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Diagnosing Neurourological Complications of Parkinson's Disease with Self-Adaptive Convolutional Neural Networks through MRI Analysis

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Abstract

Parkinson's disease (PD) is a progressive and degenerative neurological disorder that primarily disrupts the brain's motor functions, leading to symptoms like bradykinesia, stiffness, balance problems, and resting tremors. The intricate nature of PD, which often resembles other neurological conditions and involves subtle structural brain changes, complicates accurate diagnosis, resulting in a 25% diagnostic error rate. To address this challenge, the research community has employed various machine learning techniques using manually crafted features for diagnosis. This study introduces an innovative computer-aided diagnostic approach for PD based on a self-adaptive convolutional neural network (SCNN), a potent model for automatically extracting essential problem features. The Parkinson's Progression Markers Initiative (PPMI) provided the dataset used in this investigation, which includes a variety of datasets such as T2-weighted MRI scans from both PD individuals as well as healthy controls (HC). In particular, mid-slice MRI data is gathered and registered in order to be aligned. To pinpoint the region of interest in the midbrain, a 33 × 33-sized window is employed, as PD primarily affects the substantia nigra within the midbrain. Comprehensive experiments have been conducted to validate the reliability of the SCNN approach. Using common evaluation measures like area under the curve, specificity, sensitivity, and accuracy, the suggested method's performance is evaluated. Notably, the evaluation findings show that in terms of diagnostic precision, the SCNN performs better than other machine learning techniques

Key words: Parkinson's disease, SCNN, MRI analysis, CAD diagnosis, Substantia nigra and Neurodegenerative disorders.

Introduction

Parkinson's disease is a debilitating neurological ailment that substantially reduces an individual's capacity to execute motor and non-motor functions. The first comprehensive account of Shaking Palsy was given in James Parkinson's seminal work, "An Essay on the Shaking Palsy," which came out in 1817 [1]. The disease is caused by dopaminergic neurons, which are found in the substantia nigra, an important sub-cortical area of the brain that regulates movement. Parkinson's disease can present with a variety of early symptoms, including tremors, reduced handwriting, olfactory impairment, sleep disturbances, mobility issues, constipation, a progressive loss of speech volume, an expression that is uncharacteristically animated, episodes of dizziness or fainting, and a propensity to bend or hunch over. Early signs of a nervous system issue are frequently indicated by these symptoms.

The accumulation of misfolded protein molecules within cells is the main cause of Parkinson's disease, which ultimately results in neurodegeneration. Even if a number of drugs, including dopamine agonists, MAO-B inhibitors, and levodopa (L-DOPA) [2], are used as first treatments, their efficacy gradually wanes. In addition, patients frequently encounter unwanted side effects as dosages rise in order to maintain efficacy. It is important to stress that although there is no known cure for Parkinson's disease, medication can help regulate the disease's course and reduce symptoms. Sadly, there is currently no proven treatment for this illness, which emphasizes how critical it is to concentrate on early discovery and intervention. Parkinson's disease is the second most prevalent neurological disorder globally, affecting about 10 million people. In addition, individuals under the age of 50 may be affected by this condition, and it's significant to highlight that men get diagnosed with Parkinson's disease at a higher incidence than women.

The deterioration of gait, or the rhythmic pattern of movements involved in walking, is one of the most noticeable motor abnormalities associated with Parkinson's disease. One essential aspect of walking is the gait

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cycle, which consists of a sequence of synchronized physical movements. When evaluating a patient's gait, medical practitioners frequently look at criteria including shorter strides, slower walking during free ambulation, and changes in cadence rate [3]. These changes are suggestive of Parkinson's disease. Early identification of Parkinson's disease is essential, given the limits of current treatments that only offer transient symptom alleviation. The illness advances more quickly in this early stage, so it's critical to find new tools or markers for an early diagnosis. Early detection of Parkinson's disease would give rise to opportunities for more efficient management and could perhaps impede the disease's advancement. Hence the major contribution of the proposed work is,

- This article presents the use of a (CNN) for the diagnosis of Parkinson's disease. CNNs are known for excellent feature extraction and pattern recognition from complex data, making them a novel PD diagnosis tool. Using a CNN model, researchers can use deep learning to effectively identify PD from MRI scans, outperforming typical machine learning methods.
- Another benefit of the proposed computer-aided diagnostic system is better diagnostic accuracy. CNN diagnoses PD better than naive Bayes, decision trees, support vector machines, and artificial neural networks, according to the study. The research uses CNNs and the Parkinson's Progression Markers Initiative (PPMI) dataset to improve PD diagnosis accuracy by 25%. This accuracy gain is critical for early Parkinson's disease intervention and better management.

