative features and best sample to build a classification model. They have utilized the robust regression method and further develop a robust classification model for designing the CAD for PD diagnosis. Experimental results on both synthetic and publicly available PD datasets show promising results.

In this paper, a CAD is presented for diagnosing of PD by using MR T1 Images. The general steps of the proposed method is shown in Fig.1 including preprocessing, feature extraction and classification.

The remaining sections of this paper are structured as follows: Section 2 and 3 covers materials and methods, which provides details of the dataset, preprocessing and the proposed method for PD classification. The experimental results and discussion are provided in Section 4. Finally, Section 5 presents the conclusion.

2 Data Set

The data used in the preparation of this article is the T1-weighted brain MR images which is obtained from the PPMI database `www.ppmi-info.org/data`. For up-to- date information on the study, please visit `www.ppmiinfo.org`. PPMI is a landmark, large-scale, international and multi-center study to identify PD progression biomarkers [15]. The data that is used in our study contain the original T1 MR Image of 598 samples with 411 PD and 187 Control. Furthermore, it consists demographic or clinical information about age and sex of the subjects. The summary of the data base information are presented in Table 1. Based on the demographic information in this table, the balance of dataset is presented for the two type of classes which are Parkinson disease (PD) and healthy control (HC) .

Table 1: Demographics of the PPMI

Data Type	**Class**		**Sex**		**Age**		
	PD	**HC**	**F**	**M**	**(25-50)**	**(50-76)**	**(75-100)**
Number of Subjects	411	187	217	381	81	472	45

3 Proposed Method

The overview of our proposed method is presented in Fig.1 which is shown that there are 3 general steps including: 1- Preprocessing 2- Feature Extraction 3- Classification. In the next parts, each step is explained by detail. The proposed CAD system goals are as follow:

1. Extract the volume based features from the MR T1 images using the automated surface-based analysis package FreeSurfer.
2. Comparing the capability of different type of classifier for diagnosis PD.

Fig. 1: The general framework of the proposed methods.

3.1 Preprocessing

Preprocessing is one of the essential step in designing the CAD system which provides informative data for the next step analysis. In this paper, for achieving the volumetric information of the MRI subjects, several preprocessing steps have to be done. Freesurfer image analysis suite have been used in this study for performing preprocessing over the 3D MRI data. FreeSurfer is a software package for the analysis and visualization of structural and functional neuroimaging data from cross-sectional or longitudinal studies. It is developed by the Laboratory for Computational Neuroimaging at the Athinoula A. Martinos Center for Biomedical Imaging [16]. The FreeSurfer pipeline performs cortical reconstruction and subcortical volumetric segmentation including the removal of non-brain tissue (skull, eyeballs and skin), using an automated algorithm with the ability to successfully segment the whole brain without any user intervention [17].FreeSurfer is the structural MRI analysis software of choice for the Human Connectome Project which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/). In total 31 preprocessing steps has been done by using FreeSurfer which some of them are shown in Fig.2.

There are two types of failure in preprocessing step which can be categorized to hard failure and soft failure. The hard failure is related to the subjects that preprocessing is not successfully done for them and the soft failure is related to the subjects that are preprocessed but there are some problem in the results of preprocessing. Out of 568 subjects MRI images, 388 images successfully preprocessed. Other images excluded from the dataset due to poor quality of the original image or unknown CDR label.

3.2 Feature Extraction

After doing the preprocessing using FreeSurfer, a list of volume based features are extracted from the different regions of the brain. These features are captured from the segmented regions which resulted from brain parcellation using

