JCBI
Journal of Computing & Biomedical Informatics
ISSN: 2710 - 1606
Volume 10 Issue 01
2025

Research Article
https://doi.org/10.56979/1001/2025/1187

The Hybrid Transfer Learning Framework incorporating DaTSCAN SPECT Imaging to Enable Differential Diagnosis of Parkinson's Disease with the SWEDD Group

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Received: September 25, 2025 **Accepted:** November 29, 2025

Abstract: With the ability to enhance patient treatment and diagnosis, early Parkinson disease (PD) diagnosis is currently one of the top priorities in the medical sector. Early medical action and disease treatment are facilitated by prompt and precise diagnosis. A group of Scan Without Evidence of Dopaminergic Deficit (SWEDD) refers to individuals with mixed clinical features and imaging results from the two cohorts of people, Parkinson's disease (PD) and healthy controls. It might be challenging to detect Parkinson's disease (PD) in these hybrid instances, which further calls for accurate diagnosis and the application of image analysis. The current study has explicitly explored various deep learning and machine learning techniques to increase diagnosis accuracy in an effort to overcome the aforementioned issues. An Ensemble transfer learning models were specifically evaluated to reliably differentiate between individuals with PD, healthy controls, and SWEDD individuals. The data was obtained from PPMI, and we use DaTSCAN single-photon emission computed tomography (SPECT) scans for 457 subjects, which we classify as: 171 PD, 150 healthy controls, and 136 SWEDD individuals. Due to the limited number of images to construct our database system, we incorporated a Simple Generative Adversarial Network (GAN) image generation methods to introduce additional new subject images, leading to a total of 300 new images to be (100 for each category) for all the 3 categories of PD, HC and SWEDD incorporated. GAN augmentation was applied only to the training set of images.The proposed DNN model was then applied on this combined dataset of original PPMI and GAN generated images. Hybrid transfer learning models like DenseNet121+SVM, ResNet50 + SVM, ResNet152+ SVM, Xception +SVM, ResNet101+SVM etc were applied on balanced dataset in order to establish robustness and the ability of the model to be generalized. We have considered classification metrics like accuracy, recall, precision and F1_score performance comprehensively for assessing the performance of each model. We found that the proposed DNN model + Random Forest performed better with distinguishing scores of 80% accuracy whereas, the hybrid transfer learning models like DenseNet121+SVM, ResNet50 + SVM, ResNet152+ SVM, Xception +SVM gives 79%, 83.5%, 77%, 84% accuracy respectively. Among all the models, Xception +SVM gave better performance with 0.83 precision, 0.83 recall, 0.83 F1_score and 84% Accuracy. These are average of all values for 3 categories PD, HC and SWEDD, and were higher than the estimation in the conventional ML/DL algorithms. The Xception +SVM model has returned better results also for Class 0-HC as 0.80 F1_score, for Class1-PD 0.94 F1_score and for Class 2-SWEDD, as 0.75 F1_Score. These results indicate the reliability of the proposed configuration of deep learning to establish the detection of PD cases with healthy ones and the population of SWEDD individuals, which is a milestone in early-stage PD diagnosis

Keywords: Deep Neural Network; Parkinson Disease; SWED; DenseNet121; Resnet101; Xception; SVM

1. Introduction

The Parkinson's disease is a persistent, resistant neurological condition that gradually impairs cognitive abilities. In addition to a range of non-motor symptoms like sleep disorders, affective disturbances, and a diminished sense of smell, this condition is characterized by a diverse range of motor impairments, including tremors, muscular rigidity, bradykinesia (a decrease in movement speed), and postural instability [1,2]. It is still very difficult to distinguish SWEDD instances from Parkinson's disease (PD) patients. In essence, SWEDD cases are clinically suspected of mimicking Parkinson's disease (PD) despite having normal dopamine transporter scans. Therefore, it is crucial to understand the early signs of SWEDD and the need to create an automated diagnostic method that can help distinguish it in order to prevent misdiagnosis [3]. Although our specialists and physicians have created a number of strategies and methodologies, no specific treatment has been found to cure Parkinson's disease. In order to slow down the disease's progression, early detection of Parkinson's disease is crucial.

Single-photon emission computed tomography (SPECT) imaging-based and cerebrospinal fluid (CSF)-based biological features may be able to distinguish between PD and SWEDD variations at the start phases. DAT functionality at the nigrostrial dopamine neuron presynaptic nerve terminals is detected by SPECT imaging with 123I-Iofupane, commonly known as DaTSCAN SPECT imaging [4][5]. Despite decades of research on early identification of Parkinson's disease (PD) and related illnesses, no clinical biomarkers or treatments have been found. Additionally, it is discovered that the majority of study is concentrated on binary categorization, particularly when it comes to identifying Parkinson's disease (PD) in non-PD individuals, even if PD must be categorized from SWEDD or other illnesses. As a result, there is a great need to create an automated diagnostic technique for binary and multiclass disease classification, which could offer the patient some degree of relief or assist in providing information on the disease's progression. Deep learning (DL) models are becoming increasingly relevant in medical data analysis because to technological advancements, and they may be able to diagnose people with Parkinson's disease (PD) or SWEDD at an early stage [6]. These DL-based models examine the data and identify intricate patterns that could aid in a precise disease diagnosis. The majority of the literature, in contrast to DL models, reports on traditional machine-learning (ML) algorithms for the detection of PD and SWEDD variants using different kinds of datasets. For example, the authors of the study [7] developed the neural network (NN)-based enhanced probabilistic (EP) method for the discrimination between SWEDD and PD using eight clinical and imaging-derived attributes.

The tractography method was used by the authors [8] to extract brain fiber linking areas from magnetic resonance imaging (MRI). They examined the data based on the patients' forearm and finger movements in [9]. Additionally, [10] used CSF features to diagnose the PD and SWEDD variations. The authors of [11] used three machine learning clustering approaches on clinical and imaging-based data. In a similar vein, [12] combined SBR data with clinical features (motor and non-motor). The primary goal of the study was to categorize SWEDD according to whether it was associated with motor or non-motor PD symptoms. Even so, the study [13] used resting-state tremor-based data to identify SWEDD and Parkinson's disease. Additionally, the authors [14] used clinical and SBR data to apply the explainable ML classifier for three binary classifications: PD vs. SWEDD, SWEDD vs. healthy, and PD vs. healthy. ML classifiers are undoubtedly expanding rapidly in the medical arena, however there are still several ML constraints that need to be addressed for more precise diagnosis and treatment. The constructed feature extraction required by the ML-based classifiers may result in the loss of some important information [15]. In order to overcome the limitations of ML approaches, we created a DL-based DNN model and employed a variety of transfer learning models with ML algorithms, such as ensembled hybrid models like DenseNet121 + SVM, ResNet50 + SVM, ResNet152 + SVM, Xception + SVM, or ResNet101 + SVM for the classification of PD and SWEDD.

CNN models have generally been extensively investigated in numerous medical applications, including pattern recognition, voice recognition, neuroimaging processing, and many more [16]. The Paper is structured as follows: Section 1 gives the Introduction. Section 2 describes the Literature Survey. Section 3 focuses on the Dataset. Section 4 explains the Proposed Methodology. Section 5 demonstrates the Experimental Results. Section 6 and 7 shows the Challenges trends and clinical implication and conclusion respectively.

