Journal of Autonomous Intelligence (2024) Volume 7 Issue 3
doi: 10.32629/jai.v7i3.1093

ORIGINAL RESEARCH ARTICLE

Efficient machine learning model to detect early stage Parkinson's disease

Raziya Begum, T. Pavan Kumar*

Department of Computer Science & Engineering, Koneru Lakshmaiah Education Foundation, Vaddeswaram, Guntur 522502, AP, India

*** Corresponding author:** T. Pavan Kumar, pavankumar_ist@kluniversity.in

ABSTRACT

Parkinson's disease (PD) often manifests itself in memory loss and cognitive decline. The decline is inexorable, and damage to the brain's cortex has already occurred. Numerous studies have shown that by detecting dementia early and beginning treatment, the disease's course can be slowed, and any further atrophy can be prevented. Brain imaging data, such as from an MRI, is frequently used in the diagnosis of Parkinson's disease (PD). In recent years, utilizing deep convolutional neural networks has greatly improved Parkinson's disease diagnosis. However, getting to the level of quality needed for clinical use is still challenging. In this study, we introduce a machine learning-based approach for more accurately diagnosing Parkinson's disease. This research makes use of information gleaned from single-photon emission computerized tomography (SPECT) scan and positron emission tomography (PET) scans performed on patients with Parkinson's disease (PD) and healthy controls. The most crucial characteristics of these datasets are isolated with the aid of the Fisher discriminate ratio (FDR) and non-negative matrix factorization (NMF). The K-nearest neighbor, Decision Tree, Support vector machine (SVM), and Deep Convolution neural network (DCCN) classifiers with confidence bounds classify the NMF-transformed data sets with a decreased number of features. The proposed DCCN technique has a classification accuracy of up to 93.7 percent when compared to decision trees, K-Nearest Neighbor (KNN)s, and SVMs. The DCCN is now a reliable approach for classifying SPECT and PET, PD images.

Keywords: Parkinson's disease (PD); support vector machine (SVM); decision tree; DCCN; brain-imaging

ARTICLE INFO

Received: 4 August 2023
Accepted: 11 October 2023
Available online: 26 December 2023

1. Introduction

Parkinson's disease (PD) is the leading cause of dementia, affecting between 60 and 80 percent of those who are diagnosed. Parkinson's disease (PD) is now widely acknowledged as a leading cause of dementia, almost 70 years after its original description in 1906. Approximately 123 more deaths were attributed to Parkinson's disease during the years of 2000 and 2015. By 2050, one in every 85 individuals is expected to be diagnosed with Parkinson's disease, according to, experts. If PD is diagnosed correctly and treated early, it can save up to $7.9 trillion in healthcare and medical expenditures. Some recent developments in the application of machine learning approaches for Parkinson's disease diagnosis and prognosis were described by Shang et al.[1], Combining MRI data with a neuropsychological test has been shown to enhance the categorization of Parkinson's disease and its prodromal stages, as reported by Blair et al.[2] may be more prevalent in one hemisphere at certain Parkinson's disease stages. Bron et al.[3] proposed using a significance map and weights for a support vector machine. Aubin et

al.[4] suggest using multi-view learning in conjunction with support vector machines to treat Parkinson's illness. Diagnosis Using Multiple Templates for Feature Representation. Zhang et al.[5] used support vector machines (SVM) with DTI fractional anisotropy maps to categorize people with Parkinson's disease. For the purpose of early Parkinson's disease identification using the PPMI dataset, Zernike moment-based algorithms were developed by Jain et al.[6]. Cerebral neuritis plaques and overt neuronal death are hallmarks of this disorder. Typically, symptoms manifest themselves slowly but steadily, eventually becoming severe enough to interfere with everyday living. Although age is the most significant risk factor for developing PD, this condition affects people of all ages. In the early stages, the memory loss is minimal, but in the later stages, the patient's communication abilities and ability to respond rapidly decline. Parkinson's disease (PD) cannot be slowed down with current treatments, but early detection can help slow the illness's course and give patients a better quality of life. An assessment of the literature found that Parkinson's disease diagnosis is hindered by a lack of high-sample and high-dimensional brain data and pictures.

