



ARTIFICIAL INTELLIGENCE IN PARKINSON'S DISEASE DETECTION

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Abstract : Parkinson's Disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms that significantly impair quality of life. Early detection and accurate diagnosis of PD remain critical challenges due to the complexity of its symptoms and the overlapping characteristics with other neurological disorders. Artificial Intelligence (AI) has emerged as a powerful tool in medical diagnosis, particularly through the application of Machine Learning (ML) and Deep Learning (DL) techniques. This comprehensive review explores the advancements in AI-based approaches for detecting and diagnosing Parkinson's Disease, focusing on various ML algorithms and DL architectures used in image processing, voice analysis, gait assessment, and biomarker identification. The review highlights the strengths and limitations of different models, such as Support Vector Machines (SVM), Random Forests, Convolutional Neural Networks (CNNs), and Recurrent Neural Networks (RNNs), in classifying PD and predicting disease progression. Furthermore, it discusses the challenges in data acquisition, feature selection, and the need for large, diverse datasets to improve model generalizability. The integration of AI into clinical practice holds promising potential for enhancing diagnostic accuracy, reducing the burden of manual assessments, and providing personalized treatment strategies for Parkinson's patients.

Keywords: Parkinson's Disease detection, Artificial Intelligence(AI), Machine Learning(ML), Deep Learning(DP), Convolutional Neural Networks(CNN), Support Vector Machines(SVM), Recurrent Neural Networks(RNN), brain imaging, gait analysis, speech analysis , biomarkers, neurodegenerative disorders.

I. INTRODUCTION

Parkinson's Disease (PD) is a chronic, progressive neurodegenerative disorder that primarily affects movement and is often associated with tremors, stiffness, and difficulty with balance and coordination. As the second most common neurodegenerative disorder after Alzheimer's disease, PD impacts millions of people globally, and its prevalence is expected to increase with aging populations. The disease is marked by the gradual loss of dopaminergic neurons in the substantia nigra region of the brain, which leads to the hallmark motor symptoms[1]. In addition to motor dysfunction, PD can also cause a range of non-motor symptoms such as cognitive decline, sleep disturbances, and depression, complicating the clinical diagnosis and management of the disease[2]. Early and accurate detection of Parkinson's Disease is critical for improving patient outcomes, as early interventions can slow disease progression and alleviate symptoms. However, diagnosing PD in its early stages is challenging due to the overlap of symptoms with other movement disorders and the absence of a definitive diagnostic test[3].

In recent years, Artificial Intelligence (AI) has garnered significant attention in the medical field, showing great promise in aiding the diagnosis and management of various diseases[4]. The application of AI, particularly through Machine Learning (ML) and Deep Learning (DL) techniques, has revolutionized traditional medical diagnostics by offering automated, data-driven solutions that can analyze large amounts of complex data with high accuracy[5]. These AI-driven methods have demonstrated their potential in Parkinson's Disease detection, leveraging diverse datasets such as brain imaging, speech patterns, gait analysis, and wearable sensor data to identify PD-specific features and biomarkers. Traditional diagnostic methods for PD rely heavily on clinical evaluations, including medical history, neurological examinations, and response to dopaminergic treatments[6]. These assessments, while effective, can be subjective and prone to variability across practitioners. Moreover, by the time PD is clinically diagnosed, significant neurodegeneration has already occurred, limiting the potential for early intervention[7]. AI-driven approaches, on the other hand, have the potential to complement these traditional methods by providing objective, quantitative assessments based on patterns in data that may be imperceptible to human experts[8]. AI models, particularly those based on ML and DL, can be trained to detect subtle changes in voice, gait, and brain imaging that are associated with early-stage PD, enabling earlier and more accurate diagnoses[9]. Machine Learning, a subset of AI, uses statistical techniques to enable computers to learn patterns from data and make predictions or decisions without being explicitly programmed for each task. In the context of PD detection, ML algorithms such as Support Vector Machines (SVM), Random Forests, k-Nearest Neighbors (k-NN), and Decision Trees have been applied to various