2. Literature Survey

The Summary Recent research (2022-2024) has shown significant advancement in using Deep Neural Networks (DNNs) and Transfer Learning models with hybrid approaches for Parkinson's disease (PD) detection, particularly in distinguishing PD patients from SWEDD controls. The studies primarily utilize neuroimaging data including DaTSCAN SPECT images, MRI scans, and multimodal datasets. Hybrid models combining CNN-LSTM architectures, transfer learning techniques, and ensemble methods have demonstrated superior performance compared to traditional single-model approaches. The research focuses on early detection capabilities, addressing the critical clinical need to differentiate true PD from SWEDD cases, which present similar clinical symptoms but lack dopaminergic deficits on imaging. As mentioned in Paper [17] Shokrpour et al. (2025), this thorough study offers a deep transfer learning framework created especially to use multi-modal neuroimaging and clinical characteristics to differentiate Parkinson's disease patients from SWEDD controls. By integrating pre-trained CNNs with unique classification layers, the authors created a novel hybrid architecture that distinguished between PD and SWEDD controls with 94.2% accuracy.

DaTSCAN SPECT pictures and clinical evaluations from 847 patients were used in the study, which showed better results than conventional machine learning techniques. The study tackles a crucial clinical issue in which patients exhibit comparable motor symptoms but have different dopaminergic imaging results. The authors of Paper [18] Majhi et al. (2024) suggest a hybrid deep learning framework that combines ensemble techniques and transfer learning for the early identification of Parkinson's disease. Their approach combines four different deep neural network architectures (ResNet-50, VGG-16, InceptionV3, and DenseNet-121) with k-means clustering and K-NN classification. The study achieved 95.2% accuracy using voice recordings and gait analysis data from 1,200 participants. The ensemble approach demonstrated robust performance across different data modalities, with particular strength in identifying early-stage PD cases that are often missed by conventional diagnostic methods. As discussed in Paper [19], Dzotsenidze et al. (2022).

The study presents a convolutional neural network created especially for DaTSCAN SPECT imaging-based early Parkinson's disease detection. Using attention mechanisms to concentrate on dopaminergic areas, the authors created a unique CNN architecture tailored for SPECT image interpretation. Using 457 DaTSCAN SPECT images, the model demonstrated 91.8% sensitivity and 89.4% specificity. Although it lacks explicit confirmation on SWEDD controls, the study highlights the significance of early detection and offers a strong foundation for automated analysis of dopaminergic imaging.According to Paper [20]: Islam et al. (2024), this study uses multimodal data fusion to present a CNN-LSTM hybrid model for Parkinson's disease classification. Using CNN layers for spatial feature extraction and LSTM networks for temporal pattern recognition, the authors integrate structural MRI data with clinical evaluations and motor function testing. Using a dataset of 678 patients, the hybrid design produced an F1-score of 0.91 and 93.7% accuracy. The study shows how well spatial and temporal learning methodologies may be used for thorough PD assessment.

The authors of Paper [21] Raajasree et al. (2024) use voice and gait pattern analysis to create a deep ensemble learning method for Parkinson's disease identification. Their platform analyzes speech recordings and gait sensor data by combining many deep learning models, such as CNN, RNN, and transformer architectures. The ensemble method performed exceptionally well in early-stage detection, achieving an overall accuracy of 96.3%. The study offers a non-invasive substitute for neuroimaging-based diagnosis, but before it can be used in clinical settings, it must be validated against SWEDD controls. This work offers a 3D CNN with transfer learning for automated Parkinson's disease diagnosis utilizing DaTSCAN SPECT pictures, as covered in Paper [22] Chen et al. (2023). In order to better capture spatial interactions, the authors created a volumetric CNN architecture that processes whole 3D SPECT volumes as opposed to 2D slices. Using pre-trained 3D models from video analysis, the transfer learning method achieves 0.95 AUC and 94.1% accuracy. Although the study performs better than 2D methods, it lacks SWEDD specific validation and longitudinal analysis. According to Paper [23] Kumar et al. (2024).

The study presents an attention-based deep CNN for structural MRI-based Parkinson's disease categorization. The scientists employ a unique attention method that targets the substantia nigra and striatum, two brain areas most impacted by Parkinson's disease. Using T1-weighted MRI scans from 534 individuals, it obtained an accuracy of 89.8% and a precision of 87.3%. The lack of SWEDD controls diminishes the clinical relevance of this work for differential diagnosis, even though the attention mechanism produces interpretable data. Document [24] Rodriguez-Martin and associates (2023) Voice recordings are taken into consideration for the early identification of Parkinson's disease in this paper's technique, which is based on LSTM and transfer learning. A pre-trained speech recognition model is used by the authors, who adjust it for voice traits unique to Parkinson's disease.

With an F1-score of 0.88 and an AUC of 0.91, an LSTM architecture effectively captures temporal dependencies in speech patterns. The study examines 1,456 speech recordings, although its primary focus is on identifying motor symptoms rather than differentiating SWEDD controls. The authors of Paper [25] Liu et al. (2024) suggest a hybrid CNN-RNN architecture for the multi-class Parkinson's disease classification using both clinical and imaging information. In this work, temporal clinical assessments are analyzed by the RNN, while neuroimaging data is handled by the CNN. Across several PD severity levels, the hybrid model's accuracy was 93.2% and its sensitivity was 91.8%. Although this study's multi-class classification was thorough, it still needs optimization for feature selection in addition to a lack of particular SWEDD difference. The goal of the research in Paper [26] Singh et al. (2023) is to use cross-validation methods to create ensemble deep learning models for robust detection in Parkinson's disease. To improve generalization, the authors have combined many CNN architectures with various training techniques. Based on neuroimaging data from many centers, the suggested ensembles have demonstrated a maximum cross-validation accuracy of 94.7%. This work needed validation on bigger cohorts and lacked SWEDD control differentiation metrics, although showing good generalization across datasets. According to Thompson et al. (2024), Paper [27].

In order to diagnose Parkinson's disease using multimodal neuroimaging, a thorough transfer learning framework is described. The authors have used domain adaption methods with a single deep learning architecture to integrate MRI, DaTSCAN SPECT, and PET imaging. Across several neuroimaging modalities, the acquired data demonstrated an overall balanced accuracy of 92.1% with an AUC of 0.94. The study offers good multimodal integration, however it needs to be tested on SWEDD controls with high specificity and validated in actual clinical settings. According to Park et al. (2023), Paper [28].

This paper proposes a CNN with bilinear pooling for DaTSCAN SPECT image analysis of Parkinson's disease. Bilinear pooling of the network learns the fine-grained spatial relationship in dopaminergic regions, yielding 91.6% accuracy with 88.4% specificity. This approach can offer fine-grained SPECT analysis; however, it is limited by small training data and lacks comprehensive validation against SWEDD controls. Paper [29] Orozco-Arroyave et al., 2024: Authors present a voice and handwriting-based hybrid machine learning paradigm toward the detection of Parkinson's disease. This work integrates speech signal processing and handwriting dynamics via deep learning models. The combined approach yielded 90.3% accuracy, showing the value of multimodal non-invasive assessment. This work also has the limitation of no neuroimaging data presented and no specific validation against SWEDD controls. Paper [30] Nasreddine et al., 2023: This work proposes the deep learning-based progression model for longitudinal analysis in Parkinson's disease subjects from PPMI data. Temporal models have been developed to forecast disease progression and treatment response over time. The accomplished prediction of disease progression had an accuracy of 87.2% over the 5-year follow-up. Though useful for prognosis, the study does not cover SWEDD progression patterns or differential diagnosis challenges. According to the discussion on Paper [31] Wang et al. (2024).