There have been a number of recent attempts to address these issues using deep learning techniques, such as the following: stacked auto encoders, sparse regression models, and deep sparse multi-task learning. These techniques are more commonly employed to select a specific item. This issue's features recommend items with and without information load in order to increase disease detection accuracy. The Zernike moments based method is then extended by Li et al.[7] to axial, coronal, and sagittal sMRI images from the OASIS dataset. Incorporating additional correlation information into the feature selection, Pandya et al.[8] modelled it using the connectedness of an undirected network. Support Vector Machine (SVM), K-Nearest Neighbour (KNN), and Naive Bayes (NB) may all be used to categorise a dataset based on Laplace Beltrami eigenvalues, as stated by Ramaniharan et al.[9], Rahman et al.[10] and coworkers built a web-based SVM for diagnosing Parkinson's illness. In order to categorise PD, Gündüz employed the Rotated BRIEF and Oriented FAST feature extraction techniques. The next step is to assess how well our data set and machine learning algorithms work.

Motivation:

Machine learning/Deep learning has been widely used for the development of intelligent software for speech recognition, computer vision, robot control, natural language processing, and other applications. ML is gaining popularity in studying chronic diseases with applications ranging from early prevention, diagnosis to predicting treatment effect and prognosis. In medical sciences today, diagnosis of the disease is a serious task that relies on clinical examination and assessment. Thus, for cost-effective management as well as decision making decision support systems based on computers may play a pivotal role. The health care field creates a huge amount of data which comprises assessment reports including patient's clinical and physical assessments, treatment, future appointments, and a list of prescribed or no prescribed medicines. It is a tedious and complicated task to manage this data in a required manner so that it can be effectively extracted and efficiently processed. The major challenges for the healthcare professionals comprise of conditions underlying diseases that may not be directly observable or measurable as data, in 5 finding latent variables is one of the challenges. Thus, ML algorithms play a critical role in the early detection of diseases. However, other challenges could be that the disease is continuously evolving which would vary from person to person, at times the patient's information is incomplete, there could be observational differences apart from integrating the domain knowledge which is an essential step in the modeling process. Despite all these challenges, many advancements have been made in the past decade cost-effective management, as well as decision-making decision support systems based on computers, may play a pivotal role. The health care field creates a huge amount of data which comprises assessment reports including patient's clinical and physical assessments, treatment, future appointments, and a list of prescribed or non-prescribed medicines. Using ML, a variety of classifiers have been developed which can divide this health data based on their attributes. Such

classifiers form the basis of medical data analysis as well as disease detection/prediction. Further with the development of several algorithms, it has become easier to collect the data and share it in big information systems. These in turn support the physicians in a reliable decision-making process based on the correct diagnostic data in the prognosis of a novel patient with accuracy and high speed. Machine Learning algorithms can efficiently manage a huge amount of data, integrate data from various resources, and incorporate the background information in the study. Thus, using electronic health record data, ML and deep learning algorithms have been able to predict many important clinical conditions.

The aim of this paper is to compares the ml models to classify the PD Disease on MRI dataset. There exist a number of different Machine Learning (ML) models among which this paper aim is to compare (ML) models like SVM, K-NN, DCCN models.

2. Literature survey

There is an increased risk of Parkinson's disease (PD) in people with moderate cognitive impairment (MCI), which is the most common form of the neurodegenerative illness. At this point, it is impossible to predict which MCI patients will precede to Parkinson's disease, despite promising results in pattern classification for distinguishing between progressing (pMCI) and stable (sMCI) patients.

Biomarkers for Parkinson's disease (PD) have been studied for use in diagnosis and monitoring of the illness's development[11–13]. These biomarkers include genetic information, CSF cerebrospinal fluid (CSF) biomarkers, MRI, and PET. (PET). Pattern classifiers based on these parameters have shown promise in differentiating PD patients from healthy controls (HC)[14], and there is evidence to suggest that using longitudinal data rather than cross-sectional data might further enhance performance.

Changes in neuropsychological tests, the pace of cortical and subcortical volume loss[15], and the intensity/density map of brain tissue have all been researched longitudinally for their role in PD diagnosis and prognosis. Including data from numerous individuals over several time points is often required for prediction models that make use of longitudinal data. However, missing data is a major issue for longitudinal research. Replacing missing information is a common method of dealing with this issue[16].

The multi-fidelity neural process with physics (MFPC) ratings have been used to develop longitudinal models for dealing with missing or inadequate data[17]. For example, MFPC relies on a hypothesis about the latent longitudinal process that other markers might not share. Classification tasks, such as distinguishing between sMCI and pMCI, have commonly been used to model the early prediction of PD dementia. In order to define pMCI and sMCI, classification performance is first established using a cutoff follow-up time of a predetermined duration. Furthermore, regardless of diagnostic criteria, the cohorts of people with pMCI and sMCI are generally distinct. When it comes to PD dementia prediction in a categorization environment, we know very little about when persons with MCI may pass over into full-blown dementia. Multiple studies have used time-to-event analysis[18–21] with encouraging outcomes.

