Classification of Parkinson's Disease using regional features and machine learning algorithms on structural MRI

Minor project dissertation submitted to the University of Delhi in partial fulfillment of the requirements for the award of the degree of

MASTER OF SCIENCE (COMPUTER SCIENCE)

by

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Certificate

This is to certify that the minor project dissertation entitled **Classification of Parkinson's Disease using regional features and machine learning algorithms on structural MRI** being submitted by **Yash Khorwal and Vishvendra Singh** under the supervision of **Dr. Bharti,** Assistant Professor, Department of Computer Science, University of Delhi. The project work has been carried out for the partial fulfillment of the requirements of Master of Science (Computer Science) degree in the Department of Computer Science, University of Delhi. The project embodies original research work carried out at the Department of Computer Science, University of Delhi. This has not been submitted so far, in part or full, to any other University or institute for the award of any other degree or diploma.

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We hereby declare that the minor work project dissertation entitled **Classification of Parkinson's Disease using regional features and machine learning algorithms on structural MRI** which is being submitted to Department of Computer Science, University of Delhi, Delhi-110007 in the partial fulfillment of the requirements of Master of Science (Computer Science) degree is a bonafide work carried out by us. The work has been carried out under the supervision of Dr. Bharti, Assistant Professor, Department of Computer Science, University of Delhi.

The project embodies original work carried out at the Department of Computer Science. This work has not been submitted, in part or full, to any other University or Institute for the award of any other degree or diploma.

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"Data used in the preparation of this article were obtained from the Parkinson's Progression Markers Initiative (PPMI) database (www.ppmi-info.org/access-data-specimens/download-data). For up-to-date information on the study, visit www.ppmi-info.org."

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Abstract

Parkinson's disease (PD) is a neurological condition marked by rigidity, tremor, and slowness of movement. The quality of life in terms of health has been proven to be considerably impacted by Parkinson's disease.

Its early and accurate diagnosis is a prime concern for clinicians and patients. This project aims to classify PD patients from healthy subjects using structural MRI and machine learning approaches.

Further, if any disease impacts a few brain regions, we aim to learn a decision model using regional features like surface area, and volumetric loss.

In the present work, a small balanced dataset containing 30 PD and 30 healthy subjects is created from a publicly available dataset PPMI. Also, regional features including cortical thickness, grey matter volume, white matter volume, and Cerebrospinal volume are computed using multiple atlases. Then, Fisher's Discriminant Ratio, a well-known feature selection approach, is used to find relevant features and subsequently relevant regions. We experimented with six machine learning models - Logistic Regression (LR), Decision Tree (DT), AdaBoost (AB), Random Forest (RF), Support Vector Machine (SVM), and Extreme Gradient Boost (XgB).

The performance is computed using accuracy, precision, recall, and F1-score with the Leave-one-out cross-validation approach. The best accuracy is 66.67% which is achieved with Logistic Regression. We were also able to identify the affected brain regions in PD. This study may be extended for larger datasets also.

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Introduction

1.1. Background

Parkinson's disease is a brain condition that results in uncontrolled or unintentional tremors, slowness, and balance and coordination issues. Most frequently, symptoms develop gradually and worsen with time. Moving around and communicating may become challenging as the sickness becomes worse. They might also go through mental and behavioral changes, memory loss, sleep problems, depression, and weariness. Parkinson's disease is characterised by the death of nerve cells in the basal ganglia, a part of the brain that controls movement, which results in the illness's most noticeable signs and symptoms. Typically, these nerve cells, or neurons, create dopamine, a crucial neurotransmitter in the brain. The condition causes problems with movement because the degeneration or death of the neurons reduces the amount of dopamine that is produced. What leads to the degeneration of neurons is yet unknown to scientists. (“Parkinson’s Disease: Causes, Symptoms, and Treatments”).

Symptoms include

- Slow movement
- Trembling in the jaw, head, arms, or legs
- Imbalance and coordination issues, which can occasionally cause falls
- Muscular stiffness caused by persistently tightened muscles

1% of people over the age of 65 years suffer from PD (estimated about 12 lac Indians living with PD in India) (“Parkinsons Disease and the Ageing Indian Population - Healthcare Radius” 2021).