data types to distinguish between PD patients and healthy individuals[10]. These algorithms rely on the extraction of relevant features from data, such as movement patterns, vocal characteristics, or brain scans, which are then used to classify or predict the presence of the disease[11]. Machine learning techniques have also been employed to analyze longitudinal data, allowing researchers to monitor disease progression and predict future outcomes. Deep Learning, a more advanced subset of ML, has gained prominence due to its ability to automatically extract complex features from raw data without requiring manual feature selection. DL models, such as Convolutional Neural Networks (CNNs) and Recurrent Neural Networks (RNNs), have been particularly successful in analyzing high-dimensional data such as medical images, speech recordings, and sensor data[12]. CNNs have been widely used in brain imaging studies to detect structural and functional abnormalities associated with PD, while RNNs have been applied to time-series data, such as speech or gait, to capture temporal dependencies that are characteristic of the disease. The use of DL in PD detection has significantly advanced the field by providing more accurate and robust models, especially in cases where large, complex datasets are available[13]. In addition to improving diagnostic accuracy, AI has the potential to transform the way Parkinson's Disease is monitored and managed over time. By analyzing data from wearable sensors and mobile devices, AI models can continuously track patients' symptoms and disease progression in real-time, enabling personalized treatment strategies and more effective disease management. These tools can also empower patients to monitor their own symptoms and share data with healthcare providers, facilitating more informed and timely interventions[14].

Despite the promising advancements in AI-based PD detection, several challenges remain. One of the key limitations is the availability of large, diverse, and well-annotated datasets. Many AI models are trained on small, homogenous datasets, which limits their ability to generalize to broader populations. Furthermore, the variability in data acquisition methods, such as differences in imaging protocols or sensor placements, can lead to inconsistencies in model performance across different settings. There is also a need for greater transparency and interpretability in AI models, as clinicians and patients alike may be hesitant to rely on "black-box" algorithms for critical healthcare decisions. Ethical considerations, including patient privacy and data security, must also be addressed as AI becomes more integrated into clinical practice. This review aims to provide a comprehensive analysis of the current state of AI in Parkinson's Disease detection, focusing on both machine learning and deep learning approaches. We will explore the various types of data used in PD detection, including imaging, speech, and wearable sensor data, and evaluate the performance of different AI models. Additionally, we will discuss the challenges and limitations of current approaches and propose future directions for research to improve the robustness, interpretability, and clinical applicability of AI in PD detection. By advancing AI techniques in PD diagnosis, we can pave the way for earlier interventions, personalized treatment plans, and improved quality of life for patients with Parkinson's Disease in figure.1.

II. CONTRIBUTION OF PAPER:

- To makes significant contributions to the intersection of AI and healthcare by offering a detailed analysis of how AI technologies can be applied to the detection and diagnosis of Parkinson's Disease (PD).
- The examination of the strengths and limitations of different AI models, including Support Vector Machines (SVMs), Random Forests, Convolutional Neural Networks (CNNs), and Recurrent Neural Networks (RNNs), in terms of their accuracy and reliability in PD detection.
- The paper also identifies current challenges in AI applications, such as the need for larger, more diverse datasets and the importance of improving model transparency and interpretability.

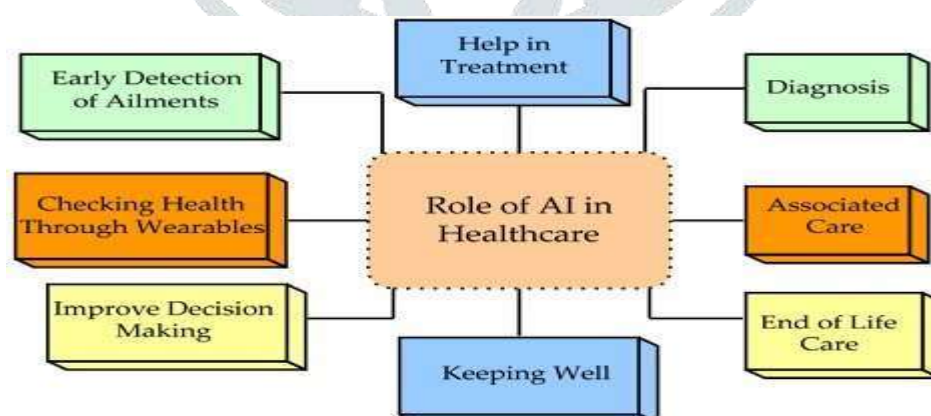


Figure.1 The function of artificial intelligence in the healthcare sector.