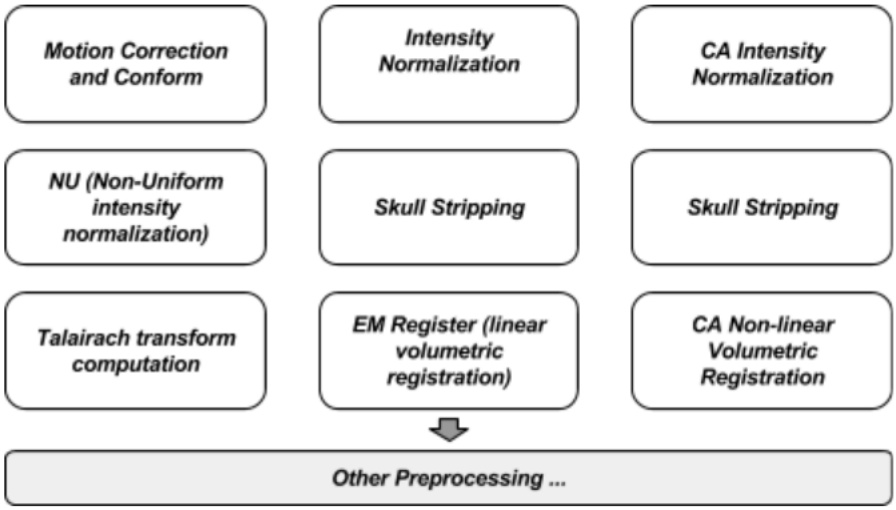


Fig. 2: Preprocessing steps

FreeSurfer. The collected features include left and right hemisphere of the brain which some of them are listed as below:

1. Left and right lateral ventricle
2. Left and right cerebellum white matter
3. Cerebrospinal fluid (CSF)
4. Left and right hippocampus
5. left and right hemisphere cortex
6. Estimated total intra cranial (eTIV)
7. left and right hemisphere surface holes
8. ...

The extracted feature data is based on the Equation 1.

$$FeatureData = \begin{bmatrix} f_{11} & f_{12}\ f_{13} \dots f_{1n} \\ f_{21} & x_{22}\ x_{23} \dots f_{2n} \\ \dots & \\ f_{s1} & f_{s2}\ f_{s3} \dots f_{sn} \end{bmatrix} \quad (1)$$

Where s is the number of subjects and n is the number of extracted features for that subject. In this study, n is 388 and m is 139.

Furthermore, there are two other type of features which are provided by the PPMI dataset which are age and sex for each subjects. Thus, these two biographical information could be added to the extracted feature which give feature data with the size $(388 * 141)$.

3.3 Classification

In this part, the aim is using the extracted volume based features for classifying the MRI data to two class of PD and HC. In our study, three types of classification algorithm is used which all of them are supervised methods. In the following, each classification method is generally explained:

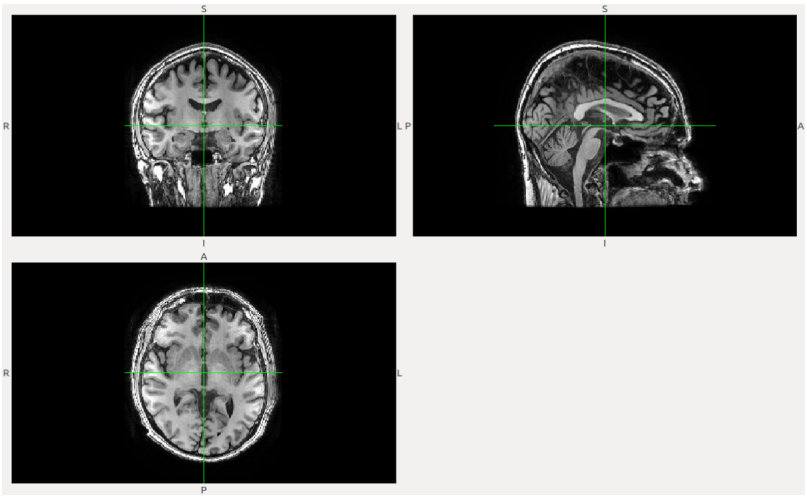
- **Logistic Regression (LR):**
  Logistic regression (LR) is a statistical technique which is used in machine learning for binary classification problems. LR belongs to the family of MaxEnt classifiers known as the exponential or log-linear classifiers [18]. Like naive Bayes, it works by extracting some set of weighted features from the input, taking logs, and combining them linearly (meaning that each feature is multiplied by a weight and then added up) [19]. Thus, this model could be a suitable binary classifier for our problem.
- **Random Forest (RF):**
  Random forests (RF) is an ensemble learning method for classification, regression and other tasks. This method is presented by Breiman [20], which creates a set of decision trees from randomly selected subset of training data. It then aggregates the votes from different decision trees to decide the final class of the test object. Each tree in a random forest is a weak classifier. A large set of trees trained with randomly chosen data will make a single decision on a majority basis. In the current stage of this research, we tested how accurate decisions can be made by random forests trained by the data coming from a single MRI volume.
- **Support Vector machine (SVM):**
  Support vector machine (SVM) [21] is a well-known supervised machine learning algorithm for classification and regression. It performs classification tasks by constructing optimal hyperplanes in a multidimensional space that separates cases of different class labels. This classification method is more popular because its easier to use, has higher generalization performance and little tunning comparing to other classifier. In our case, the kernel SVM is used.

