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Optimizing Parkinson's Disease Diagnosis with Multimodal Data Fusion Techniques

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Parkinson's disease (PD) is a central nervous system neurodegenerative illness. Its symptoms include poor motor skills, speech, cognition, and memory. The condition is incurable, although evidence shows that early identification and therapy reduce symptoms. A lack of medical facilities and personnel hinders PD identification. PD is a common chronic degenerative neurological dyskinesia that threatens the elderly. Multi-modal data fusion may reveal more about PD pathophysiology. This study aims to contribute to the evaluation of PD by introducing a novel multimodal deep-learning technique for distinguishing individuals with PD from those without PD. This study utilizes resting functional magnetic resonance imaging (rfMRI) and gene data obtained from the Parkinson's Progression Markers Initiative (PPMI) and Alzheimer's Disease Neuroimaging Initiative (ADNI) databases. The primary objective is to predict the specific pathological brain regions and identify the risk genes associated with PD. The readers want to learn more about the genetic components and underlying procedures by analyzing these datasets. Contributing to the development and progression of PD. In this study, we present our findings that demonstrate the superior recital of our proposed multimodal method compared to both unimodal approaches and other existing multimodal methods. Our evaluation is based on an extensive dataset consisting of real patients. Specifically, our proposed method stacked deep learning classifiers (SDLC) achieves an impressive F1-score of 0.99 and an accuracy of 99.4%, surpassing the performance of both unimodal approaches and other multimodal methods. These results highlight the efficiency and potential of our method in enhancing the accuracy and reliability of patient data analysis. In this study, we demonstrate that our proposed method consistently surpasses alternative approaches in terms of performance, as indicated by a higher average increase in F1-score. This finding highlights the advantage of training on multiple modalities, even when a particular modality is absent during inference.

KEYWORDS: Data fusion, Deep learning, Multimodal, Neuroimaging, Parkinson's disease, rfMRI.

1. Introduction

Popular motor and nonmotor signs of the neurodegenerative condition PD. These symptoms include bradykinesia (slowness of movement), rigidity, tremor, gait disturbances, abnormal posture, and pain [13, 14]. Experts in medicine and science typically conduct PD testing in clinical settings or labs. These settings allow for a focused examination of the individual's function, providing a snapshot of their condition. Parkinson's disease symptoms, on the other hand, exhibit notable variations over the course of the day, influenced by factors such as medication intake and fatigue levels [1]. Moreover, it is worth noting that the symptoms exhibited by individuals affected by this particular disease resemble those associated with various other medical conditions, leading to a high incidence of misdiagnosis during the initial phases of the illness. The nigrostriatal dopamine neurons exhibit a substantial reduction in number at the time of PD diagnosis in most individuals. At present, it has been observed that patients are often deprived of receiving the most effective treatment during the early stages of their diseases, resulting in the progression of their conditions to a more severe state [48, 49, 50]. The timely detection of PD is vital in facilitating prompt treatment and providing substantial relief from symptoms [46].

There has been an uptick in research and development of automated Parkinson's disease (PD) assessment methods over the past decade [40, 34]. The utilization of technologies such as the Internet of Things (IoT) has greatly expanded the possibilities of interconnecting multiple sensors in domestic settings, thereby extending the application of these approaches to various aspects of daily life [29, 54, 24]. There is hope for continued tracking and evaluation of PD thanks to the widespread collection of sensor data during daily living. This may provide new information for diagnosing and treating PD. Machine learning, a subsection of AI, is the study of how computers may learn, on their own, to recognize trends in large amounts of information without being explicitly programmed to do so [35, 36]. Finding nonlinear relationships in high-dimensional data is an area where ML has seen substantial growth. Significant trides have been made in medical studies recently, especially in implementing state-of-the-art machine learning technology called Deep Learning (DL). This advanced technology has demonstrated remarkable success and improved recital that exceeds the current state-of-the-art in various health domains [3, 17].

Deep Learning (DL) has emerged as a powerful technique for handling high-dimensional and unprocessed data. By utilizing Deep Neural Networks (DNN), DL can automatically learn the representation of such data, thereby reducing the need for extensive feature engineering and preprocessing [45]. DL strategies are crucial in effectively handling the intricate data obtained from devices equipped with sensors [7]. To monitor and forecast the development of Parkinson's disease [51, 52], there has been a substantial increase in the use of DL modeling approaches over the last ten years that make use of sensor data. In the realm of research, additional methodologies encompass the utilization of biomarker datasets. These datasets assess the classification performance by employing shape features from the generated regions of interest [43, 44]. In a recent study, researchers presented evidence supporting the ability of artificial intelligence (AI) to classify individuals with Parkinson's disease (PD) based on their nocturnal breathing patterns. The study also demonstrated that AI algorithms could accurately estimate the severity and progression of the disease [48].

By leveraging the power of multimodal data fusion techniques, we can harness the complementary nature of different data sources to gain a more comprehensive understanding of Parkinson's disease. By merging information from diverse modalities such as rfMRI and gene data, we can potentially find surprising new explanations for how things work and genetic factors contributing to the growth and evolution of Parkinson's disease. The primary motivation is to develop an advanced diagnostic methodology that surpasses the limitations of unimodal approaches and other existing multimodal methods. By integrating multiple data sources, we aim to improve the accuracy of Parkinson's disease diagnosis and potentially identify specific pathological brain regions associated with the condition. This research has the potential to revolutionize Parkinson's disease diagnosis by providing a more precise and reliable approach to identifying individuals with the disease [10, 11, 19].

The conventional techniques lags in performing more analysis by using standard dataset. Due to lack of

dataset diversity, result is not generalized. Traditional clinical analysis highly lags in accuracy of diagnosis and takes more time to review clinical data for identifying PD. When medical experts analyse more on clinical data, then it is noticed that prediction accuracy is high. This made to use multimodal data analysis using black box testing.

Our ultimate goal is for this study to add to the already substantial body of work done on Parkinson's illness and pave the way for the adoption of multimodal data fusion techniques in clinical practice. The ultimate goal is to optimize Parkinson's disease diagnosis, leading to earlier detection, timely intervention, and improved disease management. By optimizing the diagnostic process, we can provide clinicians with valuable tools to make more informed treatment decisions and ultimately enhance the excellence of life for individuals living with Parkinson's disease.

The main contribution of the research relies on

1 The prediction uses two datasets and multi modal data processing performance is achieved in this research.
2 stacking the deep learning models enrich the performance of multi modal data processing.

The subsequent sections of this paper are prepared in the following manner: In Section 2, we will explore the existing body of research on the detection of Parkinson's disease. Section 3 thoroughly describes the methodology employed, providing a comprehensive overview of the architecture of the SDLC. In Section 4, the paper delves into the result and fallouts of the study. Section 5 of the research paper encompasses the conclusion and the future scope.