There are no standard test ready to directly get detect the PD[22].

A study, Yadav et al.[23] also stated that pregnant women have less chances Parkinson's disease (PD).

As per Razzo et al.[24] study used UK Parkinson's Disease Society Brain Bank (UKPDSBB) Clinical early detection of PD with differential diagnosis can be done only 80% of diagnostic accuracy.

Dataset:

This classification system was designed with different ML models. To start the methodology a MRI dataset of 700 patients from PPMI is used with 30% of training data and 70% of testing data. In total there are 213 healthy controls, 421 Parkinson's patients have been found.

3. Proposed models

This next section goes into great length on the suggested approach. First, we'll go over what Deep Convolutional Neural Networks are, and then we'll get into the specifics of the suggested network architecture. To better understand Parkinson's disease, the following classifiers were employed and compared with the proposed methodology as shown IN **Figure 1**.

Methodology:

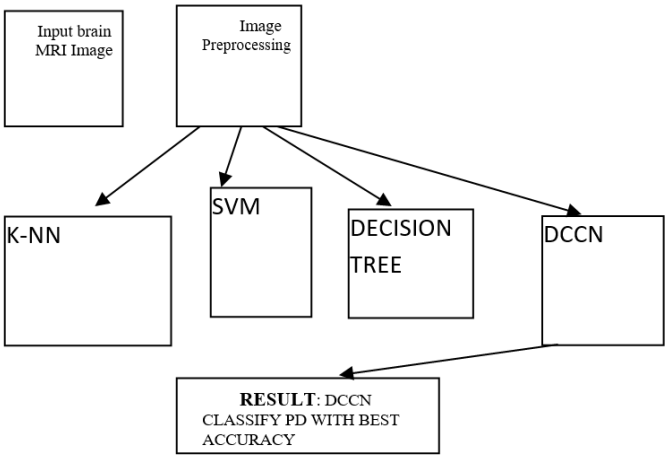

Figure 1. Proposed Methodology.

3.1. K-Nearest Neighbor (KNN)

K-Nearest Neighbour is a basic supervised learning-based machine learning technique. The K-NN technique optimizes the classification of a new instance based on its similarity to previously tagged examples. The K-NN algorithm classifies new information by comparing it to the whole database. With K-NN, novel data may be categorized quickly and accurately.

The K-NN technique is most commonly used for classification, although it may also be used for regression. Since the K-NN method is non-parametric, it makes no data-specific assumptions. This algorithm is known as a "lazy learner" because it does not immediately use the knowledge it acquires from the training set, but rather saves it for later use during the classification process. During its training phase, the KNN algorithm just has to store the dataset and place fresh data into a category that best fits it. The new piece of information, x1, might go into either Class A or Class B, and we need to decide where it fits. For this type of problem, the K-NN method is obligatory. K-NN may be used to quickly determine the class or category of a dataset. As a jumping off point, consider **Figure 2** to demonstrate this technique.

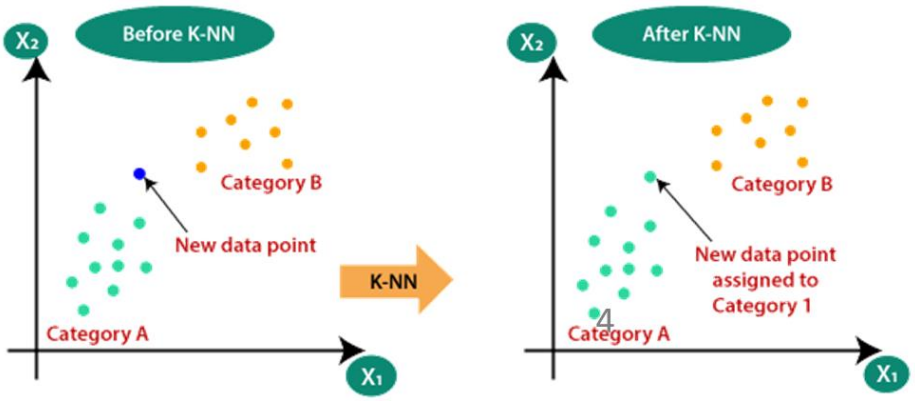

Figure 2. Classification of data points by KNN model.