1.2. Problem statement

In literature (“APDA1703_Basic-Handbook-D5V4-4web.Pdf”’) it is mentioned that a general neurologist, who is qualified to identify and treat neurologic problems, may frequently detect PD. Consultation with a movement disorder expert is advised to avoid misdiagnosis. A doctor who has completed extra specialty training in the diagnosis and treatment of movement disorders, such as PD, in addition to standard neurology training, is referred to as a movement disorder specialist.

Clinical test scores are given to the patients by the physician. But this method is subjective. If the physician is a beginner there might be chances of giving the wrong score to the patient.

That is why Magnetic Resonance Imaging (MRI) is used for PD diagnosis as it is easy to acquire and may help in objective assessments. According to the past literature (Crispino et al. 2020; Yadav et al. 2016; Shu et al. 2021; Solana-Lavalle and Rosas-Romero 2021; Samantaray, Saini, and Gupta 2022), we know that people have worked on MRI on specific radiomics features and voxel-based morphometry. The researchers have used structural MRI (sMRI) which focuses on the anatomy of the brain, to determine the changes in tissue volume due to the disease. However, the research work on the automated diagnosis of PD using machine learning algorithms is limited (Solana-Lavalle and Rosas-Romero 2021; Shu et al. 2021).

Motivated by the strength of sMRI and for the diagnosis of PD, the usage of structural alterations in PD patients to those in healthy controls (HC) to develop an automated diagnosis tool using machine learning is the main focus of the current study.

1.3. Objectives

The current study focuses on the following:

1. Finding relevant regional features namely, White Matter volume, Grey Matter volume, Cerebrospinal fluid volume, and Cortical Thickness from sMRI to capture structural changes in PD.
2. To explore the efficiency of popular machine learning algorithms to build an automated diagnostic tool for classifying PD and HC using regional features.
3. To identify affected brain regions in PD.

2. Literature Review

This section focuses on some recent research utilizing MRI to identify Parkinson's disease (PD). In literature (Samantaray, Saini, and Gupta 2022; Shu et al. 2021; Solana-Lavalle and Rosas-Romero 2021; Crispino et al. 2020; Yadav et al. 2016), research work was conducted to classify PD and healthy subjects using structural MRI data.

(Samantaray, Saini, and Gupta 2022) talked about the structural neuroimaging-based subgrouping methods used in PD that are data-driven and clinical symptom-based subgrouping approaches. The author provides a summary of the work done in structural MRI-based research on brain connectivity for PD. They provided an overview of network atlases, brain connectivity software, connectivity measures, and mathematical definitions. Finally, they explore the difficulties that will inevitably arise and offer doable advice on choosing approaches to subgroups and analyzing connections using structural MRI data.

(Shu et al. 2021) attempted to design and evaluate a radiomics model based on clinical traits and whole-brain white matter to anticipate the onset of PD. A training set and a test set were created from the entire dataset. The maximum relevance minimum redundancy (mRMR) approach was used to minimize the amount of the training dataset and create a radiomics signature. A joint model was created in the end. The prediction models were subsequently validated using the test data and evaluated for discrimination, calibration, and clinical value, and an accuracy of 82.7% which was achieved with Logistic Regression.

(Solana-Lavalle and Rosas-Romero 2021) analyzed MRI data using both qualitative and quantitative methods in order to research and comprehend PD. The regions of interest in sMRI are identified using voxel-based morphometry (VBM). Magnetic resonance images are subjected to VBM prior to classification in order to identify the areas from which features will be retrieved using first- and second-order statistical techniques. Using feature selection techniques also reduces the number of features. They employ seven classifiers and run different tests for women and men. The accuracy of 93.28% for women and 95.56% for men was achieved by Logistic Regression and Support Vector Machine respectively.

A few researchers (Crispino et al. 2020; Yadav et al. 2016) also focused on gender-based studies and attempted to identify the effect of PD in male patients in comparison to female patients.

(Crispino et al. 2020) plan to compile the most credible data on how gender affects the onset of Parkinson's symptoms and health-related quality of life on the basis of Genetic Factors, Mitochondrial Function, Inflammatory Response, Clinical Features, Cognitive Status, Motor Functions, Mood Symptoms, REM Phase of Sleep, Response to Treatment. They concluded that despite expressing more severe clinical symptoms associated with PD, women with PD had more favorable outcomes in terms of non-motor symptoms, mental abilities, and emotion management.