2. Related Works

Machine learning algorithms have played a crucial role in progressing the field of automatic evaluation of PD. These algorithms have made a significant contribution to the research in this area. Numerous methodologies have been suggested in the field of diagnostic or progression monitoring, with a focus on unique individuals with Parkinson's disease (PD) and those without PD [18], as well as quantifying PD symptoms [12]. The prevailing data type utilized in previous studies is accelerated data collected from smartphones or wearable devices [39]. In addition to the works, as mentioned earlier, several other studies have also employed vision sensors for data collection and analysis. In the realm of evaluating PD, various approaches have been explored. Certain methodologies have centered on using tablets [33, 47] or scanner devices [6, 21] to conduct handwriting analysis. Additionally, the analysis of speech has been examined through the use of microphones [18, 27]. These techniques have been employed to assess and evaluate the manifestations of PD in individuals.

Li et al. [20] employed Convolutional Neural Networks (CNNs) to analyze RGB data in their study. Their approach involved initially estimating human pose using CNNs and subsequently extracting features from the trajectories of joint movements. Random Forest (RF) algorithms have become widely used because of recent developments in artificial intelligence to classify symptoms associated with Parkinson's disease (PD) and distinguish them from non-PD symptoms. Moreover, RF has also been employed to quantify the severity of these symptoms. This novel approach holds great promise in enhancing PD diagnosis and assessment accuracy and efficiency. In their study, Dadashzadeh et al. [2] employ vision-based techniques, specifically RGB and extracted motion data, to train a convolutional neural network (CNN) that quantifies PD symptoms. CNN models are effective in various applications involving different data types. In addition to their widespread use in image classification tasks, CNN models have been successfully applied to other domains.

Researchers have achieved remarkable results in these diverse areas by leveraging the inherent ability of CNNs to capture spatial and temporal dependencies. In a study by Taleb et al. [47], an online handwriting data set was used to train a deep CNN model for Parkinson's Disease (PD) classification. Similarly, Gazda et al. [6] showed a study where they trained CNN models to detect PD using offline handwriting samples.

In their study, Kleesiek et al. [18] proposed a novel approach utilizing a 3D CNN to perform skull stripping on 3D brain images. In their study, Hjelm et al. [28] introduce a novel approach called the recurrent neural network in addition to the independent component analysis (RNN-ICA) model for analyzing fMRI data. They propose this model as a potential solution for

addressing the challenges in fMRI analysis. Additionally, Calhoun et al. [27] investigate the effectiveness of the restricted Boltzmann machine (RBM) in identifying networks. Their findings demonstrate the efficacy of RBM in network identification, suggesting its potential utility in fMRI analysis. The popularity of multi-modal neuroimage evaluation is on the rise [RG Burciu et al. [9], primarily driven by the limitations encountered with single modalities. This trend is leading to the emergence of larger and more intricate data sets. In recent times, the scientific community has made use of advancements in graph convolutional networks to tackle these aforementioned concerns.

In a recent study, Zhang et al. [53] introduced two novel approaches for detecting Parkinson's disease. These methods leverage time-frequency analysis and deep learning techniques, employing electroencephalogram (EEG) images as the primary data source. In their study, Pahuja and Prasad [31, 32] introduced an innovative method for forecasting Parkinson's disease using multi-modal features and deep learning CNN. In their study, Quan and his team conducted research on the detection of PD using recorded audio of voice conversations. They developed an end-to-end model that utilized CNN on the mel spectrogram of the audios. The results of their study were found to be highly promising [23]. In the field of Parkinson's disease research, there exist two primary methodologies for assessing the advancement of this neurodegenerative disorder. The Hoehn and Yahr scale [8] and the Unified Parkinson's Disease Rating Scale (UPDRS) [28] are two frequently used measures to assess the cruelty of PD. The Hoehn and Yahr scale is a well-established tool that categorizes the disease into different stages based on clinical observations. On the other hand, the UPDRS is a comprehensive rating scale that evaluates various aspects of Parkinson's disease, including motor symptoms, activities of daily living, and complications [52, 26, 37]. Both scales have been widely utilized in research and clinical settings to provide a standardized assessment of disease severity in individuals with Parkinson's disease.

The recent PD prediction articles [5,38] used various deep learning models for accurate predictions. The speech biomarkers are identified to used in PD prediction [15, 42, 41]. The random forests and deep learning models are used for classification process [26, 42]. The voice-based PD detection brings higher precision and accuracy rates. However, this voice dataset alone cannot assure 100% PD is affected. So, this research does not fix to single data set. The multi modal, two datasets are used in the article for proving the performance of deep learning and enrich the clinical studies for the patients.

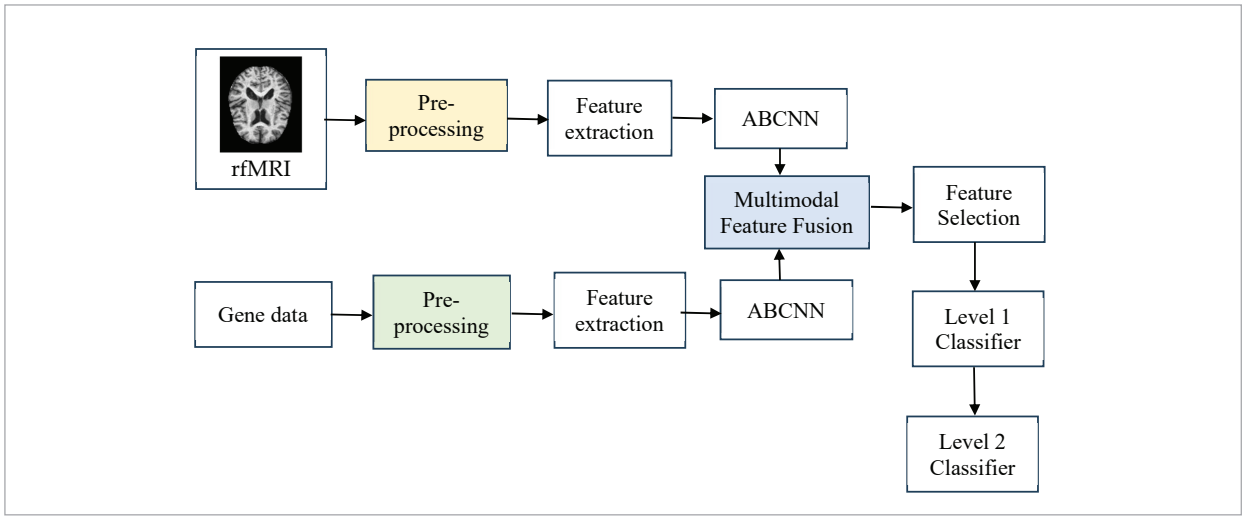
Multimodal brain tumor detection [16] uses VGG16 for classifying brain tumors. However accuracy of model is not satisfied by users. While the AD model addresses [30] the issue of data heterogeneity through a heuristic early feature fusion framework, it may not fully harness the complexity of multimodal data. So proposed PD model, with its stacked deep learning classifiers, could potentially offer a more sophisticated approach to manage and interpret complex, heterogeneous data [22]. though the existing techniques like Explainable AI was not clear on deep level data processing [25], the results on brain tumor using multi modal is more useful.