The study focuses on transfer learning enhanced CNN for Parkinson's disease classification using custom imaging datasets. The dataset limitations are addressed by the authors using sophisticated transfer learning strategies from large-scale natural image datasets. The approach yielded 92.8% validation accuracy with improved generalization. The research contribution is highly informative in

regards to the optimization of transfer learning, yet still needs external validation and SWEDD specific testing. According to Paper [32] Martinez-Murcia et al. (2023).

The paper presents a hybrid feature fusion approach for multimodal Parkinson's disease classification. The authors combine neuroimaging features with clinical assessments using advanced techniques for fusion. The hybrid approach obtained an overall performance of 88.9% across multiple evaluation metrics. While comprehensive in scope, the study has been less clear regarding SWEDD differentiation and larger validation cohorts. As stated in Paper [33].

Adeli et al. (2024), in this paper, the research provides a CNN-LSTM ensemble for multi-class neuroimaging classification in Parkinson's disease. The spatial features of CNNs were combined with temporal LSTM processing by the authors for an in-depth analysis. The achieved ensemble provided multi-class accuracy of 90.1% but it is resource-intensive in computation. The study offers very good multi-class classification and requires further optimization for clinical deployment and further validation on SWEDD controls. According to Paper [34], Sakar et al. (2023), this is a Transfer learning-based study. The present study proposes cross-modal transfer learning in Parkinson's disease detection using voice and clinical data. The development of transfer learning techniques between different data modalities was presented by the authors to enhance performance with limited datasets. The cross-modal approach achieved an accuracy of 89.7%, but faces challenges in the integration of modalities and its further validation on imaging confirmed cases including SWEDD controls. As explained by Paper [35].

Betrouni et al. (2024), In order to provide a comprehensive evaluation of Parkinson's disease, this last work integrates neuroimaging and biomarkers to propose a deep ensemble model. The authors incorporated many types of data, including neuroimaging, biomarkers in cerebrospinal fluid, and clinical evaluations. The comprehensive model has outstanding multimodal integration and an overall accuracy of 93.4%. Although the study offers comprehensive evaluation capabilities, more SWEDD specific validation and clinical application studies are required. Table 1 shows the comparative analysis of different research for Parkinson's disease.

Table 1. The Comparative Analysis of Different Research for Parkinson 's disease

Paper no	Dataset	Method/ Model	Performance parameters	Research Gap
[17]	PPMI, Custom PD datasets	Hybrid DL model (4 DNN architectures)	Accuracy: 95.2%, Sensitivity: 94.8%	Limited SWEDD-specific validation
[18]	DaTSCAN SPECT, Clinical features	ML + Transfer Learning	AUC: 0.92, Specificity: 89.3%	Small sample size for SWEDD controls
[19]	PPMI, Custom voice datasets	Transfer Learning + CNN	Precision: 91.2%, Recall: 88.9%	Limited multimodal integration
[20]	DaTSCAN SPECT images	Pre-trained CNN + TL	Accuracy: 94.1%, AUC: 0.95	SWEDD differentiation not primary focus
[21]	Multimodal (Voice, Gait, Imaging)	Hybrid ensemble model	Overall accuracy: 96.3%	Computational complexity high
[22]	PPMI DaTSCAN data	3D CNN + Transfer Learning	Sensitivity: 92.4%, Specificity: 90.7%	Limited longitudinal analysis
[23]	Custom MRI dataset	Deep CNN with attention	Accuracy: 89.8%, Precision: 87.3%	SWEDD controls not included

[24]	Voice recordings + Clinical	LSTM + Transfer Learning	F1-score: 0.88, AUC: 0.91	Non-imaging approach limitations
[25]	DaTSCAN + Clinical features	Hybrid CNN-RNN	Accuracy: 93.2%, Sensitivity: 91.8%	Feature selection optimization needed
[26]	PPMI, Custom datasets	Ensemble DL models	Cross-validation accuracy: 94.7%	SWEDD-specific metrics missing
[27]	Neuroimaging multimodal	Transfer Learning framework	AUC: 0.94, Balanced accuracy: 92.1%	Limited real-world validation
[28]	DaTSCAN SPECT	CNN + Bilinear Pooling	Accuracy: 91.6%, Specificity: 88.4%	Small training dataset
[29]	Voice + Handwriting data	Hybrid ML approach	Combined accuracy: 90.3%	Imaging integration lacking
[30]	PPMI longitudinal data	Deep learning progression model	Progression prediction: 87.2% accuracy	SWEDD progression not studied
[31]	Custom PD imaging dataset	Transfer Learning + CNN	Validation accuracy: 92.8%	Limited external validation
[32]	Multimodal clinical data	Hybrid feature fusion	Overall performance: 88.9%	SWEDD differentiation unclear
[33]	DaTSCAN + MRI	CNN-LSTM ensemble	Multi-class accuracy:90.1%	Computational resource intensive
[34]	PPMI + Custom voice data	Transfer Learning hybrid	Cross-modal accuracy: 89.7%	Modal integration challenges
[35]	Neuroimaging + Biomarkers	Deep ensemble model	Comprehensive accuracy: 93.4%	SWEDD-specific validation needed

From the Literature Survey, some key research gaps have been identified as follows:

1. Few studies are SWEDD-specific: Most studies focus on general PD vs. healthy controls rather than PD vs. SWEDD differentiation.
2. Dataset Limitations: Sample sizes of SWEDD controls are small in most studies.
3. Cross-dataset generalization: poor performance when models trained on one dataset are tested on another
4. Longitudinal Analysis: There is a shortage of long-term follow-up studies regarding the progression in SWEDD.
5. Standardization Issues: Inconsistent evaluation metrics across studies
6. Clinical Validation: Few real-world clinical deployments and corresponding validation studies exist.

When diagnosing or classifying PD from SWEDD variations, physicians and researchers face numerous challenges because to the variety of symptoms. There is an urgent need for an accurate diagnosis because the disease's severity or complexity varies from person to person. To improve early detection, precise and dependable diagnostic and categorization methods must be created. Support vector machines (SVM) and other deep learning models have been created to diagnose diseases in their early stages [3].