Related Works

The implementation of various (ML) and (DL) approaches has led to considerable breakthroughs in the classification of Parkinson's disease (PD) in recent studies. Fully automated and semi-automated methods are among these techniques:

Analysis of Gait Employing DL [4] suggests that a unique intelligent model was presented by analyzing gait data with DL methods. A 1D convolutional network was used to handle the data from 18-ID signals, which measure (VGRF) and are derived from foot sensors. The model not only detects Parkinson's disease but also predicts its severity, achieving an impressive accuracy of 98.7%. Vowel-Based PD Detection [5] an intelligent system was developed for PD detection using vowel features. The minimum average maximum (MAMa) tree and singular value decomposition (SVD) were used for the extraction of characteristics, and picking feature approaches were used to choose 50 unique features. A K-nearest neighbors (KNN) algorithm was used for classification, and 92% accuracy was attained.

CNN-Based Neuroimaging Classification [6] a convolutional neural network (CNN)-based model was presented for classifying PD and healthy controls (HC) using neuromelanin-sensitive magnetic resonance imaging (NMS-MRI). With 25 PD and 35 HC among the 45 individuals in the sample, the model's higher testing accuracy was 80%. A revolutionary intelligent system that encompassed every region of the brain and gathered feature vectors from each is provided by the Whole-Brain Network Approach [7]. Support vector machines were utilized for classification, and random forests were used for feature selection. With 169 HC and 374 PD participants in the(PPMI) data set, this model demonstrated a 93% accuracy rate throughout training and testing.

For Voice-Based PD, MLFNN Diagnosis [8] refers to a machine learning-based method of PD diagnosis that makes use of a (MLFNN). The data came from the Oxford Parkinson's datasets and comprised speech measures from 31 individuals (10 normal controls and 21 Parkinson disease patients). The model demonstrated effectiveness with a level of sensitivity of 83.3%, specific of 63.6%, and overall accuracy of 80%.

Swarm Optimization for Feature Extraction [9] where a dataset from the UCI repository was used, and swarm optimization was applied for feature extraction. Classification was performed using naive Bayes, resulting in an impressive accuracy of 97.5%. Non-Motor Features in PD Diagnosis [10] examined the use of non-motor characteristics in PD diagnosis, such as (REM), olfactory loss, and sleep behavior disorder. These non-motor characteristics were paired with additional markers such measures of CSF fluid and dopaminergic imaging. Boosted tree, SVM, random forests, and Bayes were among the several classification methods used; SVM yielded an accuracy of 96.4%. Considering non-motor symptoms alongside motor symptoms enhances diagnostic accuracy, even in the early stages of PD, and aids in differentiation from other neurological disorders. In addition to advancing PD diagnosis, these studies demonstrate the potential for applying ML and DL techniques to differentiate PD from other neurological conditions, providing valuable insights for early and accurate diagnosis and tailored treatment approaches.

Proposed Model Taxonomy

Pre-processing stage

T The original DICOM format was used to store the magnetic resonance (MR) images. Then, they were transformed into JPEG format by use of the freely available DICOM to JPEG application. There were 45 slices in the data set for each participant; however, only slice number 22 was selected for each individual due to its precise depiction of the substantia nigra, an important mid-brain region that regulates movement and motor control. The substantia nigra produces dopamine, which is a signaling chemical that communicates with the brain and other body parts regarding movement and coordination.

All of the slice number 22 photos were stacked together to provide a coherent dataset. After that, intensity-based image registration was used to align these photos, a process made possible by the OpenCV framework. Aligning brain scans or pertinent regions taken from Parkinson's disease patients is the technique of image registration. Through the establishment of a regular spatial relationship between the images, this alignment guarantees consistency and uniformity throughout the study. The process of image registration removes variations resulting from variances in patient location or scanning techniques by bringing the images into a standard coordinate system. Removing any undesired or irrelevant data that would cause the model to learn redundant and needless features was the main goal of the image registration process.

Using an area of 33 × 33 pixels, the mid-brain slice was isolated using the freehand (ROI) method in order to produce an accurate image of the substantia nigra. Given that various patients may have differing sizes of this particular organ, the freehand ROI approach was chosen. The precise control over cropping the organ's specific position was accomplished by using the freehand ROI technique. The final input for the convolutional neural network (CNN) model was this processed image.

Self-adapting Convolution Neural Network Model

CNN architecture has found application in various image-related tasks, including image classification and recognition, where it often outperforms other models. For instance, in a recent study [8], a deep CNN-based system for diagnosing COVID-19 from cough sounds was proposed, and it was shown to outperform alternative models. Another article [9] suggested the use of CNN for the classification of lung diseases, particularly on chest X-ray images, resulting in improved classification accuracy compared to previous techniques. The layers of convolution, function activation, map features, maximum pooling, and normalization are the fundamental components of the CNN architecture.