(Yadav et al. 2016) focused on evaluating, using network analysis, the variations in cortical thickness and structural alignment between the genders in PD patients. They concluded that male patients with PD were more affected than female individuals with PD, suggesting that male PD patients had more alterations in brain tissue. In PD patients, gender differences in regional cortical thickness were also seen. In order to provide PD patients with better clinical treatment, the data also points to the necessity for medications tailored to various genders.

3. Materials and Methods

3.1. Dataset Details

In the present study, a publicly available dataset "Parkinson's Progression Markers Initiative (PPMI)" is used for the preparation of a dataset. PPMI is a landmark to develop substantial open-access data collection, the project is working with collaborators throughout the world. The purpose of PPMI is to find biological indicators of Parkinson's risk, onset, and progression. The Michael J. Fox Foundation for Parkinson's Research and several other donors sponsor a public-private partnership known as PPMI. The details of the partners are available at www.ppmi-info.org/fundingpartners.

We conducted an analysis of 3D-T1 Weighted MRI of people with PD and healthy controls (HC). For this, a balanced dataset i.e., containing equal numbers of PD and HC, was constructed. Further, to avoid any bias due to gender, an equal number of male and females were considered while preparing the dataset. The details of the prepared dataset are mentioned in Table 1.

Table 1. Details of Dataset used in the work (PD vs HC)

Category	**Number of subjects**	**Age (in years)**		**Gender (M/F)**
		Range (Min-Max)	**Standard Deviation**	
PD	30	44-79	10.60	15/15
HC	30	32-85	11.85	15/15

*PD: Parkinson's Disease, HC: Healthy controls

3.2. Pre-processing

The pre-processing of the MRI includes the following steps:

A. Conversion of NifTi to DCM

The dataset consists of structural images of the brain that focuses on the anatomy of the brain. The files were in the format of **NIfTI** (.nii) that needs to be converted into **DCM** (.dcm) with the help of DICOM import (SPM Module).

B. Preprocessing using CAT12 (Gaser et al. 2022)

Using the CAT12 toolbox, we conducted the following steps:

1. T1 images are split into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF), and are then standardized to a template space (CSF).
2. On completion of the preprocessing, a quality check is performed. This could possibly be done by using several CAT12 modules. Furthermore, quality parameters are estimated and saved in xml-files for each data set during preprocessing. These quality 12 parameters can be additionally used in different modules.
3. Image data must be smoothed prior to getting inserted into a statistical model with the GM images. This is performed by the SPM module “Smooth”.

3.3. Proposed Model

3.3.1. Feature Extraction

In this work, we extracted regional features from three atlases namely, Neuromorphometrics Atlas (“Neuromorphometrics, Inc. | Building a Model of the Living Human Brain”), aparc_a20009s (“DestrieuxAtlasChanges”) and aparc_DK40 (“DestrieuxAtlasChanges”) to extract features. The features extracted from each atlas are described as follows:

Neuromorphometrics Atlas (“Neuromorphometrics, Inc. | Building a Model of the Living Human Brain”): It is an anatomical atlas that divides the brain into 136 sections based on data from several participants. It was created using anatomical MRI scans from 30 healthy participants that were manually traced. Using CAT12, we extracted (i) Volumes of the cerebral spinal fluid (CSF), (ii) white matter (WM) volume, and (iii) gray matter (GM) volume from each brain region.

Surface Atlas ("DestrieuxAtlasChanges")

Surface atlas deals with the Surface Cortical Thickness. In this work, we used two atlases:

i) **aparc_a2009s**: This atlas parcellates the cortex into 152 regions.

ii) **aparc_DK40**: This atlas parcellates the cortex into 72 regions.

Using the CAT12 toolbox, we extracted the cortical thickness of regions parcellated using these two surface atlases.