KNN-working:

The K-NN algorithm can be stated using the following formula:

Step 1: Select your neighbor's number K.

Step 2: Calculate the Euclidean distance between the K nearest neighbors.

Step 3: Using the estimated Euclidean distance, select the K closest neighbours.

Step 4: Count how many data points there are in each category among the k nearest neighbors.

Step 5: Assign the new data to the category with the greatest number of neighbours in Step 5.

Step 6: The model is finished.

Let's say we have a new piece of information that we need to classify. Take a look at the **Figure 3**.

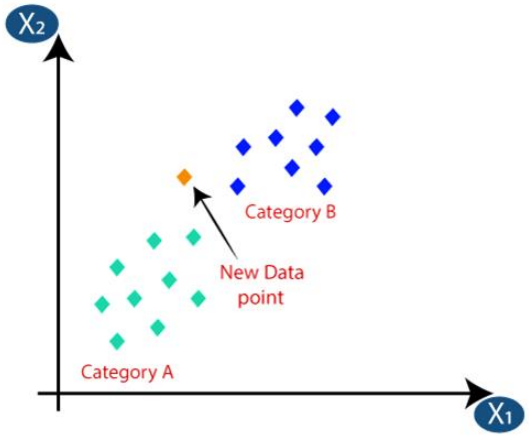

Figure 3. Classifying the data point.

3.2. Support vector machine

The Support Vector Machine (SVM) is a well-liked supervised learning technique that has been successfully applied to issues of classification and regression. However, it is frequently used to fix classification problems in machine learning. The optimal line or decision boundary that may divide n-dimensional space into classes must be developed in order to classify future data points effectively. The hyperplane represents the border of the optimal decision space.

The apexes and axes of the hyperplane are selected by SVM. We call these outlier instances "support vectors", and the corresponding computer is a "support vector machine". **Figure 4** is an example of a decision boundary in the shape of a hyperplane that divides two sets of people.

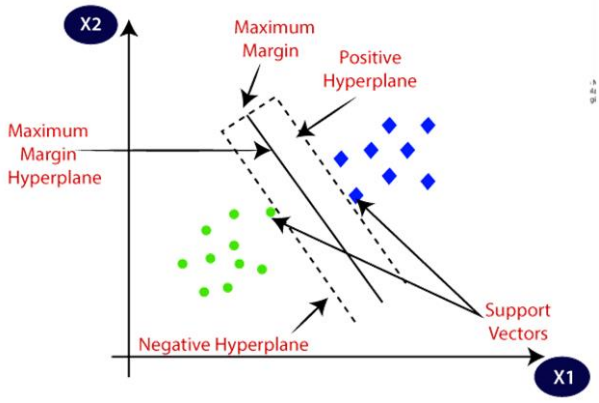

Figure 4. SVM model architecture.

3.3. Decision tree

Decision Tree is a popular supervised learning approach that is used to solve classification issues but may also be used to tackle regression difficulties. Each leaf node in a classifier organised as a tree indicates a classification outcome, while the interior nodes stand in for features in the training data and the branching symbolises the underlying decision rules. Decision Nodes and Leaf Nodes are the two types of nodes found in a decision tree. However, these decisions ultimately result in a dead end, or a leaf node. Decisions and experiments can be grounded on the dataset's characteristics.

It's a diagram that shows you the many outcomes of a decision tree. A decision tree is a structure similar to a tree that has a starting point, or root node, and branches out from there. The Classification and Regression Tree Algorithm (CART) expedites the process of creating a tree. When a question is asked of a decision tree, the tree is split into branches according to the possible responses (yes/no). The decision tree shown in the **Figure 5** has the following basic structure:

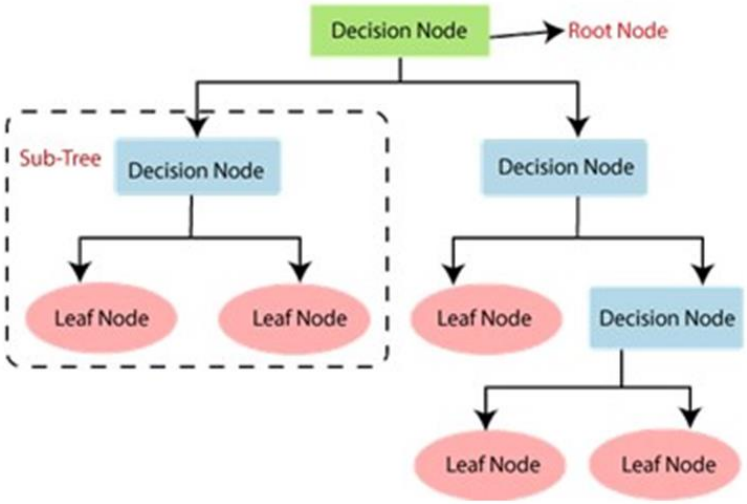

Figure 5. Decision tree working architecture.