The initial convolutional layer, a crucial part of the CNN structure, takes input data and processes local spatial information using convolutional kernels, followed by an activation function that reports activation values. Multiple convolutional layers can be stacked to create a feature hierarchy, progressively extracting and learning more intricate features. The number of convolutional filters used determines the quantity of feature maps generated. For every pixel in the feature map, the activation function represents spatial neighbourhood activation. A maximum pooling layer thereby lowers the dimensionality of the input, minimizes the danger of overfitting, and uses less computational power. To build a hierarchical design, the max pooling layer's output can be passed into an additional convolutional layer. The dense layer connects every neuron to the final feature maps, and for classification purposes, the softmax function serves as the activation function. These components collectively form the fundamental building blocks of the CNN model.

Initiating weight values

Deep learning heavily relies on appropriate weight initialization, a crucial factor that accelerates convergence and stabilizes the loss function, even after numerous iterations. In this study, we employ the Xavier initializer, designed to maintain specified levels of backpropagation gradient and activation variance [10].

$$\text{Weights} \sim Unormal\left[-\frac{\sqrt{6}}{\sqrt{wei+(wei+1)}}, \frac{\sqrt{6}}{\sqrt{wei+(wei+1)}}\right] \quad (1)$$

In Equation (1), the utilization of Unormal as a normal distribution, wei as the input layer weight, and w+1 as the output layer weight is illustrated.

Kernel Convolution stage

When convolution is applied to an image, it initiates the generation of feature maps, with each kernel producing its set of features. The calculation of the feature map F can be achieved using the formula provided,

$$F = \text{bias} + [Mk_1 * Nc_1 + Mk_2 * Nc_2 + \ldots + Mk_n * Nc_n] \quad (2)$$

where Nc represents the input channel, and Mk signifies the kernel.

Activation function

The system becomes non-linear during the activation function phase. Even though a number of mechanisms for activation have been suggested and are still being studied, each has a unique set of restrictions and might not be appropriate in all situations. For instance, the sigmoid function exhibits the vanishing gradient problem, while ReLU, despite the risk of dead neurons, often yields superior results compared to sigmoid and hyperbolic tangent functions. ReLU's tendency to disregard gradients below zero is another concern. To address these issues, the enhanced LeakyReLU incorporates a negative gradient parameter α, which can take any real value between 0 and 1.

$$f(x) = \text{maximum}(0, x) \quad (3)$$

$$f'(x) = f(x) + \alpha\text{minimum}(0, x) \quad (4)$$

Pooling layer

Pooling operations serve to reduce the dimensionality of feature maps and filter out minor variations in illumination and intensity. These days, the most popular pooling strategies are max, min, and typical pooling. Within the pooling kernel, max pooling determines the maximum value, min pooling selects the smallest value, and average pooling determines the mean value. The average impact of all the features is returned via pooling, which calculates the mean of each characteristic in the pooling kernel.

Fully connected stage with regulation

The primary goal of normalizing is to prevent the model from being overfit. Many techniques, including widely used ones like batch normalizing, global average gathering, global max pooling, and L1 and L2 regularization, can be used to avoid overfitting. Another useful strategy is called Dropout, which ensures that each person contributes to the final product by arbitrarily activating or deactivating neurons to facilitate successful learning. We use dropout with a variable p in this study, where p can take on any real number between 0 and 1. The operation of Dropout can be understood through the formula:

$$yk = \sum M \in M * Pr(m)ykM \quad (5)$$

Here, yk represents the likely result of unit k, M denotes the set of all pruned networks, y^M signifies the output of unit M, and Pr() represents the probability function.

The fully connected layers come after the convolutional layers. In these layers, every pixel in the image is treated as a neuron and communicates with every other neuron in the layer. The classification task is handled by a classifier in this last layer; Softmax is a popular classification in deep neural networks. One can define Softmax by applying Bayes' theorem.

$$p(Ck|x) = \sum j = 1\, np(x|Cj)p(Cj)p(x|Ck)p(Ck) \quad (6)$$

Here, Ck signifies the target class for identification, and Cj represents classes for j=1,2,3,...,n. Its exponential form is as follows:

$$\sigma(a1)_k = \frac{e^{a1_k}}{\sum_{j=1}^{n} a1_j} \quad (7)$$

Furthermore, evaluating the degree of alignment between the predicted values and the given ground truth label also heavily relies on the loss function. Although the loss function can be customized for a given task, categorical cross-entropy is a commonly used cost function in classification tasks, and it is formalized as follows:

$$f_{\text{cost}}(x) = -\sum_{a \in \text{voxels}} \sum_{b \in \text{classes}} c_{a,b} \log\left(\hat{c}_{a,b}\right) \quad (8)$$

Here, c represents the actual target class, and c^{(a,b)} is the class that Equation predicts(8).

Training the proposed model

Upon receiving MRI data as input, our proposed model undertakes the task of classifying the data into PD or HC categories. Our approach makes use of a deeper CNN network with compact 3 x 3 convolutional kernels. Opting for smaller convolutional kernels, which entail fewer parameters to estimate, facilitates the model's ability to learn and generalize effectively, even when trained on limited datasets. In contrast, larger convolutional kernels necessitate more abundant training data, involve a higher number of parameter estimates, and exhibit lower generalizability. To enhance model performance, we incorporate the advanced LeakyReLU activation function after each convolutional kernel. LeakyReLU modifies negative gradients during backpropagation, which successfully tackles problems such as the dying ReLU problem. Furthermore, each LeakyReLU layer is preceded by batch normalization, which speeds up the network's training process. Our network is designed to handle 33 × 33 input patches.