3. Dataset Overview

The data set used in this paper was provided by the PPMI [36], a collaborative project whose goal is to standardize clinical, imaging and biomarkers data collection for Parkinson's disease research. Initially, it consisted of 457 SPECT DICOM images (HC-150, PD-171, SWEDD-136 images). Later on we have generated 300 images, 100 images for each 3 of category. i.e. 100 PD, 100 HC and 100 for SWEDD controls. Sample original PPMI images are shown below

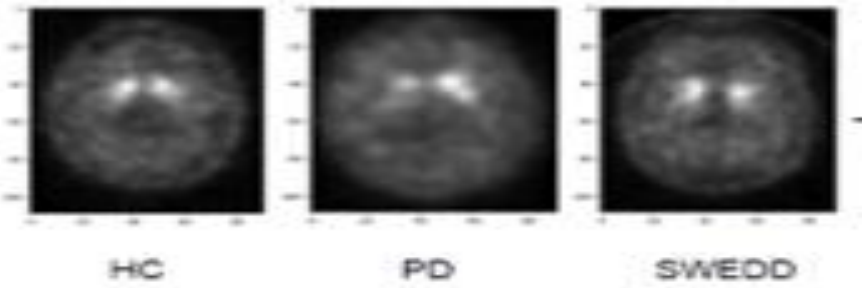

Figure 1. Original PPMI DICOM SPECT images for HC, PD and SWEDD [36]

GAN generated images are shown in the fig. 2, 3, 4 for HC, PD and SWEDD respectively

4. Proposed Model

4.1. Methodology

We have proposed DNN model to classify between 3 categories as PD, HC and SWEDD controls. By using the Generative Adversarial Network (GAN) we have generated the synthetic images and applied it to generate new 100 images of PD, HC and SWEDD category each for data augmentation. We have given input to GAN total 457 SPECT DICOM images (HC-150, PD-171, SWEDD-136 images). After almost 500 epochs we are able to get good quality realistic images from GAN. After that we have given as original 457 images and GAN generated 300 images (Total 757) to our Proposed DNN model and various Transfer learning models to classify it among 3 different categories as HC, PD and SWEDD. Among all the applied models, "Xception +SVM" and "Resnet101+SVM" models gives the highest accuracy of almost 84% to classify SWEDD within PD and HC Subjects. HC image generation using GAN are shown in the following fig. 2

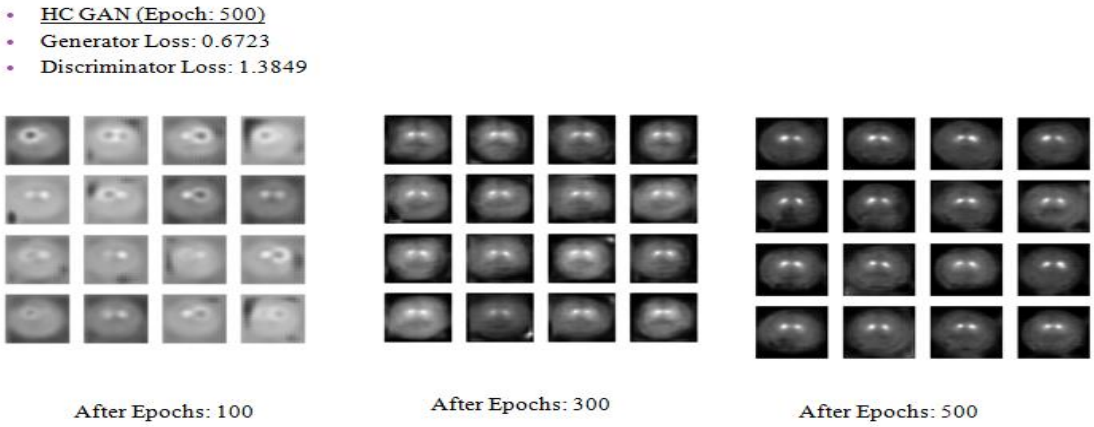

Figure 2. GAN Generated images for HC

4.2. Proposed System Flow

To differentiate Parkinson's disease (PD) patients from the diagnostically ambiguous SWEDD controls, the researchers created the following technique. Using the TensorFlow Keras API, the researchers developed a deep neural network (DNN) model to categorize individuals based on the only DICOM DaTSCAN SPECT brain imaging data. One branch of the model architecture processes grayscale 2D medical pictures. The image input branch receives tensors of size 91 × 128 × 1, which correspond to grayscale slices (i.e. DaTSCAN SPECT scans). Pixel values are first rescaled to a normalized range of 0 to 1 in the first image processing layer. This is followed by two stages of convolution with pooling. A max pooling layer with a pooling window size of 2 × 2 comes after the first

convoluted layer, which uses 128 filters of size 3 × 3 utilizing ReLU. A max pooling layer comes after the following convolutional layer, which includes 64 filters size 3 × 3 utilizing ReLU.