III. LITERATURE REVIEW ON NEUROIMAGING TO DIAGNOSE PD:

Recent advancements in Artificial Intelligence (AI) have shown great promise in improving the detection and diagnosis of Parkinson's Disease (PD), particularly through Machine Learning (ML) and Deep Learning (DL) techniques. Studies have explored the use of ML algorithms like Support Vector Machines (SVMs) and Random Forests for analysing various data types, including voice recordings, gait analysis, and wearable sensor data, to identify early signs of PD. Deep Learning models, such as Convolutional Neural Networks (CNNs), have also been successful in analysing brain imaging data, offering improved diagnostic accuracy. Furthermore, Recurrent Neural Networks (RNNs) have been applied to speech and movement data, capturing temporal patterns that are indicative of PD[15]. While these AI-driven approaches show promise, challenges remain, including data quality, model interpretability, and generalizability across diverse populations. Nonetheless, AI continues to hold significant potential in transforming PD detection and management[16].

E. Adeli et al(2019)[1]: The literature on semi-supervised discriminative classification highlights its ability to leverage both labeled and unlabeled data, making it a powerful approach in scenarios with limited labeled data. Research has focused on enhancing robustness to sample outliers and feature noise, with techniques such as noise-tolerant learning algorithms and regularization strategies improving model reliability. These methods address the challenges posed by real-world data imperfections, improving classification accuracy in noisy environments.

S.-A. Ahmadi et al(2019)[2]: The literature on computerized diagnosis of neurological stance disorders emphasizes the potential of data mining and machine learning techniques applied to posturography and sway data. Studies have explored how algorithms such as Support Vector Machines (SVMs) and Random Forests can analyze balance and postural control metrics to detect disorders more accurately. These approaches offer improvements over traditional diagnostic methods by providing objective, quantifiable assessments of stance disorders. Research highlights the promise of these techniques in enhancing early detection and personalized treatment for neurological conditions.

S. Aich et al.(2019)[3]: The literature on the application of supervised machine learning for Parkinson's Disease (PD) prediction, particularly using voice datasets, has grown significantly in recent years. Voice impairments, such as reduced vocal intensity and monotonic speech, are among the early symptoms of PD, making voice analysis a valuable non-invasive diagnostic tool. Machine learning models, including Support Vector Machines (SVMs), Random Forests, and Neural Networks, have been widely used to analyze vocal features extracted from patients' speech recordings.

H. Alaskar et al.(2018)[4]: The prediction of Parkinson's Disease (PD) using gait signals has emerged as a promising area of research, leveraging the intricate relationship between motor function and the progression of the disease. Gait abnormalities, such as reduced stride length, increased variability, and alterations in walking patterns, are often among the earliest indicators of PD.

A.S. Alharthi et al.(2019)[5]: Deep learning has increasingly gained attention for its ability to analyze ground reaction force (GRF) data, especially in the context of wide-area floor sensing applications. GRF data, which reflects the forces exerted by the ground on a body in contact with it, is crucial for understanding human movement patterns, balance, and biomechanics. Traditional methods of GRF analysis often relied on manual measurements and basic statistical techniques, which could be limited in their ability to capture complex patterns and dynamics.

L. Ali et al.(2019)[6]: The literature on evaluating speech samples for Parkinson's Disease (PD) has increasingly focused on multi-model frameworks that leverage complementary information from diverse speech characteristics. Research highlights the effectiveness of integrating various acoustic features, such as voice quality, pitch, and speech rate, to enhance diagnostic accuracy. Studies have demonstrated that combining multiple models, including traditional machine learning and deep learning approaches, can improve the robustness of PD detection by capturing subtle variations in speech patterns. This approach not only aids in early diagnosis but also provides valuable insights into the progression of the disease and its impact on communication abilities.

C. Zhu et al.(2019)[7]: The exploration of handwriting analysis as a means of detecting Parkinson's Disease (PD) has gained traction in recent years, highlighting the potential of this approach to offer non-invasive, objective diagnostic insights. Handwriting difficulties are common in PD patients, often manifesting as micrographia, tremors, and changes in writing speed and pressure. Recent studies have focused on constructing reliable systems for PD detection based on the analysis of handwritten drawings, leveraging advanced techniques such as feature selection and adaptive boosting.