First, the architecture consists of three convolutional layers. Next, there is a max pooling layer that has a 2 × 2 stride and a 3 × 3 kernel. The output, referred to as feature maps, from the initial max pooling layer consists of 64 channels and measures 16 × 16 in dimensions. By adding the max pooling layer, the total dimensionality as well as the amount of learnable parameters are decreased. The following three convolutional layers receive the feature output map from the first max pooling layer. The output feature maps generated by the sixth convolution layer, with a size of 128 × 16 × 16, are processed by the second max pooling layer, which has a 2 × 2 stride and a 3 × 3 kernel. The output feature maps that are produced from this layer of pooling have size of 128 × 7 × 7.

Two fully connected (FC) layers are involved in the processing that follows. There are 512 neurons in the first FC layer and 256 neurons in the second layer. To mitigate the risk of network overfitting, we have introduced dropout with a 0.1 value in both FC layers, representing an advanced regularization technique. At the network's conclusion, we employ a softmax layer to determine classification probabilities. A visual representation of our proposed model can be found in Figure 1, and detailed information regarding the model's architecture and parameters is presented. In Table 1, " The total amount of input channel and the feature map's or patch size's dimensions are shown in the "Inputs" column.

Table 1: Configuration of the SCNN architecture

Layers	Category	Filter	Stride size	Filters (#)	Units of fully connected layer	Input
Layer 1	Convolution	3 × 3	1 × 1	64	-	33 × 33
Layer 2	Convolution	3 × 3	1 × 1	64	-	64 × 33 × 33
Layer 3	Convolution	3 × 3	1 × 1	64	-	64 × 33 × 33
Layer 4	MaxPooling	3 × 3	2 × 2	-	-	64 × 33 × 33
Layer 5	Convolution	3 × 3	1 × 1	128	-	64 × 16 × 16
Layer 6	Convolution	3 × 3	1 × 1	128	-	128 × 16 × 16
Layer 7	Convolution	3 × 3	1 × 1	128	-	128 × 16 × 16
Layer 8	MaxPooling	3 × 3	2 × 2	-	-	128 × 16 × 16
Layer 9	FullyConnected	-	-	-	512	6272
Layer 10	FullyConnected	-	-	-	256	512
Layer 11	FullyConnected	-	-	-	2	256