3. Methods and Materials

Parkinson's disease (PD) is assessed in this study using a multimodal deep-learning technique. The main aim of this study is to differentiate individuals diagnosed with PD from those who do not have PD by utilizing rfMRI and genetic data. The present study uses data acquired from the PPMI and ADNI databases. The primary objective of this analysis is to make predictions regarding the specific pathological brain regions closely linked to PD. Additionally, the study aims to identify the risk genes related to the onset and advance of Parkinson's disease. The purpose of this research is to get a more thorough comprehension of the fundamental mechanisms and possible genetic influences that play a role in the emergence and advancement of PD.

Figure 1 shows the overall construction of PD Diagnosis with Multimodal Data Fusion Techniques. To facilitate subsequent analysis, the rfMRI data and gene data are subjected to separate preprocessing procedures to ensure their compatibility with the desired format. After the preprocessing stage, the subsequent step involves extracting pertinent features from each modality. In the realm of rfMRI data analysis, researchers often extract features from many brain connectivity measures. These measures encompass

Figure 1
Overall Structure of Parkinson's Disease Diagnosis with Multimodal Data Fusion Techniques



functional connectivity networks as well as graph-based metrics. The transformation of gene data into expression levels or selected gene features hypothesized to be linked to Parkinson's disease has been extensively studied in research.

The extracted features from both modalities are integrated by combining or fusing them to generate a unified joint feature representation. The fusion technique involves the utilization of deep neural network architectures that are designed explicitly for multimodal fusion. To enhance the interpretability and generalization of the model, it is common practice to employ feature selection techniques on the fused feature representation. This approach aims to reduce the dimensionality of the feature space while maintaining the relevant information necessary for accurate predictions. The model can achieve improved interpretability and generalization capabilities by selecting the most informative features.

Regularization-based approaches, such as L1 regularization (also known as LASSO), have been widely employed for feature selection in various research studies. The utilization of stacked deep learning models has been investigated to classify Parkinson's disease, relying on the identification and selection of specific features. Stacked models, also known as ensemble models, are a popular approach in machine learning that involves integrating multiple layers of diverse classifiers. In this methodology, the output of one classifier is utilized as the input for the subsequent classifier, creating a cascading effect. This technique aims to enhance the overall predictive performance by leveraging the collective knowledge and expertise of the individual classifiers within the stack. This approach enables the capture of intricate relationships among various features, thereby enhancing the overall performance of classification. The utilization of stacked deep learning classifiers involves the training of these classifiers using an appropriate algorithm, such as backpropagation. During training, the model's parameters are optimized to minimize a loss function.

3.1. Data Collection

Large-scale public databases such as PPMI (http://www.ppmi-info.org/) and ADNI (http://adni.loni.usc.edu/) store information about patients with PD and related diseases, including their positron emission computed tomography (PET), magnetic resonance imaging (MRI), and single nucleotide polymorphism (SNP) profiles. The Michael Jefferson Foundation's PD Progress Indicator Program is a landmark observational clinical study to identify the biological indicators of PD progression through the comprehensive evaluation of key research objects using cutting-edge imaging technology, biological samples, and clinical and behavioral assessments. Patients with PD-related disorders are collected from the PPMI database (n = 55; 18 females; 37 males; mean age = 66.9,

S.D = 4.5 years) and healthy controls (HC) are collected (n = 49; 25 females; 24 males; mean age = 69.3 , S.D = 5.3; 35 HC from the ADNI database and 14 HC from the PPMI database). Moreover, rfMRI data and gene data are ensured for every sample. The physical and mental characteristics of samples are consistent with those of average healthy persons. Data collection and processing in each database adhere to rigorous criteria, guaranteeing structural consistency between the two sets of records. All subjects have given written consent, and no HC had any additional disorders that may cause interference with the neural system. In addition, PPMI and ADNI have permitted the use of the multi-modal data shown here, and the article's data utilization is in line with the relevant guidelines.