There are a set of parameters for each classifier that need to be tuned in order to have a fair comparison.

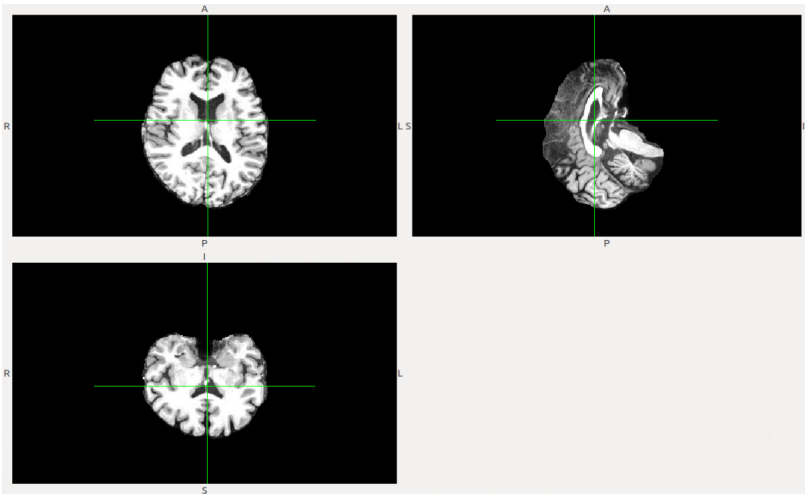
4 Results and Discussion

In this section, the experimental results for different steps of the proposed CAD system for diagnosis of PD is presented. First the preprocessing step prepare the MRI data to the next steps using FreeSurfer. Fig.3 shows the subject 3102 MRI and the resulted image after preprocessing.

After preprocessing with FreeSurfer, for each subject a list of volume-based features have been extracted. Also, age and sex feature are provided for PPMI data in their website as demographic information of the patients. Some evaluation has been done over the set of extracted features in terms of their ability



(a) Original MR Image.



(b) Preprocessed MR Image.

Fig. 3: Preprocessing results for one of the subject.

to data discrimination. Since, the PD is age related disease, the distribution of data in terms of age feature is plotted. Fig.4 shows the distribution of age in the dataset for the subjects with PD and HC labels. The distribution of all the extracted features are plotted in terms of their ability to distinguish the data to two classes of PD and HC. Some of these distribution are shown in Fig.5 . As you can see in Fig.5(a), the subjects with PD has higher brain volume comparing to the healthy one. Furthermore, the distribution in Fig.5(b) and (c) illustrate that when people are in PD category, their CSF and their CC-Anterior volume size

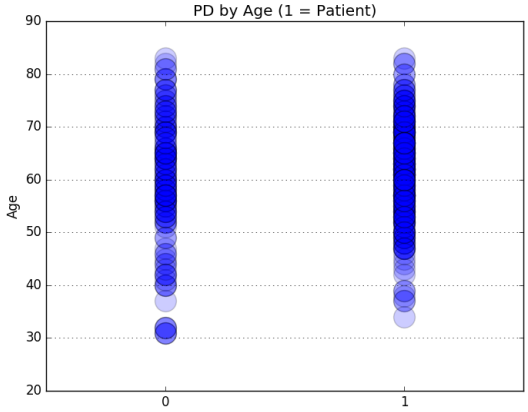


Fig. 4: Distribution of Data in terms of Age feature.

is enlarged. Fig.5(d) shows that the surface holes volume in PD is noticeably higher than the normal subjects. Another set of evaluation has been done over the extracted features. Each two features data plotted versus each other based on the corresponding class. Fig.6 shows the distribution of data based on the two pair of features including $3rd$ ventricles vs lateral ventricles and $3rd$ ventricles vs left vessels which in both of them, two features tend to have bigger value when subject is PD.

As its explained in the previous section, three types of classifiers are used in this study. These algorithm are run over 388 samples with 141 features. Internal and external cross validation is applied with $K = 10$ for external and $k = 5$ for internal (parameter tunning cross validation). The number of selected samples for the training part is 350 and for the test part is 38. Furthermore, the number of PD and HC in each group is presented in Table 2.

Table 2: Data balance in train and test part.