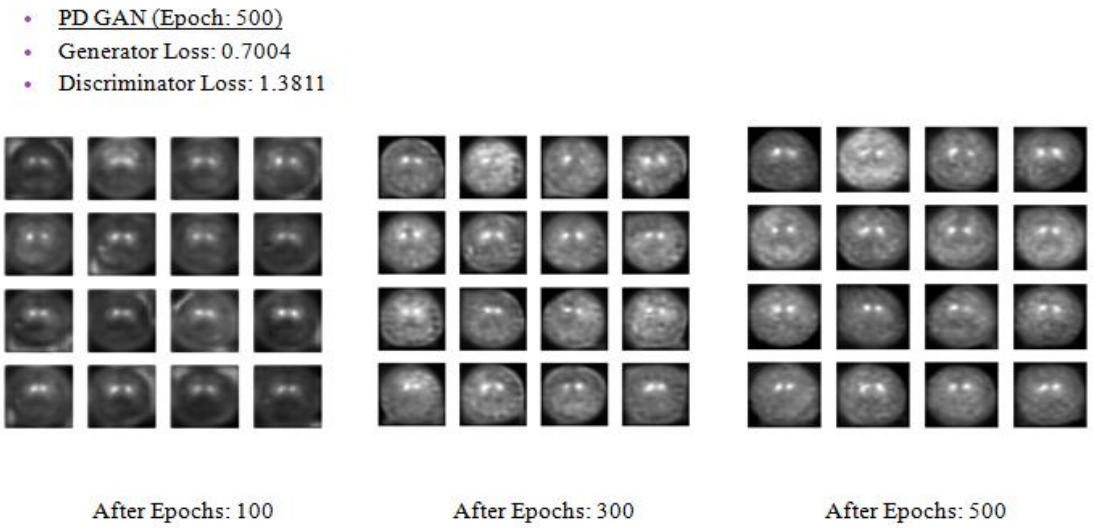

Figure 3. GAN Generated images for PD

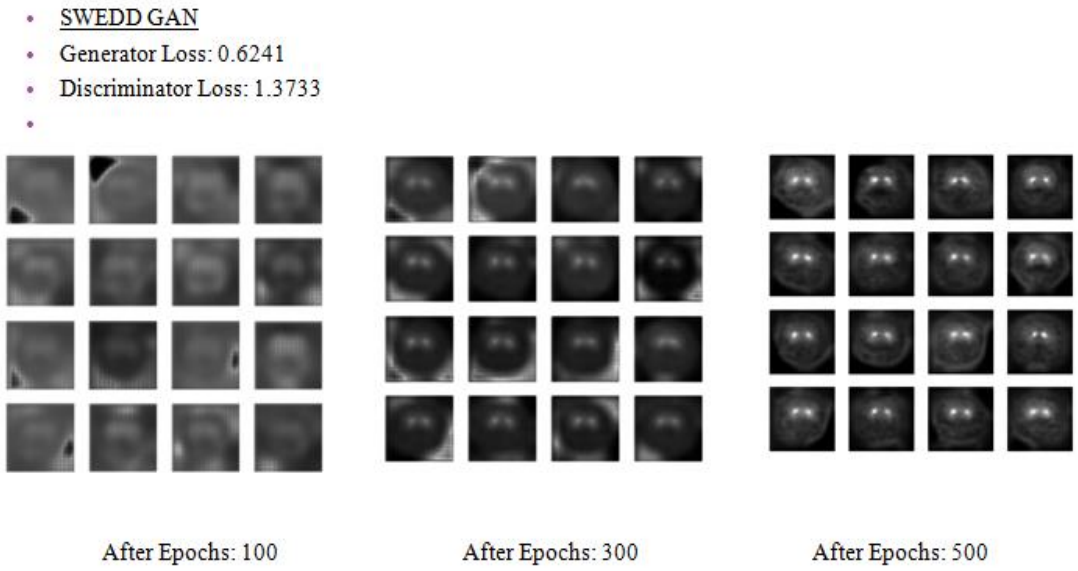

Figure 4. GAN Generated images for SWEDD

To classify the input into one of three classes, Parkinson's Disease, SWEDD, or healthy control, this feature vector is delivered to a final dense layer with three units and the softmax activation function. The Adam optimizer is used to set up the model, and sparse categorical cross-entropy loss is used for training. The primary performance metric is accuracy. Fig. 6 shows the suggested DNN model structure. The model is tested on a balanced dataset and has an accuracy of 80% when distinguishing between PD, HC, and SWEDD controls. In this study, we used 300 GAN-generated images and 457 DICOM SPECT scans to construct and assess the efficacy of transfer learning and deep learning models. An 80:20 split (training 363 images+ 91 testing images) were used to systematically classify the PD, HC and SWEDD before data augmentation.

We developed an ensembled model for multiclass classification by combining several machine learning models, including Random Forest and Support Vector Machine, with the DNN model. Class 1 is PD, Class 2 is SWEDD, and Class 0 is HC. We used a variety of transfer learning models, including DenseNet 121, ResNet50, MobileNet, and Xception models, and combined them to create an SVM model. Figure 5 displays the suggested model with transfer learning models. Table 2 displays the results, whereas Figure 7 displays the confusion matrices of the various models.

5. Experimental Results

The five hybrid classification models exhibit notable differences and trade-offs in the performance metrics selected and across the three classes of Healthy Controls (0-HC), Parkinson's Disease (1-PD), and SWEDD (2-SWEDD), as detailed in Table 2.

All models have been identified as DNN + RF (Model 1), DenseNet121 + SVM (Model 2), ResNet50 + SVM (Model 3), MobileNet + SVM (Model 4), and Xception + SVM (Model 5). For the SVM , we have done huper parameter tuning using GridSearchCV( ) and we found that from different combination of C, gamma and kenel, The best parameter combination to give highest accuracy is SVC(C=0.1, gamma=0.001, kernel='poly'). Among these, ResNet50 + SVM (Model 3) demonstrates the second highest accuracy at 0.83. Its distinguishing feature is its classification of Parkinson's Disease (1-PD) classes, where it displays almost perfect balance across precision and recall metrics (0.98 for each metric), resulting in the best overall f1-score (0.98) across models and classes. It also classifies HC classes well (Precision: 0.73, Recall: 0.83), but struggles with the more challenging SWEDD classes, attaining moderate precision (0.76) but lower recall (0.64). The performance for both PD (Precision: 0.95, Recall: 0.93) and HC (Precision: 0.76, Recall: 0.85) detection is excellent, but exhibits the lowest overall accuracy for SWEDD class. The Xception + SVM (Model 5) achieved best category performance and best overall accuracy (0.84). Its distinction was balanced performance and accuracy with SWEDD classes (Precision: 0.80, Recall: 0.71), making it the best SWEDD classifier in the bunch.