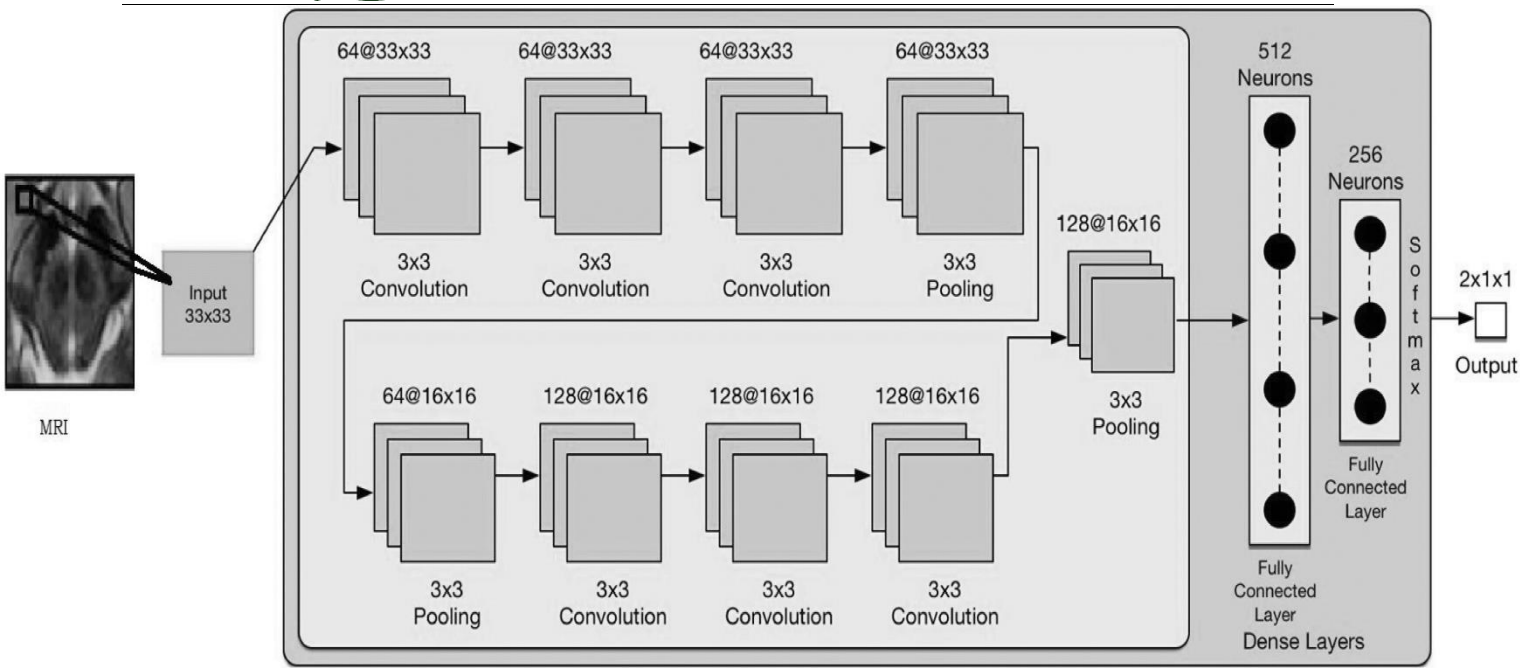

Figure 1: Proposed self-adaptive CNN model

Empirical Results

Utilized PPMI dataset for the study. PPMI dataset is a comprehensive and longitudinal resource designed for advancing research on Parkinson's disease (PD). It encompasses clinical assessments, neuroimaging data (including MRI and DaTscan), genetic information, biospecimens, and cognitive assessments collected from both early-stage PD patients and healthy control subjects across multiple international clinical sites. Finding biomarkers that can help diagnose Parkinson's disease (PD), monitor the disease's course, and maybe direct the development of new treatments is the main goal of PPMI. This open-access dataset serves as a crucial foundation for researchers worldwide, facilitating collaborative efforts to unravel the complexities of PD and improve our understanding of this neurodegenerative disorder.

Our CNN-DL classifier demonstrated remarkable performance in the context of Parkinson's disease (PD) classification. During cross-validation, it exhibited an impressive accuracy rate of 83.7% with an Area Under the Receiver Operating Characteristic (AU-ROC) score of 0.90. When tested on an independent dataset, the classifier maintained a high level of accuracy, achieving 80% with an AU-ROC score of 0.91. In comparison, traditional classifiers like CR-ML struggled, yielding a cross-validation accuracy of only 52.7% and a test accuracy of 56.5%, along with lower AU-ROC scores. The RA-ML classifier fared better with an 81% cross-validation accuracy. Figure 2 graphically illustrates the stark contrast in performance between the CNN-DL algorithm and the other two traditional methods, making it evident that deep learning approaches like CNN-DL are particularly well-suited for complex classification tasks like distinguishing PD from controls.

Detailed results, including accuracy, sensitivity, and specificity metrics, are provided in Table 2, offering a comprehensive view of the classifier's performance. Notably, radiomics-based features played a crucial role in achieving accurate classifications. Features such as run length, non-uniformity, surface-volume ratio, and grey level emphasis emerged as the most influential factors in distinguishing PD cases, as highlighted in Figure 3. The Class Activation Maps derived from CNNs (depicted in Figure 4) provide further insights into the neural activity patterns of different patients. Interestingly, a common trend emerged, with activations predominantly concentrated in the left substantia nigra pars compacta (SNc) across most patients. This observation was quantitatively analyzed and is presented in Fig. 5, revealing a statistically significant difference in the intensity of activations between the left and right SNc regions, with the left side showing a more pronounced difference (p-value = 0.09). This finding has intriguing implications for our understanding of PD pathology.

Furthermore, healthy control subjects (HCs) exhibited similar patterns of activation, with more pronounced left-side dominance. While this difference did not reach statistical significance (p-value = 0.35), it still suggests that neural activation patterns in the SNc may hold valuable insights into PD diagnosis. In summary, our PD

classification model, especially when leveraging deep learning techniques like CNN-DL, demonstrated exceptional accuracy and robustness. In cross-validation, it achieved an accuracy rate of 81.8%, which further improved to 85.7% during testing, as shown in Table 2. Figure 6 supplements these findings with visual representations of ROC curves for both cross-validation and testing, along with sample heatmaps for two distinct subjects. This study underscores the potential of advanced machine learning approaches in enhancing our ability to diagnose and understand PD.