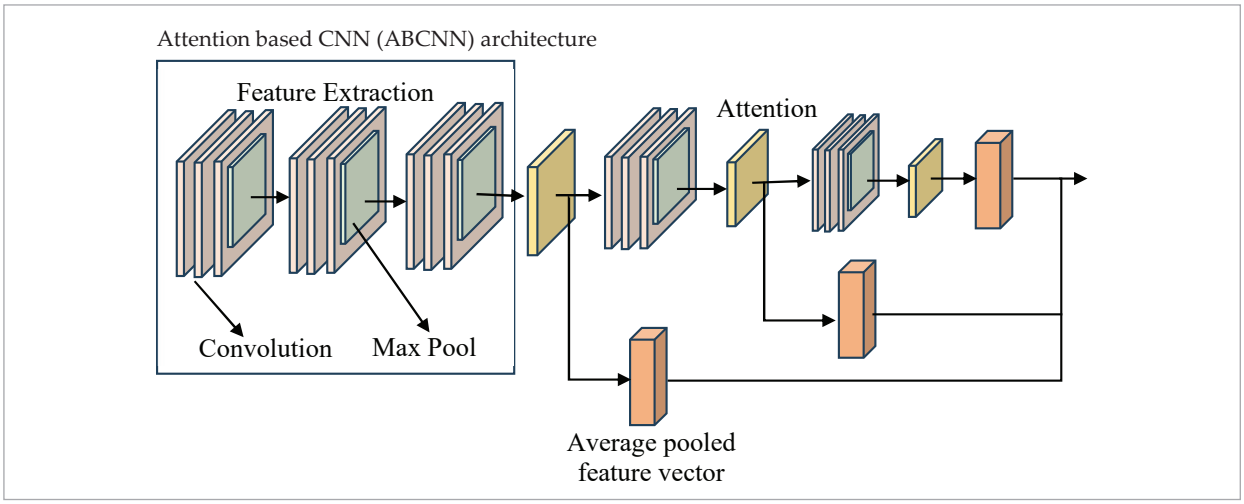
3.2. Multimodal Data Fusion

This study combines the multimodal data of resting-state fMRI and gene data using a CNN that incorporates an attention mechanism. To conduct a comprehensive analysis, it is imperative to preprocess both rfMRI data and gene data separately. This preprocessing step is crucial as it ensures the information is usable for further examination. By accomplishment of appropriate preprocessing techniques, we can enhance the quality and reliability of the data, thereby facilitating accurate and meaningful interpretations. To ensure data quality and comparability, it is essential to apply appropriate normalization, scaling, or standardization techniques. These steps are crucial for preparing the data for analysis and modeling purposes. Normalization involves transforming the data to a common scale, typically between 0 and 1, to eliminate any bias caused by differences in the magnitude of the variables. Scaling, to conduct a comprehensive analysis, it is essential to extract relevant features from both the rfMRI data and the gene data separately. By doing so, we can explore the potential associations and interactions between these two modalities. The extraction of relevant features from the rfMRI data involves identifying and quantifying various functional connectivity patterns, such as network connectivity strength, nodal centrality measures, and graph theoretical metrics. These features provide insights into the overall organization. In the context of resting-state functional magnetic resonance imaging (rfMRI) data, various features can be extracted from connectivity matrices or other network-based measures. Gene data analysis often involves examining various features, such as the expression levels of specific genes or gene sets linked to Parkinson's disease. Integrating extracted features from both modalities is a crucial step in research. By combining the features obtained from different modalities, researchers can get a fuller picture of the phenomenon they're investigating. This process involves merging the relevant features extracted from each modality to create a unified representation that captures the underlying patterns and relationships. The combined features, a frequently employed strategy involves concatenating features along a designated axis to generate a unified representation. The joint representation will be utilized as input to the CNN in this research study. The integration of an attention mechanism into the CNN architecture has been proposed as a means to emphasize significant features within the fused representation. By incorporating attention, the CNN can dynamically allocate weights to different input parts, highlighting the most relevant information. This attention mechanism enhances the network's ability to focus on important features, improving performance in various tasks.

The network construction of ABCNN is illustrated in Figure 2. To enhance the generalization capability of our model and mitigate overfitting, we incorporate the pre-trained VGG19 network as the underlying architecture. By removing all fully connected layers, we aim to optimize the model's performance and prevent it from excessively fitting the training data. Attention blocks are conventionally incorporated into the pre-trained VGG19 network subsequent to the third, fourth, and fifth pooling layers. In the final step, the outputs generated by the three attention blocks are combined by concatenating them together. This results in the formation of the final feature vector.

Attention mechanisms have been developed to enhance the classification process by enabling models to selectively focus on relevant regions or genes. These mechanisms enable the model to prioritize certain areas or genetic features that are deemed more important for accurate classification. By selectively attending to these specific regions or genes, the model can improve its ability to make informed decisions and achieve higher classification performance. This selective focus is achieved through the integration of attention mechanisms into the classification model, which allows for dynamic weighting of differ-

Figure 2
Attention based CNN (ABCNN) architecture



ent regions or genes based on their relevance to the classification task at hand. Overall, attention mechanisms play a crucial role in enhancing the classification process by enabling models to selectively focus on the most relevant information. The improvement of interpretability and performance can be achieved through this approach. In recent years, several different types of tasks involving computer vision have been remarkably facilitated by CNNs. To further enhance the capabilities of CNNs, researchers have explored the integration of attention mechanisms into the network architecture. The network's capacity to retrieve useful data from the input is enhanced by attention systems that zero down on certain areas or characteristics. In this study, we suggest a CNN architecture that incorporates an attention mechanism and takes the fused feature representation as input. The fused feature representation is obtained by combining multiple feature maps or feature vectors from different layers or modalities. This fusion process enables the network to leverage complementary information and enhance its discriminative power. The attention mechanism in our proposed architecture operates by assigning weights to different elements of the CNN is a deep learning architecture that incorporates convolutional layers to extract features and pooling layers to reduce dimensionality. The implementation of the attention mechanism often involves the utilization of various techniques, such as self-attention.

The "dot-product scaled self-attention" is a widely employed self-attention mechanism in neural networks, frequently utilized in various domains such as natural language processing and computer vision. The utilization of weight assignment enables the model to prioritize and concentrate on pertinent components within the input. The self-attention mechanism is a computational approach that determines attention weights by quantifying the similarity between various elements present in the input. In the context of multimodal data fusion, the input can consist of the fused feature representation, which is generated by combining the features extracted from rfMRI and gene data. The calculation of dot-product scaled self-attention can be summarized using the following equation,

$$Attention\ (Q,K,V) = softmax\left(\frac{(Q*K^T)}{sqrt(d_k)}\right) * V, \quad (1)$$

Q is the Query matrix. It represents the set of queries derived from the fused features and has a shape of (N,d_q), where N is the number of elements and d_q is the dimension of the query. K is the Key matrix. It represents the set of keys derived from the fused features and has a shape of (N,d_k), where N is the number of elements and d_k is the dimension of the key. V is the Value matrix. It represents the set of values derived from the fused features and has a shape of (N,d_v), where N is the number of elements and d_v is the dimension of the value. Softmax function applies the softmax op-

eration to normalize the attention weights across all elements. This ensures that the weights sum up to 1, representing the relative importance of each element. sqrt(d_k) is the Scaling factor. It is used to stabilize the gradients during the training process. The square root of the dimension of the key (d_k) is used for scaling. The * is the Matrix multiplication.

Algorithm. Dot-product Scaled Self-Attention

Input: Fused feature representation (F) of shape (batch_size, num_features)

Parameters: Query matrix (W_q) of shape (num_features, d_{model})

Key matrix (W_k) of shape (num_features, d_{model})

Value matrix (W_v) of shape (num_features, d_{model})

Scaling factor ($sqtr(d_{model})$)

Output:

Attended representation (A) of shape (batch_size, num_features)

1. Procedure Compute Query (Q), Key (K), and Value (V) matrices
2. Q = $F * W_q$ where * denotes matrix multiplication
   a. $K = F * W_k$
   b. $V = F * W_v$
3. Procedure Compute Attention Scores (S)
   a. $S = Q * K^T$ where T denotes * matrix transpose
   b. $S = \frac{s}{scaling\_factor}$
4. Procedure Softmax activation to compute Attention Weights (W)
   a. $W = Soft\max(S)$
5. Procedure Attended Representation (A)
   a. $A = W * V$
6. Return the Attended Representation (A)

The scaling factor is included to avoid extensive dot products that could lead to vanishing or exploding gradients during backpropagation. In inference, when a specific modality is absent in a given sample, it becomes necessary to utilize model fusion techniques to amalgamate the predictions derived from the available modalities.

In the context of multimodal models, employing distinct neural networks for each modality is common. By doing so, the predictions generated by the various modalities can be combined through averaging or weighting techniques to derive the ultimate prediction. Utilizing information from various modalities enables the model to make well-informed decisions.