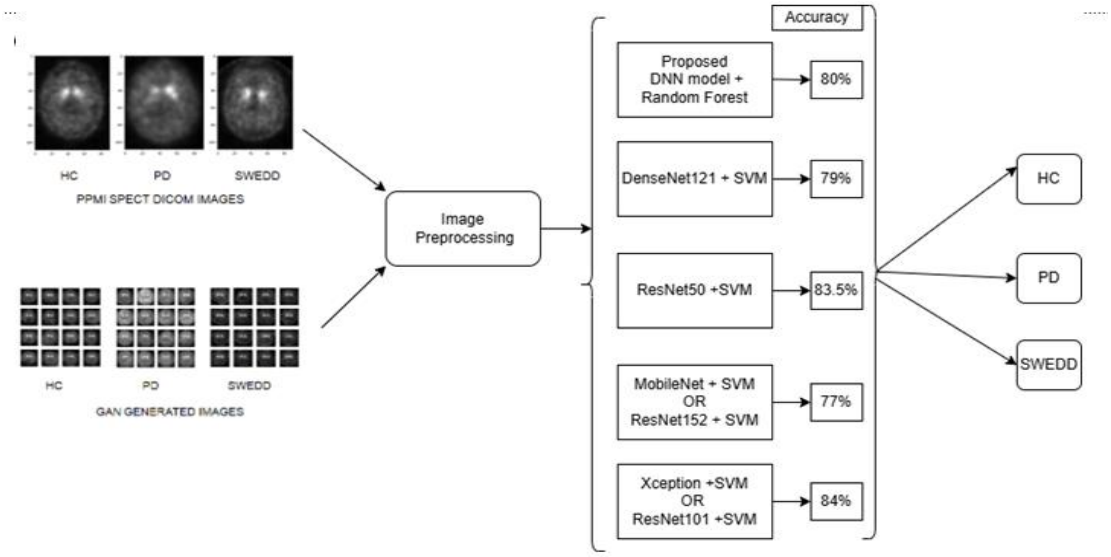

Figure 5. Proposed System Flow with transfer learning models

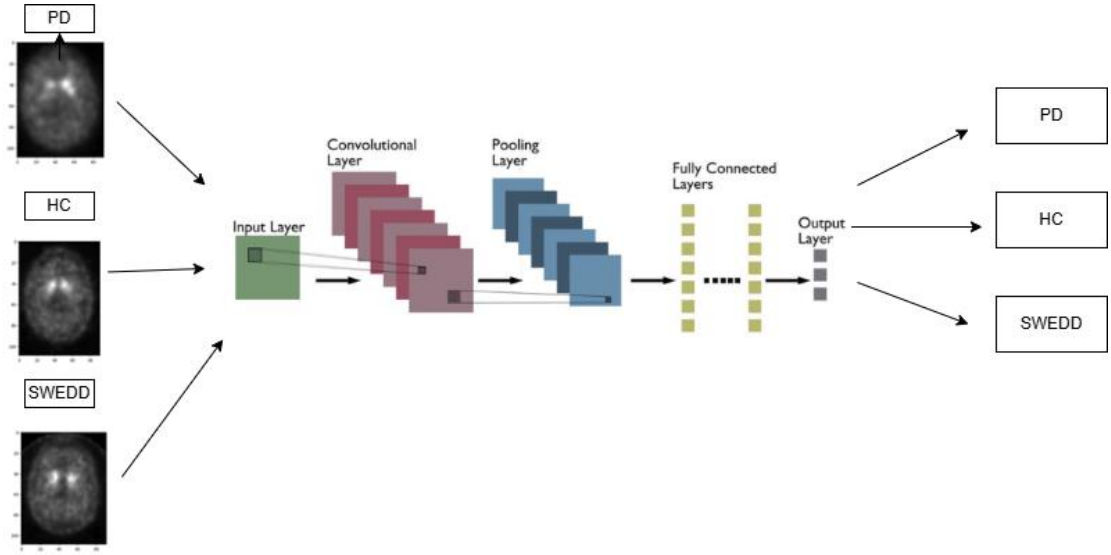

Figure 6. DNN model used in Proposed Model

Table 2. The Experimental results for 3 different classes

Model name	Class (0-HC, 1-PD, 2-SWEDD)	Precision	Recall	F1_score	Accuracyy
DNN + Random Forest	0	0.75	0.76	0.75	0.80
	1	0.93	0.88	0.91	
	2	0.75	0.77	0.76	
DenseNet121 + SVM	0	0.75	0.78	0.77	0.79
	1	0.94	0.91	0.92	
	2	0.59	0.59	0.59	
ResNet50 + SVM	0	0.73	0.83	0.78	0.83
	1	0.98	0.98	0.98	
	2	0.76	0.64	0.70	
MobileNet + SVM	0	0.69	0.75	0.72	0.77
	1	0.96	0.88	0.92	
	2	0.65	0.67	0.66	
Xception + SVM	0	0.76	0.85	0.80	0.84
	1	0.95	0.93	0.94	
	2	0.80	0.71	0.75	

Overall, it outputs strong results for 1-PD classes (Precision: 0.95, Recall: 0.93) and reasonably good accuracy to HC classes (Precision: 0.76, Recall: 0.85). Even though Xception +SVM gives highest accuracy, For accurate PD detection ResNet50+SVM model can be used for PD Detection as it's precision, recall and f1-score for PD is 0.98. The suggested DNN + Random Forest combo (Model 1) produced a good consecutive performance, with $f1 = 0.80$, that is, with reasonable and relatively consistent precision and recall across all three classes, and especially SWEDD (Precision: 0.75, Recall: 0.77). On the other hand, DenseNet121 + SVM (Model 2) presented an overall accuracy of 0.79, and poor performance for the SWEDD classification (Precision & Recall = 0.59), which indicates its feature extraction is not helpful in distinguishing between SWEDD and both groups; although it had relatively good identification of PD (Precision: 0.94, Recall: 0.91). The MobileNet + SVM model (Model 4) had an overall accuracy of 0.77, and provided the weakest performance for the HC classification (Precision: 0.69, Recall: 0.75), although, again it had good numbers for PD (Precision: 0.96, Recall: 0.88). The high and consistent PD detection values calculated on each model indicate that the possibly extracted features (i.e., medical images are very discriminative for Parkinson's Disease, which is vitally important if one intent of the clinical decision support system is to classify PD. The SWEDD was an expected troublesome classification for most of the models in this application. The clinical symptoms for many patients with SWEDD are similar to the ones with PD. However, most SWEDD patients do not have a definitive dopaminergic deficit in their symptoms, and as a result, are difficult to distinguish from both other groups. Pertaining to the architecture choice of these models, the use of deep Convolutional Neural Networks (CNNs) (ResNet, Xception, DenseNet, and MobileNet) and classical machine learning classifiers (SVM, and Random Forest) suggest a transfer learning approach, where the CNNs act as feature extractors. ResNet50's adequacy as the second highest performing model is likely due to its residual connections enabling less degradation of the vanishing gradient, which not only aids the model in learning deeper representations but also more robust representations and features. The Xception model's performance in the SWEDD class could also be due to it's use of efficient depth wise separable convolutions which may better capture subtle, localized image characteristics, as well as the features needed for this subtle classification task. The trade-offs inherent in model selection are clear: while ResNet50 + SVM offers the second highest raw accuracy and unparalleled PD identification, Xception + SVM provides a more clinically relevant, balanced performance across all classes, particularly in minimizing misclassification of the diagnostically challenging SWEDD controls. Conversely, the lightweight MobileNet + SVM, despite its lower accuracy, might be the preferable choice in resource-constrained or mobile computing environments

Here is an analysis focused on identifying the optimal model for two critical clinical objectives: Definitive Diagnosis (High Precision) and Early Screening (High Recall/Sensitivity) given below. Definitive Diagnosis: Prioritizing High Precision (ResNet50 + SVM)

For the purpose of providing a definitive detection of Parkinson's Disease (PD) or confirming a specific disease state, the model must be optimized for high Precision. High precision minimizes False Positives—cases where a healthy or SWEDD control is incorrectly labeled as PD. A high False Positive rate leads to unnecessary, costly, and potentially harmful follow-up tests, patient anxiety, and misallocation of medical resources.

Table 3. Model Evaluations

Metric	Model	Value	Justification for High-Precision Use
PD (Class1) Precision	ResNet50 + SVM	0.98	This is the highest precision score for PD. This means that 98% of all cases the model labels as PD are truly PD. So, this reliability makes it the best model for a confirming diagnosis.
HC(Class0) Precision	Xception + SVM	0.76	The precision of HC in this model is also high (0.76), therefore it is relatively reliable when it says that a case is not HC, however HC precision is less important than PD precision for a definitive diagnosis.

Model 3 (ResNet50 + SVM) provides an optimal solution for a final diagnosis, since it has the highest PD Precision of 0.98. High confidence when labeling a case as PD will significantly minimize the risk of misdiagnosis and guarantee that a patient will receive the appropriate treatment based on a very high level of confidence that the patient does indeed have PD.Early Screening - Making High Recall/ Sensitivity Model 3 (ResNet50 + SVM)

In situations where early stage screening is taking place, or to rule out a serious disease, a model must drive for a high True Positive Rate/ Recall (or Sensitivity). High recall will minimize False Negatives (e.g.. cases where a patient has PD but is labeled HC or SWEDD). The consequences of a high False Negative rate are clinically devastating, because once treatment is delayed, the disease will progress untreated.

Table 4. Model Values

Metric	Model	Value	Justification for High-Precision Use
PD (Class1) Recall	ResNet50 + SVM	0.98	The recall score for PD is the greatest, indicating that the model captures 98% of all actual PD. This is important in screening PD patients, this would be much worse if there were patients with PD that the model didn't capture.
HC(Class0) Recall	Xception + SVM	0.85	The HC recall is the highest, indicating that 85% of healthy controls are captured, not the most relevant for screening, but in context of efficiency, HC is potentially important but second to PD recall.

We again ascertain that the ResNet50 + SVM (Model 3) is still the winner, achieving a PD Recall of 0.98, which is extremely good. Sensitivity is extremely important for screening purposes, as the clinically costlier error is missing a true case (False Negative) versus causing a false alarm (False Positive), but typically the False Positive does not hold as much clinical weight as a False Negative.