3.4. Deep convolutional neural networks

Deep learning is a type of machine learning that may be used to create AI systems. It's built on the idea of artificial neural networks (ANNs), which are essentially networks of artificial neurons designed to do complex analysis on vast data sets. There are several DNNs, or deep neural networks, available. Deep convolutional neural networks (CNN or DCNN) are a type of neural network that are commonly used for pattern detection in images and videos. DCNNs evolved from traditional ANNs by using a three-dimensional neural pattern similar to that of the animal visual brain.

Red, green, and blue are all processed simultaneously by a three-dimensional neural network in a DCNN. When compared to standard feed-forward neural networks, this requires a fraction of the number of artificial neurons to process an image. A deep convolutional neural network processes images to train a classifier. Mathematical operations known as "convolutions" are used instead of matrix multiplication in the network.

Layers of convolution, pooling, activation, and completely linked are typical components of a convolutional network's architecture as shown in **Figure 6**.

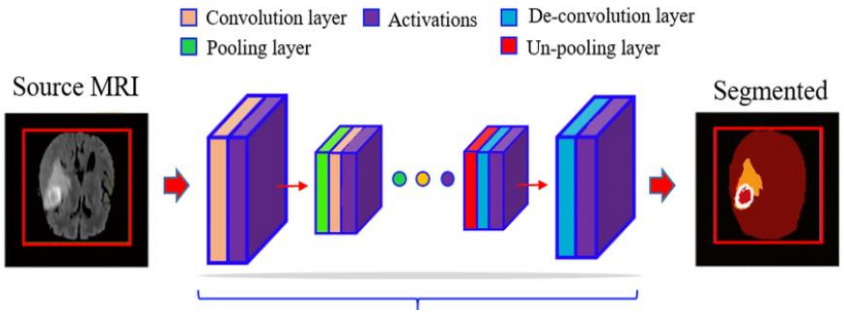

Figure 6. DCCN working model.

Output: Parkinson or healthy.

DCCN working steps: The step-by-step procedure for PDclassification using Pre-trained DeepCNN is given in algorithm.

Input: Pre-trained Model (L_m), training MR Images I_{train} = I_r,validation images (I_{val}),

- Iterations per stage Z = <Z_i … Z_x>,
- Total number of stages X,
- Training data per stage I_{train} = I_{train}^1 … I_{train}^Z,
- Validation data I_{val}
- Validation accuracy ɣ

Output: Hyper-parameters h^*, Predicted labels: 0- for health controls, 1 for PD Patients.

- **Training:**

  – For I Iterations

  For each I €I_{train}

  L L_m

  L.fc.pop()

  L.dense(2.Activation_function)

  for stage x = 1 to X do

  for j = 1 to k

  $ɣ_j$ = evaluate ɣ (h_j.I_{train}^s.I_{val})

  End

  End

  End

- **Validation:**

for iterations

for I € I_{val}

loss←$∫_{Crossentropy}$ (L)

UPDATION OF L_m with loss

Reset $h_{i,k}$ = best k configs € (h_1,h_2,……..h_x)

End

Return h* = maxargs $_{h \in h(x1,x2,…..xz)} ɣ_i$

The Deep convolutional layer uses the image pixels as input for the convolution operation. This makes a convolved map.

- A corrected feature map is produced by passing the convolved map through a ReLU function.
- A number of convolutional and ReLU layers are utilised to pinpoint picture details.
- There are many different ways to use filters and pooling layers to separate parts of an image.
- The final result of the pooled feature map must be flattened and put into a fully linked layer.

4. Implementation

For DCCN model consist of 6 convolutin layers with input size of 512 × 512 × 3. Each layer has the following gradually increasing neuron count with the kernel size as 3 × 3. The details are given in **Table 1**.

Table 1. DCCN layer s neuron count.