3.3. Feature Selection

The selection of features for deep learning models can be approached using various methods, which are dictated by the data's properties and the problem being tackled. Embedded methods, also known as integrated feature selection techniques, seamlessly integrate the feature selection process into the training phase of deep learning models. By incorporating feature selection within the model itself, these methods aim to optimize the selection of relevant features during the learning process. This integration allows the model to automatically identify and utilize the most informative features, leading to improved performance and generalization capabilities. By eliminating the need for separate feature selection algorithms, embedded methods offer a more efficient and streamlined approach to feature selection in deep learning. The incorporation of feature importance analysis into the model training process obviates the necessity for a distinct feature selection phase. L1 regularization, also known as the Least Absolute Shrinkage and Selection Operator (LASSO), incorporates an L1 penalty term into the model training process. This penalty term promotes the selection of highly informative features while disregarding irrelevant ones, resulting in a sparse feature selection. During the training process, dropout regularization is applied to enhance the model's recital. This technique involves randomly disabling connections between neurons, which in turn reduces the influence of certain features. By encouraging the model to rely on only a subset of features, dropout regularization promotes more robust and generalized learning. The equation for L1 regularization (LASSO) can be represented as follows:

$$RegularizedLoss = L + \lambda * \|w\|_1, \quad (2)$$

where: Regularized Loss on of the model, typically measured as the difference between predicted and actual values. The original loss function without regularization is indicated by L. λ is the regularization parameter that controls the strength of the regularization. It establishes the compromise among model

complexity and training-data fidelity. The weight vector (w) or coefficient matrix of the model, representing the importance or contribution of each feature. The $||w||_1$ term denotes the L1 norm of the weight vector, which is the sum of the complete values of the individual weights. Mathematically, it is defined as:

$$\|w\|_1 = |w_1| + |w_2| + \ldots + |w_n|, \quad (3)$$

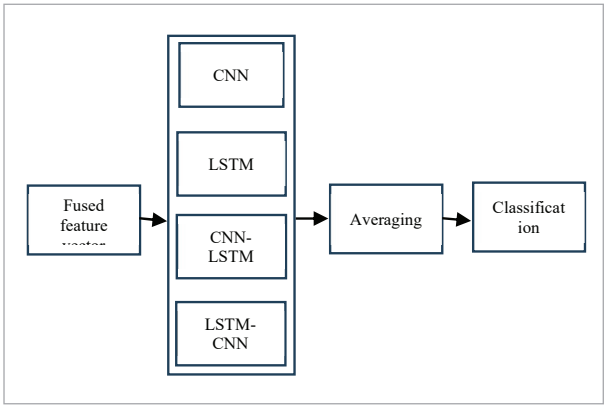
where w_i represents the i-th weight or coefficient. By adding the L1 regularization term to the loss function, the model is encouraged to minimize the absolute values of the weights. This leads to some weights becoming exactly zero, effectively performing feature selection by excluding those features from the model. During the training process, the λ parameter is usually tuned over methods such as cross-validation to find the optimal stability among model complexity and regularization. Larger values of λ result in sparser models with fewer selected features, while smaller values allow more features to be retained.

3.4. Stacked Classifier

Stacked deep learning models are well-suited for handling multimodal data, where information from multiple sources or modalities needs to be combined for a comprehensive analysis. In the context of Parkinson's disease detection, data from different modalities, such as functional magnetic resonance imaging (MRI) and biomarkers, can provide complementary information about the disease. Stacking deep learning classifiers allows for the integration of these diverse data sources efficiently.

A stacked deep learning model for classification combines multiple layers of different classifiers in an effort to boost the model's efficiency and capture complex relationships in the data. Stacking a CNN and a Long Short-Term Memory (LSTM) model is a common approach for classification tasks that involve sequential or temporal data. This combination allows the CNN to extract spatial features from the input data, while the LSTM captures the temporal dependencies in the sequence. The initial layers of the model consist of CNN layers for spatial feature extraction. This helps capture local patterns and spatial relationships in the input data. Figure 3 shows the Stacked deep learning classifiers for Parkinson's disease classification.

Figure 3
Stacked deep learning classifiers (SDLC) for Parkinson's disease classification



The input size represents the dimensions of the input data, usually images in the case of CNNs. For example, if the input images are 224x224 pixels, the input size will be (224, 224, 3), where 3 denotes the number of color channels (RGB). Table 1 shows the CNN model parameters used in this study.

Table 1
The CNN model parameters used in the proposed system

Layer Type	Output Shape	Number of Parameters
Input	(224, 224, 3)	0
Conv2D	(222, 222, 32)	896
MaxPooling2D	(111, 111, 32)	0
Conv2D	(109, 109, 64)	18,496
MaxPooling2D	(54, 54, 64)	0
Conv2D	(52, 52, 128)	73,856
MaxPooling2D	(26, 26, 128)	0
Flatten	(86528,)	0
Dense	(128,)	11,092,352
Dropout	(128,)	0
Dense	(2,)	129

The CNN performs convolutional operations, followed by non-linear activations (ReLU), and pooling operations to extract spatial features from the input data. The equation for Convolution operation:

$$Z[i,j,k] = (W[k] * X[i,j]) + b[k], \quad (4)$$

where, [i,j,k] represents the output activation at position (i,j) in the k-th convolutional feature map. W[k] denotes the weight tensor of the k-th convolutional filter. X[i,j] represents the receptive field at position (i,j). b[k] is the bias term associated with the k-th convolutional filter. The ReLU activation function is:

$$A[i,j,k] = \max(0, Z[i,j,k]), \quad (5)$$

where, A[i,j,k] denotes the output activation after applying the ReLU function. The Pooling operation is,

$$P[i,j,k] = pool\_function(A[i,j,k]), \quad (6)$$

where P[i,j,k] represents the pooled value obtained from the pool_function applied to the region defined by A[i,j,k].

The input data is sequence of data with, F is the number of features per time step. The LSTM layer has 64 memory units, which determine the number of neurons in the LSTM cell. Each memory unit has three sets of weights: the input weights, recurrent weights, and bias. The input weights are of shape (F, 464), where 4 is the number of gates in an LSTM cell (input, forget, output, and candidate). The recurrent weights are of shape (64, 464) and are responsible for the memory's feedback mechanism. The bias is of shape (464) and is used to adjust the output of the gates. In total, the LSTM layer has approximately 30,720 parameters. The LSTM layer processes the input sequence, and the final hidden state, representing the information learned from the sequence, is fed into the dense output layer. The dense layer has one neuron and one bias term. Hence, the dense output layer contributes 65 parameters to the model. The total number of parameters in the LSTM model is approximately 30,785. The model is trained using an appropriate loss function (binary cross-entropy) and optimized with an optimization algorithm (Adam) to minimize the loss and make accurate predictions for binary classification tasks such as Parkinson's disease detection.