3.3.2. Feature Selection

Fisher's Discriminant Ratio (FDR) Score was used to determine the best features. Out of all the features, the ones that had more FDR score values were chosen for the next step. The FDR is defined as

$$FDR\ Score = \frac{|\mu_1 - \mu_2|^2}{\sigma_1^2 + \sigma_2^2}$$

where μ_1 and μ_2 are the mean of class 1 and 2 respectively while σ_1^2 and σ_2^2 are the variance of class 1 and 2 respectively.

3.3.3. Classification

The next step after feature selection was to learn a decision model. In the present work, the training dataset was learned on different machine learning models namely, Logistic Regression, Decision Tree, Random Forest, AdaBoost, Support Vector Machine, and XGBoost. Since the size of the dataset was small thus, classification performance was assessed using the Leave-One-Out Cross-Validation (LOOCV) technique.

Leave one out Cross-validation is used when there is an exact match between the number of folds and the total instances in the data set. As a consequence, the learning algorithm is built using all examples apart from one as a training set, and the one that was left out serves as a test set for a single item. Each instance is utilized as a test instance just once throughout this procedure.

A brief description of utilized machine learning methods is as follows:

1) Logistic Regression

When the dependent variable is dichotomous or binary, a statistical technique called logistic regression is applied. Using logistic regression, data and the relationship between a

dependent variable and one or more independent variables are obtained. It uses a logistic function, also known as the sigmoid function. The value of this logistic function lies between 0 and 1. The decision rule for a test sample is defined as if the logistic function returns a value higher than or equal to 0.5 for a particular test case, the test instance is placed in class 1, otherwise in class 2.

2) Decision Tree

A decision tree classifier recursively divides the input data into subsets according to the information gain, or the Gini index, or a predetermined criterion based on the values of certain attributes. The instance space is then divided by each internal node into two or more sub-spaces in accordance with the attribute values of the input data. Each leaf node has a class assigned to it that indicates the ideal goal value. Test samples are categorized based on the results of the test nodes along the route, which traverses the tree from the root node down to a leaf.

3) Random Forest

Decision tree methods are combined to create the random forest classifier. To provide more precise and reliable predictions, the decision trees produced by the random forest classifier are combined. Given the number of decision trees involved in the classification process, the random forest classifier is a very reliable and accurate approach.

4) AdaBoost

An approach for iterative class ensembles is called AdaBoost (Adaptive boosting). AdaBoost is a powerful classifier that is created by merging two or more subpar classifiers to produce a powerful classifier with high accuracy. Weak learners create very short (typically one-level) decision trees and successively added to the ensemble in the AdaBoost classifier. The predictions produced by the preceding model are therefore corrected by the following models.

5) Support Vector Machine

Both classification and regression are done using the Support Vector Machine (SVM), a family of supervised machine learning techniques. The SVM approach looks for a hyperplane in N-dimensional space that can classify the data points. The hyperplane's size depends on how many features there are.

6) XGBoost

Extreme Gradient Boosting, or XGBoost, is a decision tree-based classifier that employs the boosting technique to enhance its performance. Powerful machine learning classifier XGBoost excels in situations where accuracy and speed are priorities. As opposed to other boosting classifiers, XGBoost has a lot of hyper-parameters that can be tweaked, which is its major benefit.

Overall, in this work, we have extracted regional features like volume and cortical thickness using different atlases. Then, we applied feature selection followed by machine learning algorithms to train a decision model. The pipeline of the trained model is shown in Figure 1.