Table 1. Comparative research on Parkinson's disease diagnosis using machine learning approaches

Reference	Tools	Modality	Objective	Algorithms Used	Performance
Sakar et al., 2019 [17]	JupyterLab with python programming language	Speech	The classification of PD from HC	Support Vector Machine	Accuracy (ACC.)—86%
Hsu S-Y et al., 2019 [18]	Weka	Handwriting Patterns	The classification of PD from HC	Support Vector Machine	ACC.—84.2%
Yasar A. et al., 2019 [19]	MATLAB	Speech	The classification of PD from HC	Artificial Neural Network	ACC.—94.93%
Cibulka et al., 2019 [20]	Not mentioned	Handwriting Patterns	Classification	Random Forest	Not mentioned

Ouhmida, A, 2021 [21]	Not mentioned	Speech	Classification of PD from HC	SVM, K-NN, Decision Tree	AUC-98.26%
Drotár, P et al., 2016 [22]	Python [scikit-learn library]	Handwriting Patterns	Classification of PD from HC	Ensemble AdaBoostClassifier, Support Vector Machine Classification of PD from HC	ACC.—81.3%
Marar et al., 2018 [23]	R programming	Speech	Classification	Naive Bayes	ACC.—94.87%
Fabian Maass et al., 2020 [24]	Python [scikit-learn library]	Handwriting Patterns	Classification	Random Forest	ACC.—92.87%
Sheibani R et al., 2019 [25]	Python programming	Speech	Classification of PD from HC	Ensemble-Based Method	ACC.—90.6%

2.1 Machine Learning

Machine learning (ML) is a subset of artificial intelligence (AI) in which the machine uses previous information from its previous interactions to construct a prediction model, predicts the outcome for new data, and improves its performance over time. It is distinct from normal programming. Traditional programming does not explicitly learn principles from the data; rather, they are written in a programming language. In contrast to conventional programming, machine learning generates models that are predictive by utilizing data, which are consequently employed to make predictions based on data that has not yet been observed. The design of a based-on rules program for certain issues may be exceedingly difficult due to the code's complexity. In these circumstances, ML may be implemented provided that there is an abundance of germane data [23]. Supervised learning (SL), unsupervised learning (UL), and reinforcement learning (RL) are the three categories into which machine learning (ML) can be classified, as illustrated in Figure 6. In SL, the ML model is provided with sample-labeled data as the training set, and it predicts the outcome based on this data [22]. The algorithm is obligated to make decisions autonomously to the data, and the ML model was developed with an accumulation of unlabeled and unclassified, or uncategorized data in UL. The primary goal of UL is to restructure the input data into an ensemble of objects with related structures or new features [24]. RL is a type of machine learning approach in which an intelligent agent (computer program) interacts with the environment and acquires the ability to operate within it. RL aims to determine the most effective "policy" by accruing the greatest benefits over time. The policy determines the appropriate course of action in a specific situation in figure.2.