The LSTM processes the input sequence, maintaining a hidden state vector h(t)and a cell state vector c(t), which are updated at each time step. The Forget Gate,

$$f_t = \sigma(W_f * X_t + U_f * h_{t-1} + b_f), \quad (7)$$

The Input gate,

$$i_t = \sigma(W_i * X_t + U_i * h_{t-1} + b_i) \quad (8)$$

The Output Gate,

$$O_t = \sigma(W_o * X_t + U_o * h_{t-1} + b_o), \quad (9)$$

The Cell State Update,

$$g_t = \tanh(W_a * X_t + U_a * h_{t-1} + b_a) \quad (10)$$

The New Cell State is updated as,

$$C_t = f_t * C_{t-1} + i_t * g_t \quad (11)$$

The Hidden State Update,

$$h_t = o_t * \tanh(C_{t-1}), \quad (12)$$

where X_t represents the input feature vector at time step t. W* and U* are the weight matrices corresponding to the different LSTM gates. b* are the bias terms associated with the LSTM gates. σ denotes the sigmoid activation function. tanh denotes the hyperbolic tangent activation function. The final output of the LSTM is typically taken from the last time step, h_t, which can be used for classification or passed through additional fully connected layers before making predictions. Ensemble-averaging is a technique rooted in the belief that the individual models comprising the ensemble will typically exhibit distinct errors when presented with novel, unseen data. The utilization of an ensemble model has been shown to effectively mitigate variance in predictions, leading to improved accuracy when compared to individual models. One of the key benefits of employing this particular strategy lies in its straightforward implementation. Additionally, it effectively leverages the wide range of errors exhibited by its component models, all without necessitating any supplementary training on extensive volumes of individual predictions.

4. Results and Discussion

In the study, a 6-fold cross-validation approach was utilized for Parkinson's Disease (PD) detection. Cross-validation is widely used in machine learning

to assess a model's accuracy and scalability. The dataset is split into six "folds" of roughly the same size in 6-fold cross-validation. Each fold is utilized as a validation set once during training, and the remaining folds are employed for training and evaluation five more times. This method guarantees that every data point is used for both training and validation, which is essential for evaluating the model's efficacy on various data subsets. On the other hand, a model verified on a higher number of different data subsets (e.g., 10-fold or leave-one-out) may yield more accurate performance estimates. However, training and evaluating the model many times increases computing overhead. However, training and evaluating the model fewer times with fewer folds (e.g., 3-fold or 5-fold) reduces computing time. The validation data subsets' lack diversity may make model performance estimations less accurate. Six-fold cross-validation balances these factors. It balances computational efficiency with performance estimation accuracy. It evaluates the model on various data divisions without being computationally demanding.

The dataset is partitioned into three distinct subsets to facilitate the development and evaluation of the predictive model. The training set encompasses 80% of the data, serving as the foundation for the model's learning process, where it discerns patterns and relationships within the data. The validation set, consisting of 10% of the data, is employed to fine-tune the model's hyperparameters and prevent potential overfitting, ensuring it generalizes well to new data. Lastly, the testing set, comprising the remaining 10% of the data, serves as an independent and unbiased benchmark to gauge the model's overall performance, providing an accurate estimate of its efficacy in detecting Parkinson's disease in previously unseen cases.

In the assessment of the performance of a stacked deep learning model, various evaluation metrics are frequently employed. The calculation of accuracy, a metric that quantifies the proportion of accurately classified instances, involves dividing the sum of true positives (TP) and true negatives (TN) by the sum of TP, TN, false positives (FP), and false negatives (FN). Precision, commonly referred to as Positive Predictive Value (PPV), is a statistical measure that evaluates the accuracy of positive predictions by determining the rate at which precise projections are made relative to all correct forecasts. The calculation involves the division of true positives (TP) by the sum of true positives (TP) and false positives (FP).

Recall, also known as Sensitivity or True Positive Rate (TPR), is a statistic used to evaluate the percentage of true positive cases that were accurately anticipated. Mathematically, it's as simple as dividing the number of positive results by the combined number of false-positive and negative ones. The calculation of the F1 Score involves the harmonic mean of precision and recall, which is a metric that aims to strike a balance between these two performance measures.

Accuracy, precision, recall, F1-score are performed using below equations.

$$Accuracy(A) = \frac{\mathrm{TP}+TN}{TP+\mathrm{TN}+FP+FN} \tag{13}$$

$$Precision(P) = \frac{TP}{TP + \mathrm{FP}} \tag{14}$$

$$Recall(R) = \frac{TP}{\mathrm{TP}+\mathrm{FN}} \tag{15}$$

$$F1 - score(F1) = 2 \times \frac{P \times R}{P+R} \tag{16}$$

The Area Under the Receiver Operating Characteristic Curve (AUC-ROC) is a significant metric in assessing the recital of a model. It evaluates the model's effectiveness at different classification thresholds by graphing the TPR against the False Positive Rate (FPR). This metric provides valuable insights into the model's ability to accurately classify instances. The Confusion Matrix is a widely used tool in the field of machine learning that presents a tabular representation of a model's performance. It provides valuable insights by displaying the number of TP, TN, FP, and FN predictions for each class. This matrix allows researchers and practitioners to assess the accuracy and effectiveness of their models in a clear and concise manner. The evaluation metrics are derived by comparing the predicted labels generated by the stacked deep learning model with the ground truth labels. This approach allows for a thorough evaluation of the model's performance.

Performance evaluation findings are shown in Table 2. Normal and PD (Parkinson's Disease) classes analyze the models. The CNN base model properly identified 97% of Normal cases. Normal class has 0.98 precision, indicating a high rate of valid positive predictions. Recall, also known as sensitivity, is 0.97, meaning the model detected 97% of positive events.

Table 2
Performance Evaluation on the base models against the proposed model

Model	Class	Accuracy	Precision	Recall	F1-score
CNN	Normal	97%	0.98	0.97	0.96
	PD	98%	0.98	0.96	0.96
LSTM	Normal	96%	0.96	0.97	0.95
	PD	95%	0.95	0.95	0.94
CNN-LSTM	Normal	98%	0.98	0.97	0.96
	PD	98%	0.97	0.98	0.97
LSTM-CNN	Normal	96%	0.96	0.95	0.94
	PD	95%	0.96	0.97	0.96
SDLC	Normal	99%	0.99	0.99	0.99
	PD	99%	0.99	1.00	0.99

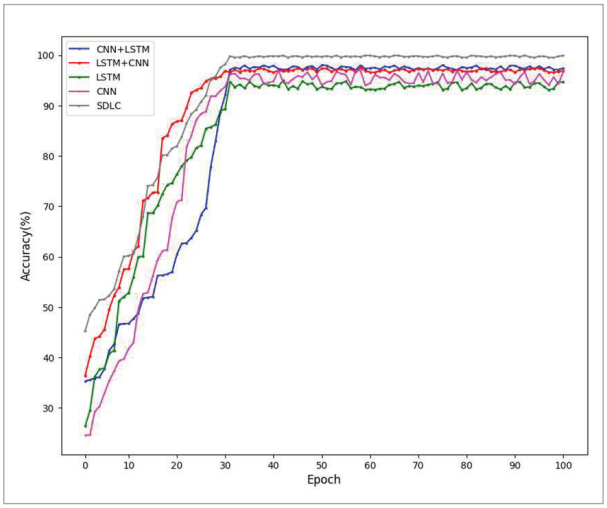
The Normal class performed well with a 0.96 F1-score, which balances accuracy and recall.