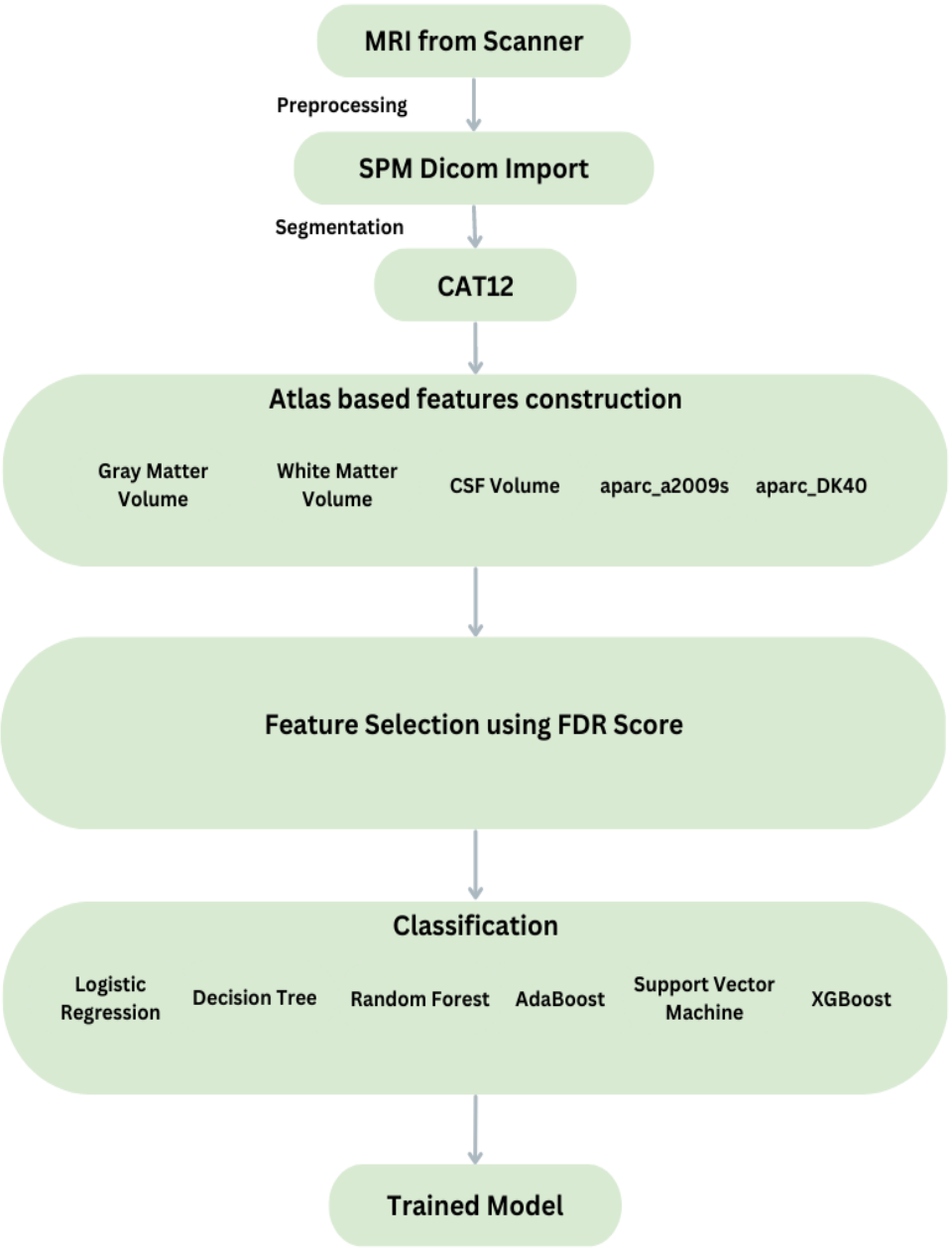

Figure 1. The pipeline for training a decision model

4. Experimental Setup & Results

In the present study, pre-processing of sMRI was conducted using the CAT12 toolbox of SPM12 ("SPM - Statistical Parametric Mapping") on the MATLAB platform. The learning models are trained on the COLAB platform. MRIcron ("NITRC: MRIcron: Tool/Resource Info") was used to view the NIfTI format images (MRI). Libraries used in COLAB are Pandas, Numpy, Matplotlib, Sklearn, and Xgboost.

4.1. Classification results

The experiments were performed using the LOOCV approach and the performance is measured using Accuracy, Recall, Precision, and F1-Score measures. The average performance of six classifiers without and with FDR is reported in Tables 2 to 6. Also, Tables 2 to 6 include one column #Feat which represents the number of features with which maximum classification accuracy was achieved with FDR.