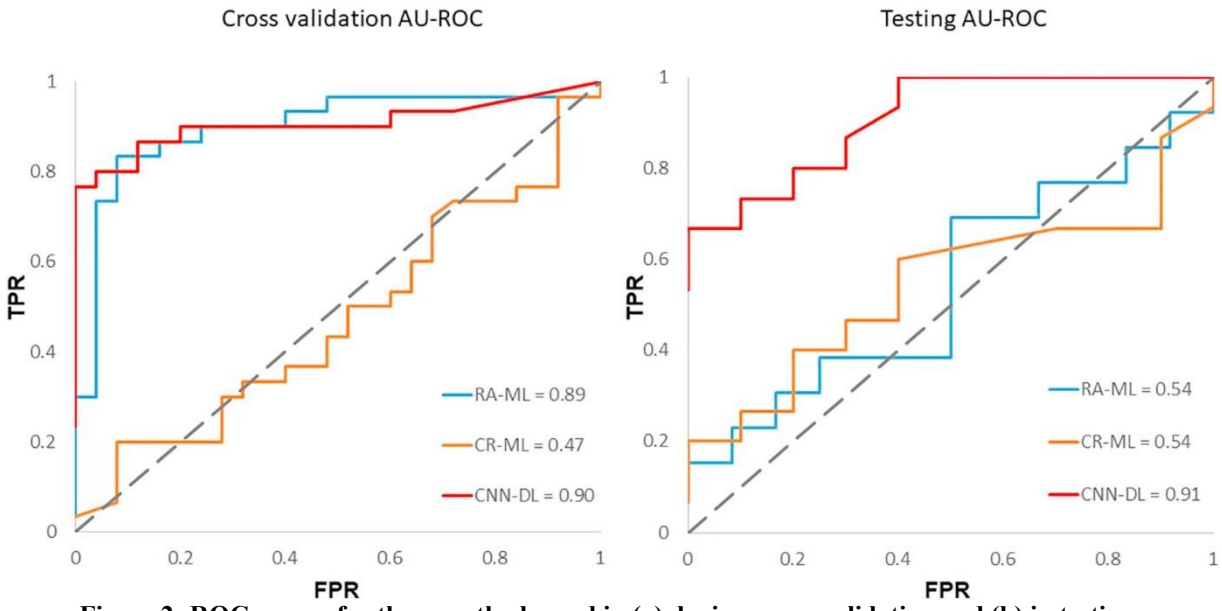

Figure 2: ROC curves for three methods used in (a) during cross-validation and (b) in testing

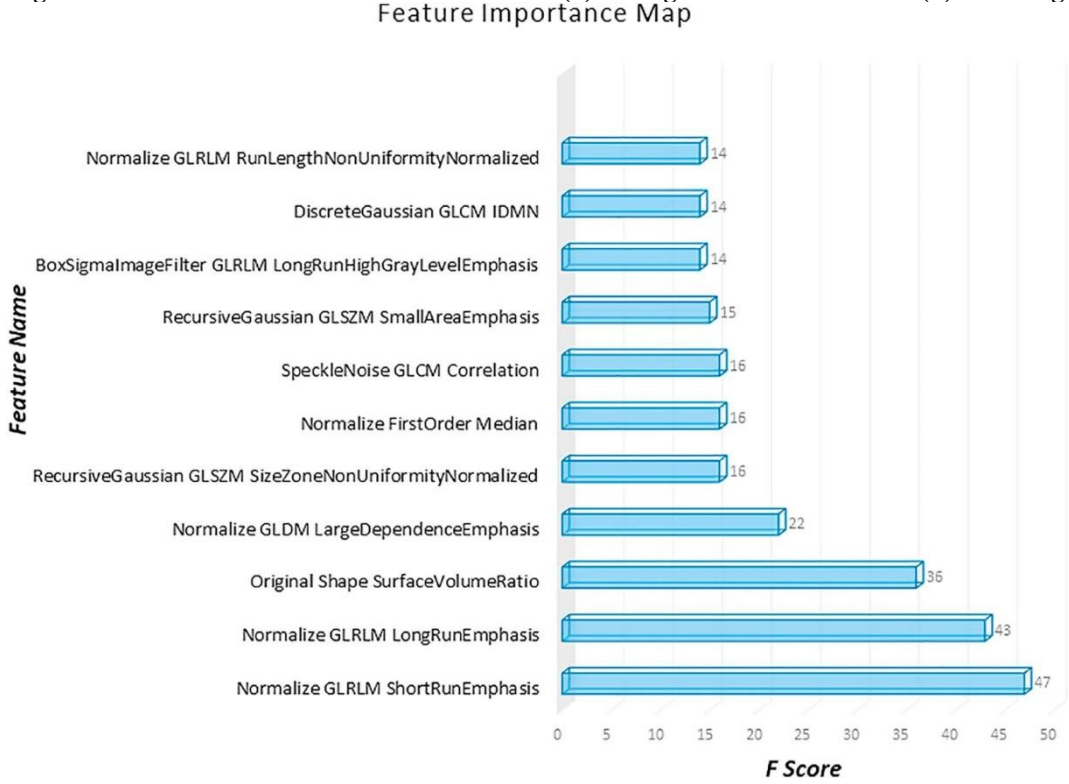

Figure 3: Feature vs F-score

The findings of this study highlight the significant potential of advanced machine learning, particularly convolutional neural networks with deep learning (CNN-DL), in the classification of Parkinson's disease (PD). The performance of the CNN-DL classifier, with a cross-validation accuracy of 83.7% and a test accuracy of 80%, underscores its ability to effectively discriminate between PD patients and healthy controls. These results