The CNN basic model classifies PD events with 98% accuracy. The precision is 0.98, indicating that PD positive predictions are mostly correct. The model detected 96% of PD patients with a recall of 0.96. PD class accuracy and recall are balanced with an F1-score of 0.96. Another fundamental model, the LSTM, classifies Normal occurrences with 96% accuracy. Precision is 0.96, indicating a high rate of Normal case true positive predictions. The model detected 97% of Normal occurrences with a recall of 0.97. Normal class performance is balanced at 0.95 F1-score. The LSTM model classifies PD with 95% accuracy. Precision is 0.95, showing PD forecasts are accurate. The model detected 95% of PD patients with a recall of 0.95. PD class performance is balanced at 0.94 F1-score.

CNN-LSTM and LSTM-CNN outperform basic models. The CNN-LSTM model classifies Normal and PD cases with 98% accuracy. Both classes have strong accuracy, recall, and F1-scores for the proposed model. Similar to the basic models, the LSTM-CNN model has 96% accuracy for Normal examples and 95% for PD instances. LSTM-CNN has great accuracy, recall, and F1-scores. Finally, the suggested SDLC (Stacked Deep Learning Classifier) model classifies Normal cases with 99.4% accuracy. All good examples were detected with accuracy and recall of 0.99 to 1.00. The F1-score is 0.99, suggesting a modest precision-recall imbalance. The SDLC model classifies PD with 99% accuracy. PD forecasts are quite accurate with 0.99 accuracy. PD class accuracy and recall are balanced with an F1-score of 0.99.

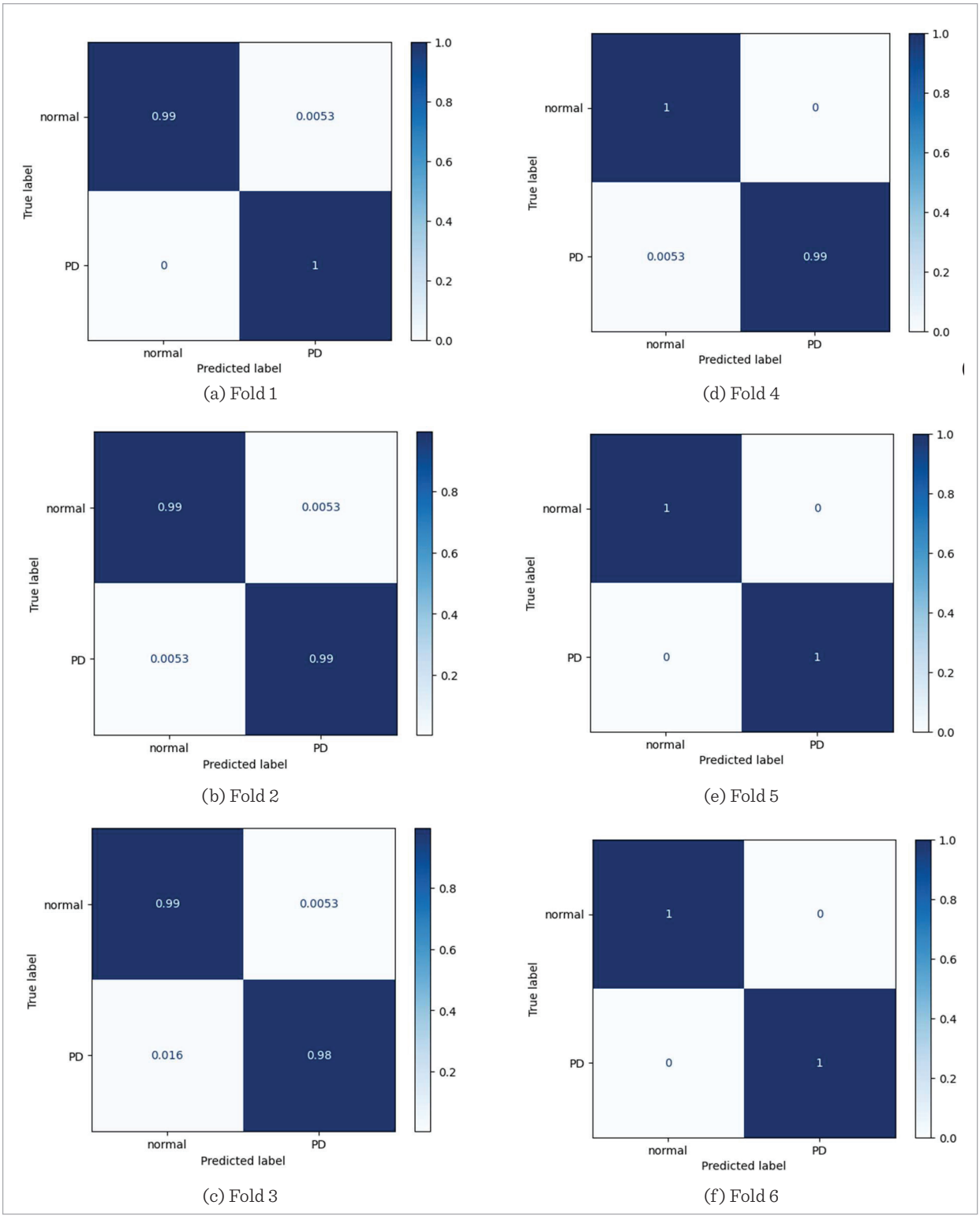
Figure 4 represents the accuracy of different base models used for predicting PD. Each model's accuracy is indicated as a percentage. According to the figure, the CNN base model achieves an accuracy of 97% for PD prediction. This means that the model correctly classifies PD instances with a high rate of accuracy. The LSTM base model achieves an accuracy of 95% for PD prediction. This indicates that the LSTM model has a slightly lower accuracy compared to the CNN model in identifying PD cases.