Table 2: Classification results for GM volume features

Classifier	Without FDR (in %age)				With FDR (in %age)				
	Accuracy	Recall	Precision	F1-Score	#Feat	Accuracy	Recall	Precision	F1-Score
Logistic Regression	40.00	53.33	42.11	47.06	8	60.00	60.00	60.00	60.00
Decision Tree	53.67	52.00	53.84	52.85	14	**66.67**	63.33	67.86	65.52
Random Forest	52.67	45.33	53.19	48.74	8	58.33	53.33	59.26	56.14
AdaBoost	40.00	33.33	38.46	35.71	17	60.00	53.33	61.54	57.14
Support Vector Classifier	55.00	50.00	55.56	52.63	14	56.67	63.33	55.88	59.38
XGBoost	56.67	56.67	56.67	56.67	11	**66.67**	66.67	66.67	66.67

Table 3: Classification results for WM volume features

Classifier	Without FDR (in %age)				With FDR (in %age)				
	Accuracy	Recall	Precision	F1-Score	#Feat	Accuracy	Recall	Precision	F1-Score
Logistic Regression	61.67	66.67	60.61	63.49	8	**66.67**	63.33	67.86	65.52
Decision Tree	46.67	47.00	46.68	46.81	11	51.67	53.33	51.61	52.46
Random Forest	51.83	46.33	52.23	48.97	8	63.33	50.00	68.18	57.69
AdaBoost	57.67	56.67	57.84	57.24	8	60.00	66.67	58.82	62.50
Support Vector Classifier	56.67	56.67	56.67	56.67	14	63.33	56.67	65.38	60.71
XGBoost	50.00	56.67	50.00	53.13	11	**66.67**	66.67	66.67	66.67

Table 4: Classification results for CSF volume features

Classifier	Without FDR (in %age)				With FDR (in %age)				
	Accuracy	Recall	Precision	F1-Score	#Feat	Accuracy	Recall	Precision	F1-Score
Logistic Regression	41.67	53.33	43.24	47.76	14	61.67	70.00	60.00	64.62
Decision Tree	62.00	69.33	60.51	64.59	14	**65.00**	63.33	65.52	64.41
Random Forest	51.67	42.67	51.99	46.62	14	48.33	40.00	48.00	43.64
AdaBoost	71.67	76.67	69.70	73.02	14	56.67	60.00	56.25	58.06
Support Vector Classifier	71.67	70.00	72.41	71.19	14	58.33	53.33	59.26	56.14
XGBoost	58.33	56.67	58.62	57.63	14	55.00	53.33	55.17	54.24

Table 5: Classification results for aparc_a2009s features

Classifier	Without FDR (in %age)				With FDR (in %age)				
	Accuracy	Recall	Precision	F1-Score	#Feat	Accuracy	Recall	Precision	F1-Score
Logistic Regression	51.67	46.67	51.85	49.12	17	50.00	46.67	50.00	48.28
Decision Tree	36.33	34.00	35.73	34.82	11	**61.67**	70.00	60.00	64.62
Random Forest	48.50	41.67	47.70	44.24	11	53.33	40.00	54.55	46.15
AdaBoost	44.17	35.00	42.64	38.41	17	55.00	53.33	55.17	54.24
Support Vector Classifier	66.67	60.00	69.23	64.29	17	53.33	46.67	53.85	50.00
XGBoost	48.33	50.00	48.39	49.18	17	58.33	56.67	58.62	57.63

Table 6: Classification results for aparc_DK40 features

Classifier	Without FDR (in %age)				With FDR (in %age)				
	Accuracy	Recall	Precision	F1-Score	#Feat	Accuracy	Recall	Precision	F1-Score
Logistic Regression	45.00	40.00	44.44	42.11	11	**63.33**	63.33	63.33	63.33
Decision Tree	47.17	47.33	47.06	47.15	14	51.67	60.00	51.43	55.38
Random Forest	46.67	41.00	46.06	43.27	14	60.00	50.00	62.50	55.56
AdaBoost	40.00	36.67	39.29	37.93	14	51.67	53.33	51.61	52.46
Support Vector Classifier	48.33	46.67	48.28	47.46	11	60.00	60.00	60.00	60.00
XGBoost	43.33	33.33	41.67	37.04	17	48.33	43.33	48.15	45.61

The following can be observed from the Tables 2 to 6:

- Using FDR, the performance of the classifiers improved, and a small subset of discriminating features were identified.
- The maximum classification accuracy of 66.67% with Decision tree and XGBoost for GM volume is achieved. However, XGBoost gave the best classification accuracy with a smaller number of features in comparison to the decision tree.
- Using WM volumetric features, 66.67% of classification accuracy with logistic regression and XGBoost is achieved. However, Logistic Regression gave the best classification accuracy with a smaller number of features in comparison to XGBoost.
- For CSF volumetric features, 65.00% of classification accuracy with the decision tree is achieved.
- For surface-based cortical thickness analysis, 61.67% accuracy is achieved using decision tree for aparc_a2009s atlas and 63.33% accuracy is achieved using logistic regression for aparc_DK40 atlas.