Deep convolution layer	Neurons
First Convolution Layer	16
Second Convolution Layer	32
Third Convolution Layer	64
Fourth Convolution Layer	64
Fifth Convolution Layer	128
Sixth Convolution Layer	128

For all convolution layers 'ReLu' Activation function was applied. 'MaxPooling' layer was applied after every convolution layer with the kernel size of 2 × 2. This was followed by three Fully connected Layer (FCL) as follows.

Layer one—512neurons with ReLu Activation function

Layer two—256 Neurons with SoftMax activation function

Layer three—2 neurons and SoftMax Activation function

Lastly Adam Optimizer is applied.

In this implementation a region of substantia nigra of 512 × 512 MRI image is fed to DCNN model to classify the region is PD or not.

5. Results

Experiments were carried out in this part to test the classification performance of several classifiers, such as KNN, decision trees, and SVM. 70% of the data set was used to train the classifiers, while 30% was used to test them. In addition, the classifiers provided all of the necessary model parameters. Classifier performance was evaluated using applied performance evaluation measures. It is important that all features are standardised and normalised before being used in classifiers.

Classification results of machine learning classifiers

A variety of classifiers have been trained and tested on the various datasets, including KNN, decision trees, and support vector machine and DCCN. **Table 2** exhibit the experimental findings of these classifiers.

Table 2. Compares the performance of various classifiers for classification.

Models	Performance of model		
	Accuracy (%)	**Specificity (%)**	**Sensitivity (%)**
KNN	89.3%	82.6	80.3
DCCN	93.7%	89.4	88.7
SVM	91.2%	82.1	84.2
Decision Tree	90.6%	86.4	85.7

The suggested DCCN approach has a classification accuracy of up to 93.7%, which is higher than decision trees at 90%, KNN at 89.3%, and SVM at 91.27% as shown in **Figure 7**.

The comparison is shown in **Table 3**.

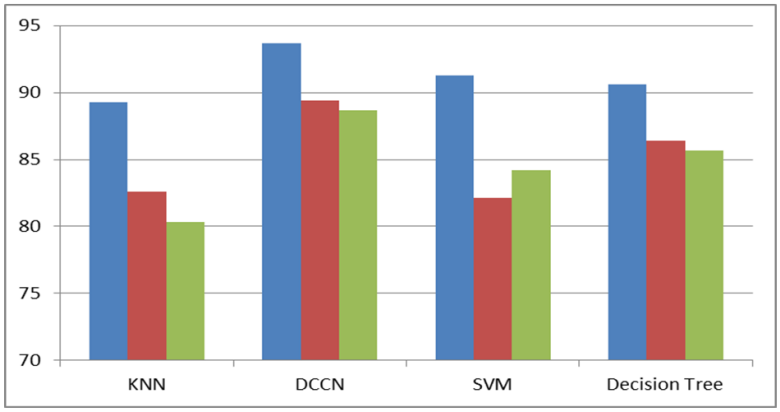

Figure 7. Different models' performances on datasets are depicted.

Table 3. Compares the performance of various classifiers on the database with each other.

Models	Performance of model		
	Accuracy (%)	**Specificity (%)**	**Sensitivity (%)**
KNN	88.8	85.4	86.3
DCCN	94.2	90.4	90.7
SVM	88.2	83.3	84.8
Decision Tree	89.6	88.4	83.3

The comparison of different models performance as shown in **Figure 8**.

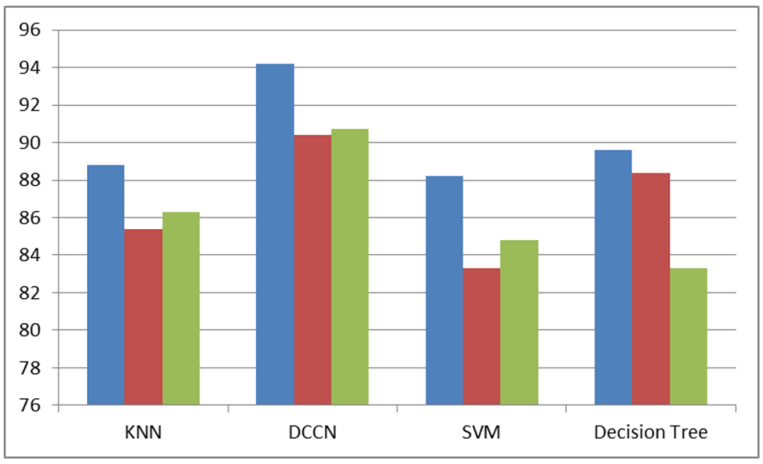

Figure 8. Performance of different models on the dataset.