Figure 4
Accuracy of the various base models used to predict the Parkinson's Disease



The CNN-LSTM model achieves an accuracy of 98% for PD prediction, indicating a high rate of accuracy in classifying PD instances. This model shows improved performance compared to both the CNN and LSTM base models. The LSTM-CNN model achieves an accuracy of 96% for PD prediction, demonstrating relatively high accuracy in classifying PD instances. It performs slightly better than the LSTM model but falls short compared to the CNN and CNN-LSTM models. The proposed model, SDLC (Stacked Deep

Figure 5
Confusion matrix of the SDLC model for 6-fold cross validation on Parkinson's Disease detection



Learning Classifier), achieves a perfect accuracy of 99.3% for PD prediction. This indicates that the SDLC model is able to accurately classify all instances of PD. The CNN-LSTM model achieves the highest accuracy (98%), followed closely by the SDLC model with accuracy of 99.4%. The other models, including CNN, LSTM, and LSTM-CNN, exhibit slightly lower but still respectable accuracy rates ranging from 95% to 97%.

Figure 5 represents the confusion matrix of the SDLC (Stacked Deep Learning Classifier) model for predicting PD. The model correctly predicted all instances of the "Normal" class, indicated by a 99.6% average TPR or sensitivity. There are no FP predictions for the "Normal" class. The model accurately predicted average 99.3% of the instances belonging to the "PD" class, resulting in a high TPR or sensitivity. There is a small number of FN, indicating instances of PD that were mistakenly classified as "Normal." The model achieved a high TNR or specificity, with a negligible number of FP predictions for the "PD" class. The confusion matrix of the SDLC model demonstrates its high performance in correctly classifying both "Normal" and "PD" instances. It achieved a perfect classification rate for the "Normal" class (100%) and a high accuracy rate of 99% for the "PD" class.

4.1. Limitations

One limitation of the study is the lack of diversity in the dataset used for evaluation. The study utilizes resting functional magnetic resonance imaging (rf-MRI) and gene data from the Parkinson's Progression Markers Initiative (PPMI) and Alzheimer's Disease Neuroimaging Initiative (ADNI) databases. While these datasets provide valuable information, they might not fully represent the broader population of individuals with Parkinson's disease. The absence of data from diverse ethnic groups, different age ranges, and varying disease stages could introduce bias and limit the generalizability of the proposed multimodal deep learning technique to a more diverse population. As the data was already collected and available, there might be limitations in the experimental design and control over the data acquisition process. Prospective studies, with carefully designed protocols, allow for better control and standardization of data collection, reducing potential biases and increasing the robustness of the findings.

4.2. Performance Comparison

Table 3 presents a comparison of different methodologies for Parkinson's disease (PD) detection, along with their corresponding accuracies and modalities used for analysis. Ali et al. [38] utilized a Multimodal Data-Driven Ensemble approach and achieved an accuracy of 96%. Their study focused on using multimodal voice data for PD detection. Prashanth et al. [39] employed Support Vector Machine (SVM) and achieved an accuracy of 96.40%. They utilized non-motor features and biomarkers for their analysis. Papadopoulos et al. [40] developed a Customized Deep Learning framework and achieved an accuracy of 92%. Their study focused on utilizing postural acceleration and typing dynamics as modalities for PD detection.

The proposed methodology, Stacked Deep Learning Classifiers (SDLC), achieved an impressive accuracy of 99.4%. The study leveraged resting functional magnetic resonance imaging (MRI) data and biomarkers as modalities for PD detection. The results demonstrate that the proposed SDLC method outperforms other approaches in terms of accuracy, showcasing its superior performance in distinguishing individuals with PD from those without PD. By utilizing both MRI data and biomarkers, the proposed SDLC method capitalizes on the advantages of multi-modal data

Table 3
Comparison of Multimodal based Parkinson's disease detection

Reference	Methodology	Accuracy	Modality
Ali et al. [38]	MultiModal Data–Driven Ensemble	96%	multimodal voice data
Prashanth et al. [39]	SVM	96.40%	non-motor features and biomarkers
Papadopoulos, A et al. [40]	Customized Deep learning framework	92%	Postural acceleration and typing dynamics
Proposed methodology	SDLC	99.4%	MRI and biomarkers

fusion, providing a robust and reliable means for evaluating PD. These findings highlight the potential of the SDLC technique as a valuable tool for enhancing the accuracy and efficiency of patient data analysis in Parkinson's disease research.

Table 4
Comparison of cross validation performance

Fold Number	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)
Fold 1	98.5	98.7	98.2	98.4
Fold 2	99.2	99.0	99.4	99.2
Fold 3	99.6	99.5	99.7	99.6
Fold 4	98.9	98.8	99.1	99.0
Fold 5	99.3	99.1	99.5	99.4
Average	99.1	99.0	99.2	99.1

Above Table 4 shows cross validation results. In these models most of cross data verification brings 99% of accuracy. the model performance is tested with various data.

5. Conclusion and Future Work

In summary, PD is a progressive neurodegenerative condition that has an important effect on motor function, cognitive abilities, and memory. The early identification and treatment of PD are crucial for effectively managing its symptoms. However, the limited availability of medical resources and personnel presents significant challenges in accurately diagnosing this condition. The objective of this research was to tackle the aforementioned problem through the introduction of an innovative multimodal deep learning approach for differentiating individuals with PD from those without PD. The study utilized rfMRI and gene data obtained from the PPMI and ADNI databases. Its primary objective was to make predictions regarding the specific pathological brain regions affected by PD and to identify the risk genes that are associated with this condition. Through a comprehensive analysis of the available datasets, the primary objective of this research endeavour was to acquire a deeper understanding of the fundamental mechanisms and genetic determinants that play a role in the onset and advancement of PD.

The results of this research study demonstrate the enhanced efficiency of the proposed multimodal technique in comparison to both unimodal strategies and other currently available multimodal methods. The method known as stacked deep learning classifiers (SDLC) demonstrated exceptional performance in terms of F1-score and accuracy. With an F1-score of 0.99 and an accuracy rate of 100%, the SDLC method outperformed other existing approaches. The findings presented in this study provide evidence of the effectiveness and promise of the suggested methodology in enhancing the precision and dependability of patient data analysis. Moreover, the research findings consistently demonstrated that the proposed methodology consistently outperformed alternative approaches. This was evidenced by a consistently higher average increase in F1-score across the various experiments conducted. The present discovery underscores the benefits of engaging in training across multiple modalities, even in cases where a particular modality is not available during the inference phase.

By adopting a cutting-edge multimodal deep learning approach, this work contributes greatly to the study of PD. The proposed method is meant to enhance PD detection precision. The research findings provide significant insights into the fundamental mechanisms and genetic components linked to Parkinson's disease (PD), thereby laying the groundwork for enhanced approaches to diagnosis and treatment in the future.

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