4.2. Identification of affected regions

For each feature extraction approach, we backtracked the features/regions with which maximum accuracy is achieved. Since feature selection was carried out in each LOOCV iteration, we computed the frequency of features/regions, and the regions with maximum frequency are reported here.

- **Using analysis of GM Volume based features**

  The most relevant features are the 4th Ventricle, Right Accumbens Area, Left Accumbens Area, Cerebellar Vermal Lobules VIII-X, Right AOrG (Anterior Orbital Gyrus), Right MCgG (Middle Cingulate Gyrus) and Right SCA (Subcallosal Area).

- **Using analysis of WM Volume based features**

  The most relevant features are Right Cun cuneus, Left SMC (Supplementary Motor Cortex), Right SMG (Supramarginal Gyrus), Left SOG (Superior Occipital Gyrus), and Left TTG (Transverse Temporal Gyrus).

- **Using analysis of CSF Volume based features**

  The most relevant features are the 3rd Ventricle, Right MSFG (Superior Frontal Gyrus Medial Segmen), and Left TTG (Transverse Temporal Gyrus).

- **Using analysis of aparc_a2009s cortical thickness-based features**

  The most relevant features are rG_temp_sup-Plan_polar, rS_central, lS_orbital_med-olfact, rS_precentral-sup-part and lS_suborbital.

- **Using analysis of aparc_DK40 cortical thickness-based features**

  The most relevant features are the rcaudalmiddlefrontal, lprecuneus, rtemporalpole, and linsula.

4.3. Comparison with existing work

We compared our results with the existing works and Table 7 represents the comparison. The results of the literature work are not repeated. We are reporting the results from their respective work.

Table 7. Comparison with existing works

Research work	Details of Features & classifier	Accuracy (in %age)
Shu et al. (2021)	WM with Logistic Regression	82.7
Solana-Lavalle (2021)	VBM with Logistic Regression	93.28
	VBM with SVM	95.56
Our work	GM with Decision Tree	66.67
	GM with XGBoost	66.67
	WM with Logistic Regression	66.67
	WM with XGBoost	66.67

Table 7 shows that the Research's results are maximum. We work to improve our performance in the future.

5. Conclusion & Future Work

In this work, we developed a PD and HC classification system based on machine learning. We constructed a balanced dataset of T1-weighted MRI containing 30 PD patients and 30 HC from a publicly available PPMI dataset. We investigated six classifiers, namely Logistic Regression, Decision Tree, Random Forest, AdaBoost, SVM, and XGBoost. Features are extracted from Neuromorphometrics, aparc_a2009s, and aparc_DK40 atlases and are used for training a decision model. Also, a subset of relevant features is extracted using FDR.

The best accuracy of 66.67% was achieved with WM using Logistic Regression and XGBoost and with GM using Decision Tree and XGBoost. The affected regions are the Right Cun cuneus, Left SMC (Supplementary Motor Cortex), Right SMG (Supramarginal Gyrus), Left SOG (Superior Occipital Gyrus), Left TTG (Transverse Temporal Gyrus), 4th Ventricle, Right Accumbens Area, Left Accumbens Area, Cerebellar Vermal Lobules VIII-X, Right AOrG (Anterior Orbital Gyrus), Right MCgG (Middle Cingulate Gyrus), Right SCA (Subcallosal Area), 3rd Ventricle, Right MSFG (Superior Frontal Gyrus Medial Segmen) and Left TTG (Transverse Temporal Gyrus). Some of these are also listed in the literature. (Solana-Lavalle and Rosas-Romero 2021)

The study can be extended to large datasets and more features can be extracted.

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