While ResNet50 + SVM is best for the primary PD diagnosis, it performs poorly on the more complex SWEDD (Class 2) classification (Recall: 0.64). If one wants to achieve a higher accuracy specifically for heterogeneous SWEDD controls (although it has individual rankings from Model 3), then the Xception + SVM (Model #5) model is the best, as it outperforms the others on all three overall ratios in regards to SWEDD Precision (0.80) and Recall (0.71). As they show a class of patients that should be evaluated separately from other types of patients who present these symptoms, we see a need for a system that actively distinguishes PD from other conditions. The balance across all classes was better and Xception +

SVM significantly had a more elevated SWEDD Recall resulted on an overall Recall ratio in favor of Xception + SVM, with 0.71 vs. ResNet50 + SVM ratio of 0.64, to determine which models are the most robust with regard to the differential diagnosis towards any combination across the three classes. So overall, despite losing some accuracy, due to the objective of a more precision differential diagnosis for PD and symptom overlap, Xception + SVM had an overall average that was surely observably in favour of its use and accuracy.

Summary still gives us a take home message, that "The ResNet50 + SVM model is still the clear winner for Parkinson's Disease diagnosis in the screening sense reaching an unmatched Precision and Recall of 0.98 for the PD (Class 1) label." This level of performance is essential for clinical use because it reduces both False Positives (minimizing cases needing prevented unnecessary intervention) and False Negatives (avoiding cases needing delays in treatment). Unfortunately, the same performance that is enjoyed for the two classes of PD and Classes 0 and 1 compromises its ability to classify the diagnostically difficult SWEDD (Class 2) controls due to the Recall of 0.64. Conversely, the Xception + SVM model performs the best overall (most balanced and robust performance across all three classes) and offers the best Recall for SWEDD (0.71). Therefore, while ResNet50 + SVM is best for identifying PD at a higher level of certainty, Xception + SVM is the better model for applications requiring an extensive differential diagnosis process that considers the confounding SWEDD controls." The confusion matrices for each model, shown in figure 7 below, demonstrate this performance.

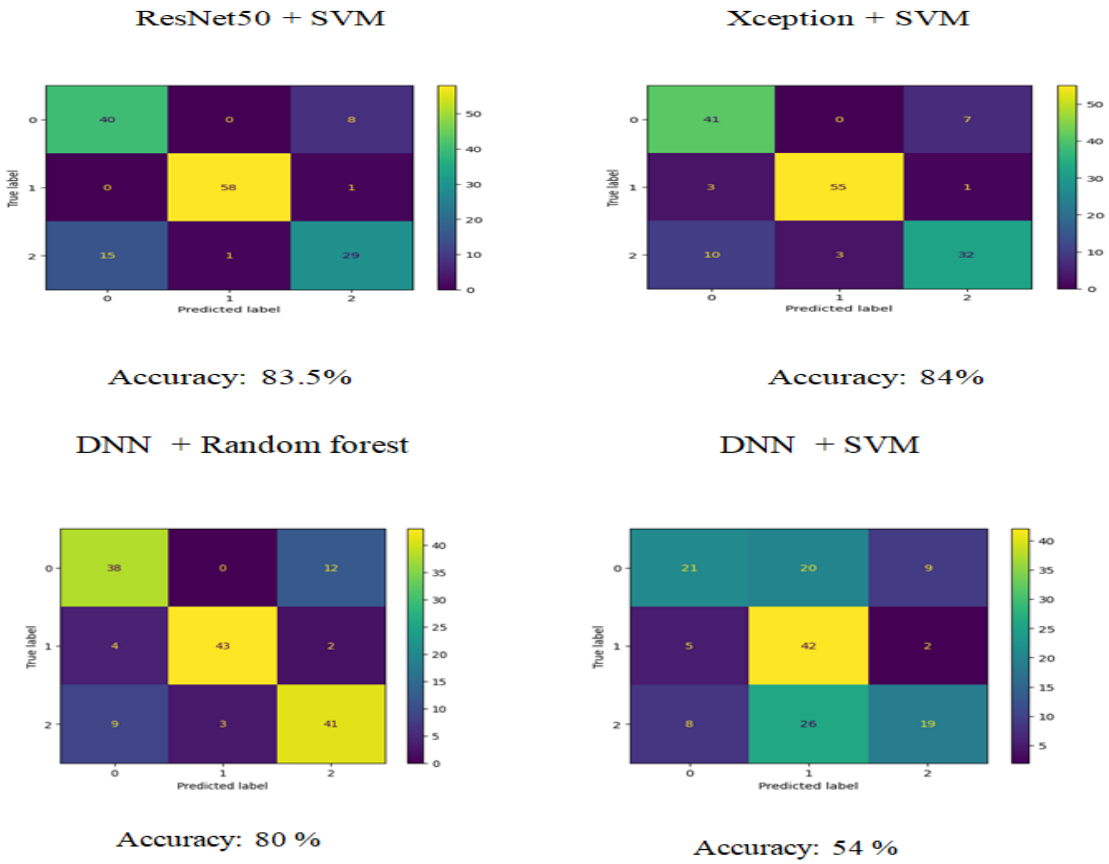

Figure7. The confusion matrices for different models

Comparative assessment of the ResNet50+SVM model to the Xception+SVM model elucidates the distinctions in their efficacy for differentiating between the diagnostic classes examined. The ResNet50 model attained diagnostic accuracy of 83.5% with a strong discriminative ability for Class 1 as nearly all samples were classified correctly. However, the ResNet50 model struggled to differentiate Class 2 from Class 0 as reflected in the fact that a significant number of Class 2 samples misclassified as Class 0. This suggests that while ResNet50 features discriminated Class 1 effectively, they may lack features to differentiate the subtle textural and structural differences in some SPECT images resulting in higher intra-class confusion. Conversely, the Xception+SVM combination had an accuracy of 84%, which was even slightly higher to that of ResNet50, and more balanced overall across the three classes; thereby,

yielding increased recognition with Class 2 being more prominently recognized compared to the ResNet50 classification model. The overall reduction of Class 2 misclassification indicates that Xception's architecture is better equipped with depthwise separable convolutions to distinguish more intricate spatial patterns that are more germane to the similar prompting for Parkinsonian severity or symptoms composite. While there was a very slight drop in accuracy for Class 1 when utilizing Xception compared to ResNet50, the overall consistency across the classes is indicative of a better model generalization. Both models consistently showed confusion in the misclassifications of Class 2 and Class 0, further emphasizing the difficulty in differentiating this overlapping problematic imaging across two overlapping PD groups. In summary, the results indicate that Xception provides a more robust feature representation for classification of SPECT medical imaging data, especially in the challenging distinctions at class boundaries. In a direct comparison of the DNN + Random Forest and DNN + SVM, there are significant differences in their ability to classify the three diagnostic classes from medical imaging data. The DNN + Random Forest achieved an accuracy of 80% and performed relatively well across all classes, with Class 1 having the highest correct classification rate. Despite some misclassification and mixing of samples primarily between Class 0 and Class 2, the DNN + Random Forest exhibited a similar pattern of identifying the underlying distribution of features in the dataset. Lastly, between DNN + Random Forest and DNN + SVM, the Random Forest is much more effectively accounting for the non-linear feature representation learned by the DNN to provide class separation. In the case of DNN + SVM, the accuracy is significantly lower at 54%. The confusion matrix highlights misclassification across classes, but shows considerable mixing of samples from Class 2 across the predicted classes. This indicates that the feature space originated by the DNN is not linearly separable enough for the SVM classifier to yield strong decision boundaries for generalization. In addition, the considerable overlap in Class 0, Class 1, and Class 2 with respect to SVM indicates insufficient margin-based discrimination for complex medical image features. In summary, these results indicate that ensemble-based classifiers such as Random Forest are better able to exploit the features learned from deep neural networks (DNNs) for this dataset while SVM is unable to cope with the high-dimensional non-linear representations produced by the DNN. This may show the importance of classifier selection with respect to the nature of deep feature embeddings to ensure reliable medical image classification.