The proposed DCCN approach achieves up to 94.2 percent classification accuracy, compared to 89.6 percent for decision trees, 88.8 percent for KNN, and 88.2 percent for SVM.

Figure 9 below shows the comparison of models using various databases.

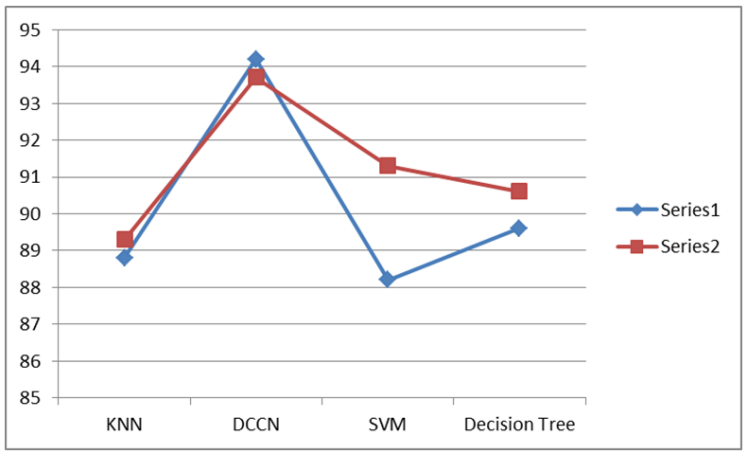

Figure 9. Comparison of different models.

When comparison to the other models, the DCCN model performed admirably. This model produced 94.2 percent of the results using the PET database.

6. Conclusion

This paper has listed out the 4 different ML models on MRI brain images to classify the disease. The accuracy of different machine learning classifiers' predictions of Parkinson's disease was examined in this study. KNN, decision tree, support vector machine, and DCCN have been used to classify this data. The DCCN classifier outperformed the KNN, the SVM, and the DT in terms of accuracy. Our results show that DCCN is an effective classifier for predicting Parkinson's disease based on data from PET and SPECT scans. Using techniques like feature selection and optimization, it will be easier to spot PD. DCCN Machine Learning model generated the 94.2% Accuracy, 90.4 Specificity and 90.7% sensitivity is best among all the other models.

Author contributions

Conceptualization, RB and TPK; methodology, RB; software, RB; validation, RB and TPK; formal analysis, RB; investigation, RB; resources, RB; data curation, RB; writing—original draft preparation, RB; writing—review and editing, RB; visualization, RB; supervision, TPK; project administration, RB; funding acquisition, RB. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

References

1. Hou Y, Shang H. Magnetic Resonance Imaging Markers for Cognitive Impairment in Parkinson's Disease: Current View. Front Aging Neurosci. 2022; 14. doi: 10.3389/fnagi.2022.788846
2. Blair JC, Barrett MJ, Patrie J, et al. Brain MRI Reveals Ascending Atrophy in Parkinson's Disease Across Severity. Front Neurol. 2019; 10. doi: 10.3389/fneur.2019.01329
3. Bron EE, Smits M, Niessen WJ, Klein S. Feature Selection Based on the SVM Weight Vector for Classification of Dementia. IEEE J Biomed Health Inform. 2015; 19(5): 1617-1626. doi: 10.1109/jbhi.2015.2432832