	PD	Hc	Total
Training	236	114	350
Test	26	12	38

As its mentioned before, the classification algorithm need a set of parameters for tunning which is selected as follow:

– logistic Regression (LR):
Regularization = $[1e-1, 1e-2, 1e-3, 1e-4, 1e-5]$, Tolerance = [1e-1, 1e-2, 1e-3, 1e-4, 1e-5]

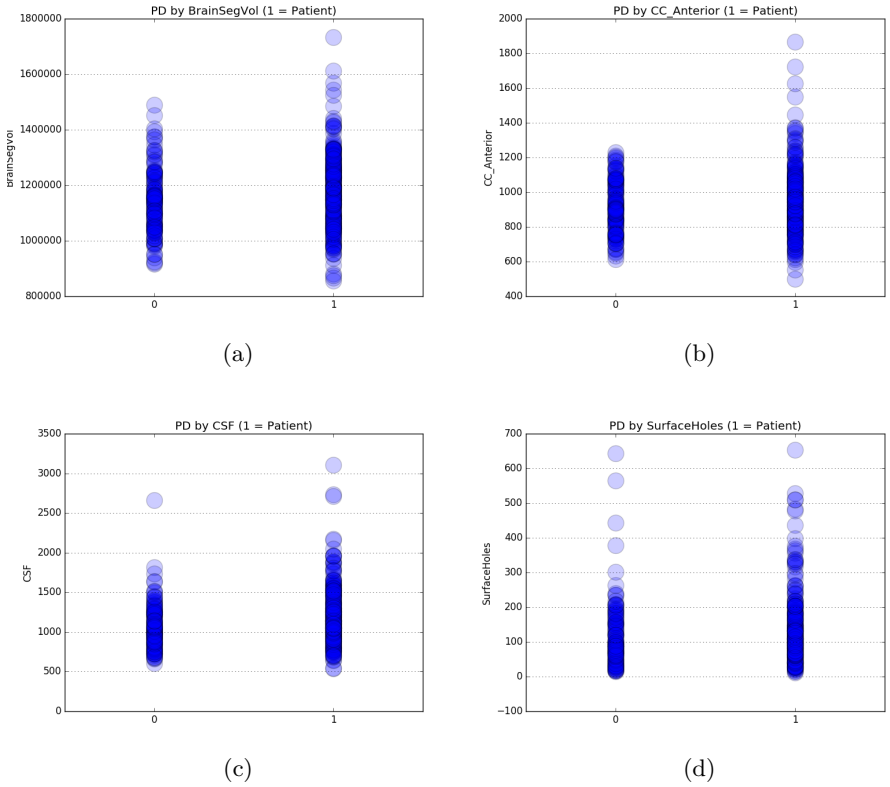
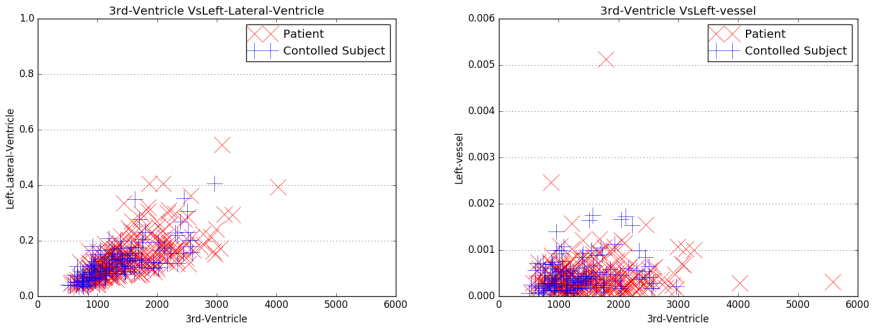


Fig. 5: data distributions in terms of the class labels and corresponding features which are: (a) Brain segmented volume. (b) CC- Anterior. (c) CSF. (d) Surface holes.

- Random Forest (RF):
  Number of estimator $=[5, 10, 15, 20, 25]$, Max depth $= [2 - 10]$
- Support Vector Machine (SVM):
  C $= [0.1, 1, 10, 100, 1000]$, Gamma $= [10, 1, 1e{-}1, 1e{-}2, 1e{-}3, 1e{-}4]$, kernels $= [linear, rbf, poly]$

The evaluation metrics that is used in this paper for comparing the result of the classification algorithms include accuracy, confusion matrix (recall, precision) and AUC (area under ROC curve). The classification results for LR, RF and SVM are Tables 3, 4, and 5, respectively.