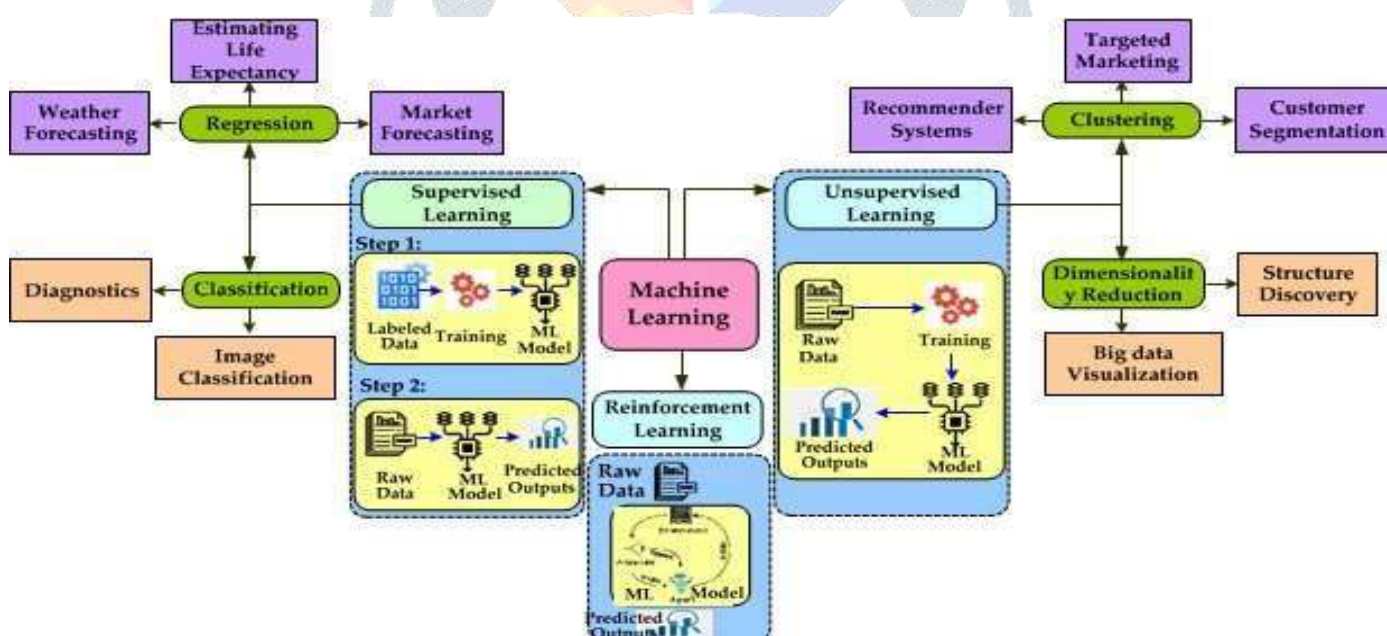


Figure.2 Categorizations of machine learning algorithms.

2.2 Deep Learning

Deep organized learning is a branch of the machine learning methodologies that is based on ANN with representation learning. DL has enormous potential in the healthcare and medical sectors as a result of the significant volume of data that is being generated (150 exabytes, or 1018 bytes, in the United States alone, growing by 48% annually) and the increasing prevalence of medical devices and electronic health records [26]. DL algorithms are frequently successful when dealing with higher-dimensional data, including audio, video, and images. Algorithms for deep learning are dynamically generated to execute throughout multiple layers of neural networks, which are essentially an ensemble of decision-making networks the fact that have been especially pre-trained to perform a specific task. Following the completion of fundamental layered visualizations, each of them is subsequently advanced to the subsequent layer. However, the majority of machine learning techniques are optimized to perform exceptionally well on datasets that contain hundreds of features or columns. ML frequently fails to identify a simple image with dimensions such as 800 x 1000 in RGB, irrespective of the organization or structuredness of the data set. It might involve rather impractical for a standard ML system to manage such depths [27]. DL approaches are those recently introduced to automate the detection and classification of PD by utilizing speech and handwriting patterns that are recorded by a smart pen . CNN and ANN are examples of deep learning. ANNs, which are networks of computational units that emulate the functionality of neural networks in biology, are frequently used for an assortment of applications, such as regression modelling, classification, along with time series analysis. They consist of multiple processor layers, with the first layer containing the input samples and the final layer delivering the prediction. Furthermore, CNN is a spatial filter-based adaptation of ANN that employs convolutional layers in order to identify the intrinsic properties, structures, and shapes of images [28]. Pooling is also employed to generate dependable features by sub sampling the features acquired by the convolutional layers, . The primary benefit of the methods mentioned earlier is their ability to autonomously learn EEG characteristics and identify anomalies based on these features in show figure.3.