4. Aubin PM, Serackis A, Griskevicius J. Support Vector Machine Classification of Parkinson's Disease, Essential Tremor and Healthy Control Subjects Based on Upper Extremity Motion. In: Proceedings of 2012 International Conference on Biomedical Engineering and Biotechnology; 2012. doi:10.1109/icbeb.2012.387
5. Zhang Y, Burock MA. Diffusion Tensor Imaging in Parkinson's Disease and Parkinsonian Syndrome: A Systematic Review. Front Neurol. 2020; 11. doi:10.3389/fneur.2020.531993
6. Gupta D, Julka A, Jain S, et al. Optimized cuttlefish algorithm for diagnosis of Parkinson's disease. Cognitive Systems Research. 2018; 52: 36-48. doi: 10.1016/j.cogsys.2018.06.006
7. Li T, Li W, Yang Y, Zhang W. Classification of brain disease in magnetic resonance images using two-stage local feature fusion. PLoS ONE. 2017; 12(2): e0171749. doi: 10.1371/journal.pone.0171749
8. Pandya S, Zeighami Y, Freeze B, et al. Predictive model of spread of Parkinson's pathology using network diffusion. NeuroImage. 2019; 192: 178-194. doi: 10.1016/j.neuroimage.2019.03.001
9. Ramaniharan AK, Manoharan SC, Swaminathan R. Laplace Beltrami eigen value based classification of normal and Alzheimer MR images using parametric and non-parametric classifiers. Expert Systems with Applications. 2016; 59: 208-216. doi: 10.1016/j.eswa.2016.04.029
10. Rahman A, Rizvi SS, Khan A, Afzaal Abbasi A, Khan SU, Chung TS. Parkinson's Disease Diagnosis in Cepstral Domain Using MFCC and Dimensionality Reduction with SVM Classifier. Mobile Information Systems. 2021; 2021: 1-10. doi: 10.1155/2021/8822069
11. Goldman JG, Litvan I. Mild cognitive impairment in Parkinson's disease. Minerva Med. 2011; 102(6): 441-459.
12. Li S, Lei H, Zhou F, et al. Longitudinal and Multi-modal Data Learning for Parkinson's Disease Diagnosis via Stacked Sparse Auto-encoder. 2019 IEEE 16th International Symposium on Biomedical Imaging (ISBI 2019). Published online April 2019. doi: 10.1109/isbi.2019.8759385
13. Davatzikos C, Fan Y, Wu X, Shen D, Resnick SM. Detection of prodromal Alzheimer's disease via pattern classification of magnetic resonance imaging. Neurobiology of Aging. 2008; 29(4): 514-523. doi: 10.1016/j.neurobiolaging.2006.11.010
14. Prashanth R, Dutta Roy S, Mandal PK, Ghosh S. Automatic classification and prediction models for early Parkinson's disease diagnosis from SPECT imaging. Expert Systems with Applications. 2014; 41(7): 3333-3342. doi: 10.1016/j.eswa.2013.11.031
15. Zhang J. Mining imaging and clinical data with machine learning approaches for the diagnosis and early detection of Parkinson's disease. npj Parkinsons Dis. 2022; 8(1). doi: 10.1038/s41531-021-00266-8
16. Dickson DW. Parkinson's Disease and Parkinsonism: Neuropathology. Cold Spring Harbor Perspectives in Medicine. 2012; 2(8): a009258-a009258. doi: 10.1101/cshperspect
17. Perez C, Roca YC, Naranjo L, Martin J. Diagnosis and Tracking of Parkinson's Disease by using Automatically Extracted Acoustic Features. J Alzheimers Dis Parkinsonism. 2016; 6(5). doi: 10.4172/2161-0460.1000260
18. Gündüz H. Deep Learning-Based Parkinson's Disease Classification Using Vocal Feature Sets. IEEE Access. 2019; 7: 115540-115551. doi: 10.1109/access.2019.2936564
19. Previtali F, Bertolazzi P, Felici G, Weitschek E. A novel method and software for automatically classifying Alzheimer's disease patients by magnetic resonance imaging analysis. Computer Methods and Programs in Biomedicine. 2017; 143: 89-95. doi: 10.1016/j.cmpb.2017.03.006
20. Islam J, Zhang Y. A novel deep learning based multi-class classification method for Parkinson's Disease detection using brain MRI data. In: Proceedings of International Conference on Brain Informatics; Beijing, China; 2017. pp. 213–222.
21. Lawton M, Ben-Shlomo Y, May MT, et al. Developing and validating Parkinson's disease subtypes and their motor and cognitive progression. J Neurol Neurosurg Psychiatry. 2018; 89(12): 1279-1287. doi: 10.1136/jnnp-2018-318337
22. Jankovic J. Parkinson's disease: Clinical features and diagnosis. Journal of Neurology, Neurosurgery & Psychiatry. 2008; 79(4): 368-376. doi: 10.1136/jnnp.2007.131045
23. Yadav R, Shukla G, Goyal V, Singh S, Behari M. A case control study of women with Parkinson's disease and their fertility characteristics. Journal of the Neurological Sciences. 2012; 319(1-2): 135-138. doi: 10.1016/j.jns.2012.05.026
24. Rizzo G, Copetti M, Arcuti S, et al. Accuracy of clinical diagnosis of Parkinson disease. Neurology. 2016; 86(6): 566-576. doi: 10.1212/wnl.0000000000002350