are particularly promising in the context of a complex and multifaceted disorder like PD, where early and accurate diagnosis is crucial for timely intervention. In comparison, traditional classifiers, such as CR-ML and RA-ML, fell short in terms of accuracy and robustness. These results emphasize the superiority of deep learning techniques, which can automatically learn relevant features from the data, over handcrafted feature-based methods. The ROC curves presented in Figure 2 vividly illustrate the disparity in performance between the CNN-DL algorithm and traditional approaches, further affirming the potential of deep learning in PD diagnosis. Radiomics-based features emerged as key contributors to the success of the CNN-DL classifier. Features like run length, non-uniformity, surface-volume ratio, and grey level emphasis played pivotal roles in distinguishing PD cases. This underscores the importance of leveraging advanced feature extraction methods in combination with deep learning models to harness the full discriminatory power of medical imaging data. Figure 3 provides a visual representation of the significance of these radiomics-based features, shedding light on the factors that influence accurate PD classification.

Class Activation Maps generated from CNNs revealed intriguing insights into the neural activity patterns associated with PD. The consistent activation of the left substantia nigra pars compacta (SNc) across most patients suggests a potential biomarker for the disease. While the difference between left and right activations was statistically significant in PD patients (p-value = 0.09), a similar trend was observed in healthy control subjects (p-value = 0.35). This intriguing finding warrants further investigation and could potentially aid in early PD diagnosis. The classification model's strong performance during cross-validation and testing, with accuracy rates of 81.8% and 85.7%, respectively, underscores its robustness and potential clinical utility. The ROC curves in Figure 6 provide a visual representation of the classifier's discrimination ability, highlighting its effectiveness in both validation and real-world testing scenarios. In conclusion, this study demonstrates the promise of CNN-DL-based approaches in PD diagnosis, offering high accuracy and valuable insights into disease-related neural activity patterns. These results may improve the early detection of Parkinson's disease (PD), resulting in earlier therapies and better patient outcomes. Subsequent studies could examine the application of these artificial intelligence models in clinical settings and delve more into the molecular principles underlying left SNc activation in Parkinson's disease.

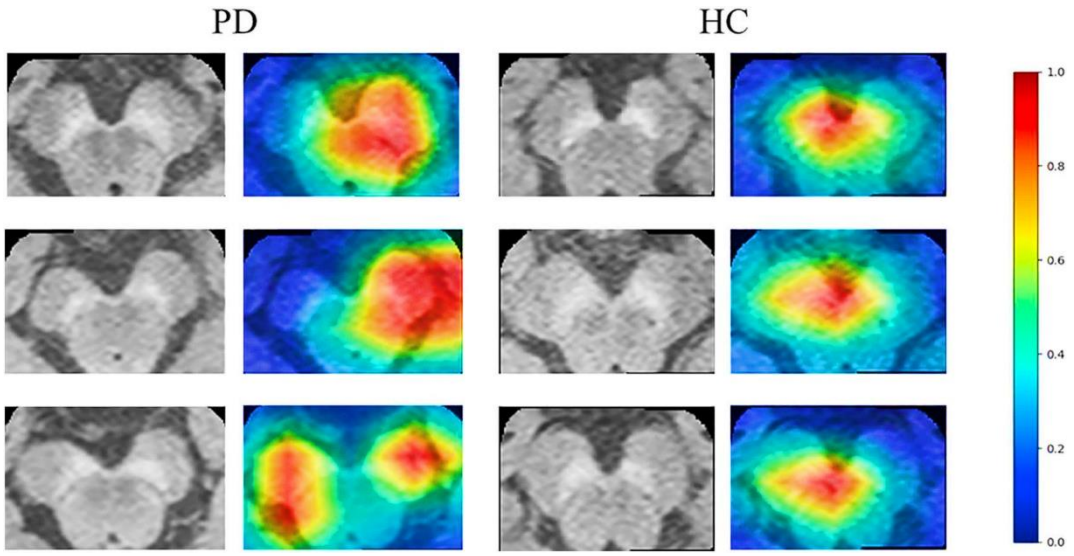

Figure 4: The Class Activation Maps of PD patients indicate significant activity in the SN region during the classification of PD individuals from controls. In the case of the third subject, both the left and right SNcs exhibit activation, whereas the first two subjects only activate the left SNc