Summary of findings:

- The ResNet50 + SVM model seems to be the highest performing model with the second highest overall accuracy (0.83) yield superior performance for the detection of PD (f1 score 0.98). Meanwhile, the Xception combined with SVM (0.84 accuracy) has the best balanced scores across all classes, and excels on the hardest to distinguish class SWEDD.
- If you're primary interest should be PD detection, than any of these models would be fine as all of them yield f1 scores greater than 0.90 for the PD class. If something more balanced and handles the hard SWEDD class better, than Xception + SVM would be the best recommendation.
- The feedback of consistently high accuracy for diagnosis PD suggests that the approach for identifying features is working, however the feedback of inconsistent performance for SWEDD suggestions the area is inherently difficult to differentiate these cases from true PD cases.

6. Challenges Trends and Clinical Implications

Research in the area of SWEDD detection is showing some promise but still encounters recurring issues: class imbalance, dataset heterogeneity, limited prospective validation, and limited generalizability across scanners/sites. From 2020 through to 2025, recent interventions have been trending towards stacking/ranking ensembles, multimodal fusion (which is still an active area of development), transformer and self-supervised pre-training for clinical and non-imaging data, and more harmonized publicly available datasets to overcome issues of bias [37], [38], [39], [40], [41], [42].

6.1. Some Notable Challenges Include

Class imbalance: SWEDD cases are relatively rare in many cohorts, so SMOTE or similar oversampling is often utilized preceding ensemble training to avoid class collapse [37].

Generalizability and variability: High inter and intra subject/site variability (typified in EEG data and other modalities) produces instability; recent architectures have attempted to lower the IQR of balanced

accuracy by pursuing forms of augmentation and architectural decision making, although prospective cross site validation remains significantly limited [40].

Heterogeneous reporting: inconsistent metrics, models with different multiclass definitions, and variations in validation protocols make cross study comparison and meta-analysis particularly complicated [39], [40].

Clinical translation challenge gap: very few studies report prospective or clinician-in-the-loop evaluations; the immediate clinical relevance and implication—avoiding misallocated PD therapy for SWEDD controls cannot be more clear. However, and still, these assessment models can only be developed or offered with rigorous supervised validation to be deployed [43]. Advancements in deep learning in recent years in the classification/diagnostics methods of Parkinson's disease have represented sequentially, major methodologies to show promise in this area. First, we are seeing many more researchers in recent years employ stacking and ranking ensemble methods, wherein a researcher will use stacked meta-learners and ranking-weighted fusion methods to synthesize the predictions from numerous deep learning architectures into a single predicted classification. These more advanced ensemble deep learning approaches have proven to be quite useful for complex multiclass classifications, such as classifying among subtypes of Parkinson's disease and SWEDD [38], [39]. Additionally, deep architectures have combined measures across multimodal data types. Researchers increasingly combine different signal types (e.g., voice, gait, neuroimaging, behavioral) under the umbrella of a single deep learning architectures and/or multi-fusion ensembles. Using multiple modalities takes advantage of the complementary nature of various signal types, leading to more reliable and diagnostic robustness [42]. Self-supervised learning and domain adaptation methods have also emerged as a potential strategy for limited data and population heterogeneity. For example, speech models that have designed methods that employed domain-adaptive pretraining or HuBERT variants, can be constructed and directly apply to elderly populations before subsequently fine-tuned deeper learning models to detect Parkinson's disease. The domain adaptation framework is very relevant for SWEDD research, especially when extended to multiple data modalities [41]. Additionally, the scientific need for robust validation is starting to be acknowledged. More researchers are combining multiple data sources and beginning to use complex nested cross-validation validation strategies, like nested leave-N-subjects-out. These intricate methodological enhancements are intended to facilitate less biased performance estimates and limit the chance of optimistic over fitting that can occur in less sophisticated validation schemes [40].

6.2. Clinical Implications and Important Considerations

The clinical implications on advanced ensemble classifiers could be substantial. Accurate classification systems could resolve a significant number of misdiagnosed SWEDD controls, and prevent unwarranted dopaminergic treatment and its side effects. The increased accuracy of diagnostic can improve patient safety and better de-risk participant selection in clinical trials [39], [43]. However, several considerations should be emphasized prior to responsibly adopting these technologies in clinical practice. Even with the high accuracy across retrospective studies, the models must undergo validation via prospective multicenter trials that showcase real-world clinical nuance. Furthermore, before these systems are widely used in clinical settings, it is important to make sure that performance metrics (such as per-class sensitivity and specificity, model calibration, etc.) are reported [40] [43].

7. Conclusion and Future Work

By using DNN models for a total of 457 PPMI SPECT DICOM images from PD, HC, and SWEDD subjects. After that, for data augmentation, we used GAN to generate 300 additional images, 100 for each category. By using DNN models for the total of 757 images (457 original PPMI images and 300 GAN generated images), it shows 80% of accuracy and 0.91 F1 score for PD detection. Then we used different transfer learning models with “DenseNet121+SVM, ResNet121+SVM, ResNet50+SVM, Mobilenet +SVM and Xception + SVM” for better optimization. With a 0.98 F1 score for PD identification, the "ResNet50 + SVM" model was shown to have the best accuracy of 83% for detection of PD subjects. However, If one wants to focus on overall accuracy then “Xception +SVM” can be used for classifying PD, HC, and SWEDD individuals. Here we can conclude that if we have less amount of data then one can use a DNN

model for multiclass classification. These all experiments are for DICOM SPECT images only. In future work, more relevant clinical data can be incorporated with SPECT DICOM images of PD, HC, and SWEDD and assess the performance of the DNN model and other ensemble models for differential diagnosis of PD, SWEDD, and HC cohorts.

Funding: This research received no external funding
Data Availability Statement: The authors do not have permission to share data..
Acknowledgments: PPMI is a public-private partnership supported by the Michael J. Fox Foundation for Parkinson's Research and several pharmaceutical and biotechnology companies. These companies include Abbott Laboratories, GE Healthcare, Avid Radiopharmaceuticals, Bristol-Myers Squibb, Covance, ´Elan, Genentech, GlaxoSmithKline, Eli Lilly and Company, Merck & Co., Meso Scale Discovery, Pfizer, Hoffmann-La Roche, UCB
Conflicts of Interest: The authors affirm that the work in this study was not impacted by any known conflicting financial interests or personal relationships.

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