Table 6 shows the general comparison between these methods. As you see the best result is for RF. As you see in the table there are two set of result which is related to using age/sex feature or doing the classification just based on the extracted volume based features from FreeSurfer.



(a) (b)

Fig. 6: Data distribution based on the pair of features: (a)3rd ventricle and left lateral ventricle. (b) 3rd ventricle and left vessel.

Table 3: Logistic regression performance

Logit	Train Accuracy	Test Accuracy	TN	FP	FN	TP	AUC
K_0	0.6867	0.6500	3	10	4	23	0.5413
K_1	0.6781	0.6750	0	13	0	27	0.5000
K_2	0.6819	0.7179	2	11	0	26	0.5769
K_3	0.6733	0.6666	3	10	3	23	0.5576
K_4	0.6991	0.5384	2	11	7	19	0.4423
K_5	0.6618	0.6153	0	13	2	24	0.4615
K_6	0.6657	0.6842	1	11	1	25	0.5224
K_7	0.7057	0.6578	2	10	3	23	0.5256
K_8	0.6857	0.6052	1	11	4	22	0.4647
K_9	0.6742	0.6315	0	12	2	24	0.4615

Based on the literature review, most the presented paper use VBM for data analysis and feature extraction. In this paper, one of the important goal was evaluating the FreeSurfer features for PD MRI images using machine learning techniques. Generally, the experimental results show that the classification models need more information about the data that should be added to the current features since these are the low-level features and we need a set of high-level features as well. In the future research, were going to find out the useful general feature that we can combine them with the volume based extracted features.

5 Conclusion

The presented work in this paper, is an automatic CAD system for diagnosing the Parkinsons Disease (PD) which is the second neurodegenerative disease mostly affected elder people. This disease is exposed by loss of the neurotransmitter that control the body movement and there is no fixed cure for that but the earlier

Table 4: Random forests performance

RandomFrest	Train Accuracy	Test Accuracy	TN	FP	FN	TP	AUC
K_0	0.7270	0.6750	0	13	0	27	0.5000
K_1	0.7327	0.6500	1	12	2	25	0.5014
K_2	0.7507	0.6923	1	12	0	26	0.5384
K_3	0.7392	0.6923	1	12	0	26	0.5384
K_4	0.7335	0.6666	2	11	2	24	0.5384
K_5	0.7277	0.7179	2	11	0	26	0.5769
K_6	0.7399	0.6578	0	12	1	25	0.4807
K_7	0.7171	0.6578	0	12	1	25	0.4807
K_8	0.7257	0.6315	1	11	3	23	0.4839
K_9	0.7199	0.7105	1	11	0	26	0.5416

Table 5: Support Vector Machine performance

SVM	Train Accuracy	Test Accuracy	TN	FP	FN	TP	AUC
K_0	0.7528	0.6000	3	10	6	21	0.5042
K_1	0.7471	0.6000	7	6	10	17	0.5840
K_2	0.7134	0.6923	5	8	4	22	0.6153
K_3	0.7335	0.5128	2	11	8	18	0.4230
K_4	0.7478	0.6666	3	10	3	23	0.5576
K_5	0.7449	0.5897	4	9	7	19	0.5192
K_6	0.7228	0.7105	4	8	3	23	0.6089
K_7	0.7400	0.4473	3	9	12	14	0.3942
K_8	0.7171	0.5789	4	8	8	18	0.5128
K_9	0.7428	0.5789	3	9	7	19	0.4903

diagnosis results the better and more efficient treatment for the patients. In this paper, MR T1 image form PPMI data set is used which is the public dataset for PD . The FreeSurfer has been used for feature extraction and preprocessing. The decision model for classification of the extracted feature data is based on LR, RF and SVM methods. In the experimental results, the ability of these three types of classifiers for PD diagnosis are compared with each other. In future, the efficiency of the proposed method could be improved by adding high level feature to the current features.

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Table 6: Comparing the performance of the different classifiers

Methods/Criteria	Age/Sex Feature	Train Accuracy	Test Accuracy	AUC
LR	No	0.6806	0.6467	0.4912
LR	Yes	0.6858	0.6313	0.4794
RF	No	0.7425	0.67	0.4647
RF	Yes	0.7396	0.6673	0.5086
SVM with rbf kernel	No	0.6752	0.6753	0.500
SVM with rbf kernel	Yes	0.6752	0.6753	0.500
SVM with linear kernel	No	0.7362	0.5977	0.521
SVM with linear kernel	Yes	0.7259	0.5927	0.5273

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