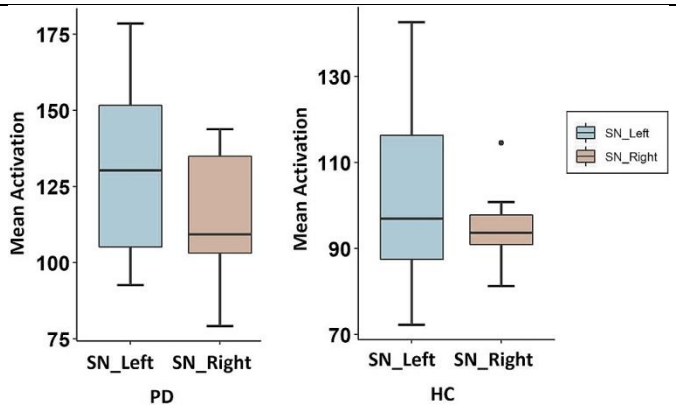

Figure 5: Boxplot of SCNN

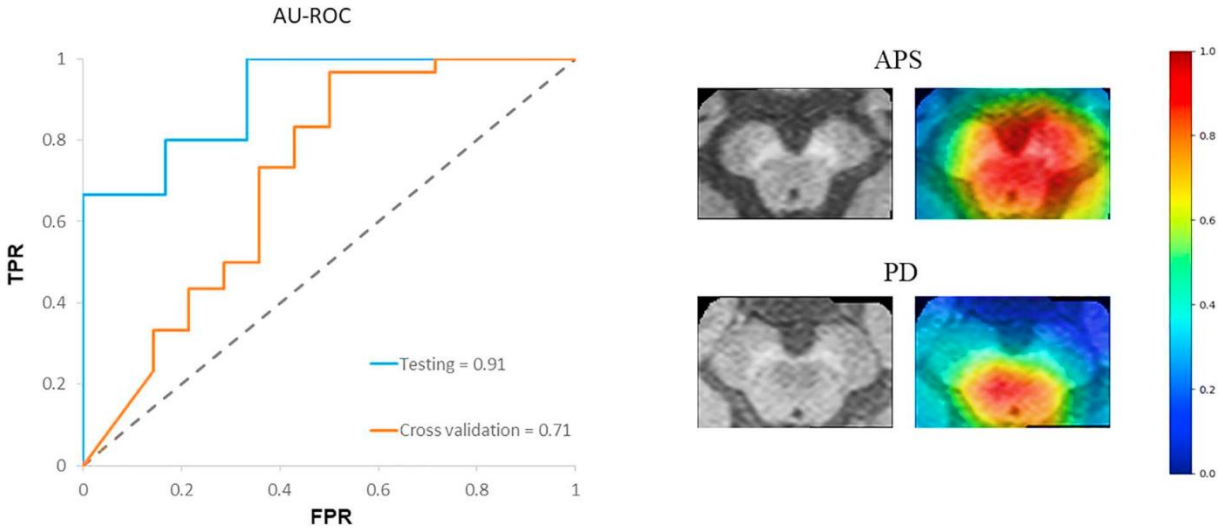

Figure 6: (a) ROC curves for the PD-APS classifier, including both cross-validation and testing data. (b) Example heatmaps for a single APS subject and a single PD subject

Table 2: Comparison of the proposed vs existing models

Description	Contrast ratios-ML	Radiomics-ML	CNN	SCNN
Cross Validation				
Accuracy	52.9	81.9	83.8	82
Specificity	0.7	0.8	0.8	0.51
ROC	0.49	0.80	0.96	0.72
Sensitivity	0.27	0.75	0.88	0.97
Testing				
Accuracy	57	60.1	80.1	85.5
Specificity	0.6	0.51	0.72	0.50
ROC	0.50	0.50	0.93	0.92
Sensitivity	0.54	0.67	0.85	1.1

Conclusion

In conclusion, this article introduces a tailored Computer-Aided Diagnosis (CAD) system that adeptly classifies MRI patches into either Parkinson's disease or healthy patterns through the application of self-adapting convolutional neural networks (CNNs). The model's impressive performance results from its capacity to autonomously extract and assimilate critical patterns from the training samples provided by the benchmark Parkinson's Progression Markers Initiative (PPMI) dataset. Notably, our findings demonstrate the model's ability to discern precise Parkinson's disease characteristics independently. Nevertheless, it is essential to acknowledge the challenges posed by overfitting when dealing with relatively small datasets. Fortunately, the thoughtful

integration of a dropout layer within the model effectively mitigates this issue. Our research underscores the superiority of CNNs over radiomics in terms of accuracy, underscoring their potential for enhanced diagnostic capabilities. The consistent disparities in activation maps between PDs and both healthy controls (HCs) and atypical parkinsonian syndromes (APS) corroborate the distinct neuro-melanin contrast within the substantia nigra pars compacta (SNc) as a discernible feature facilitating the prediction of underlying PD pathology.

Looking ahead, future research can explore the refinement and extension of CNN-based diagnostic models for Parkinson's disease. This could involve the integration of additional imaging modalities, such as functional MRI or advanced neuroimaging techniques, to further enhance accuracy and early detection capabilities. Moreover, the investigation of larger and more diverse datasets may provide deeper insights into the subtle nuances of PD pathology. Additionally, efforts to translate these machine learning models into clinical practice could pave the way for more accessible and efficient PD diagnosis. Finally, ongoing research should continue to explore novel biomarkers and innovative approaches to further unravel the complexities of PD, ultimately leading to improved patient care and therapeutic interventions.

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