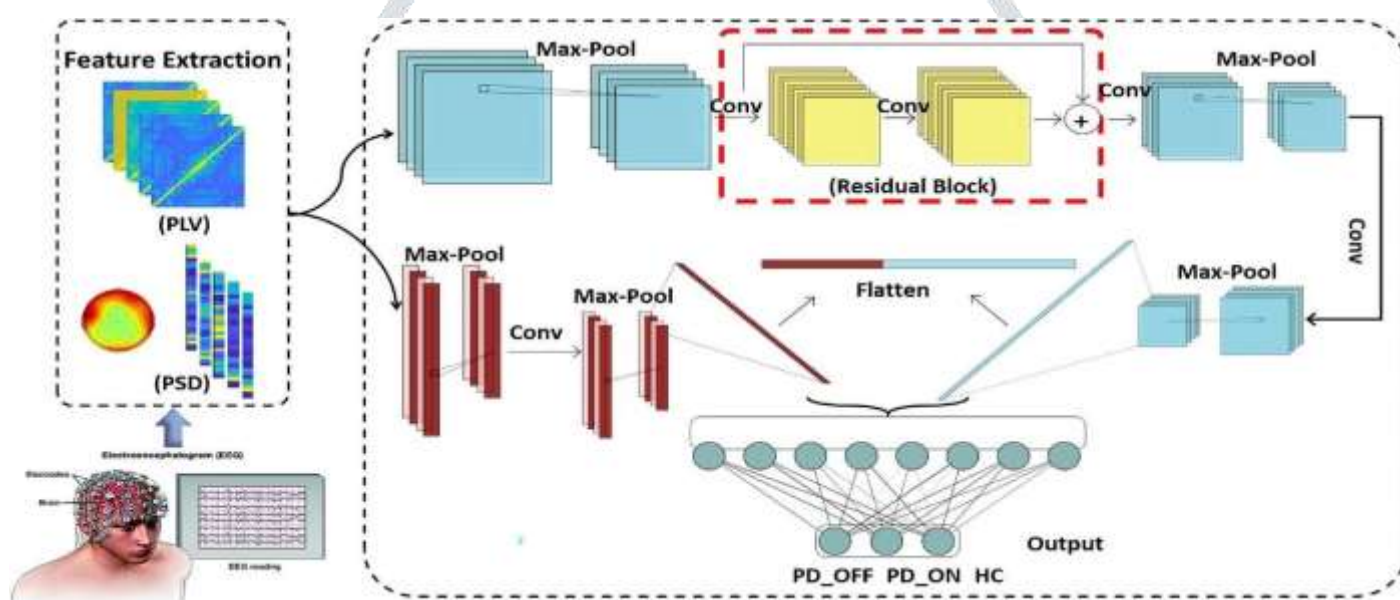


Figure.3 CNN and ANN are employed to represent the deep learning model.

2.3 Parkinson's Disease: An Overview

PD is the result of nerve cell declension in the substantia nigra area of the brain. This region of the brain produces dopamine, which is a neurotransmitter that was produced by nerve cells. Dopamine's functionality is to establish an association between the brain along with the sensory systems that regulate and direct how the body moves [29]. The brain contains a reduced amount of dopaminergic when those neurons are damaged or perish. This implies that the region of the brain that regulates mobility is dysfunctional, resulting in unpredictable, undesirable, and lethargic movements of physical elements [30]. Nerve cell death occurs progressively. After around eighty percent of the nerve cells in the substantia nigra are destroyed, signs associated with Parkinson's disease begin to emerge. at present, the disease's etiology is believed to be a combination of genetic mutations and ecological variables. Even though certain genetic factors have been demonstrated to raise one's likelihood of developing Parkinson's disease, the exact mechanism by which these factors render certain individuals more susceptible to the disease remains obscure. The dysfunctional genes are transmitted from parents to children, which is why Parkinson's disease can develop in families. However, this is a rare kind of legacy due to the medical condition. According to certain experts, the likelihood of developing Parkinson's disease may be elevated by ecological factors. Based around their motor symptoms (risk factors), the AI-based algorithm may classify individuals as having PD or not (non-PD). The dataset that was generated during the patient evaluation may be employed to construct the training model. Numerous risk factors for Parkinson's disease are established, which involves both motor and non-motor variables. Despite the fact that the symptomatic data is unable to statistically resolved, it is feasible to enhance the detection of Parkinson's disease by employing a machine learning or deep learning approach for better understanding both data classes [27]. While investigating the symptomatic biology of the disease, the most effective approach is to employ in-feature AI to accurately

predict Parkinson's disease. The following subjective and diverse evaluation methods have been employed to evaluate the severity and status of PD, which is characterized by its progressive nature: MoCA, evaluation questionnaire that GDS, RBD, UPDRS, STAI, PIGD score, SCOPA-AUT, and MMSE . The category of PD is illustrated in Figure 4.

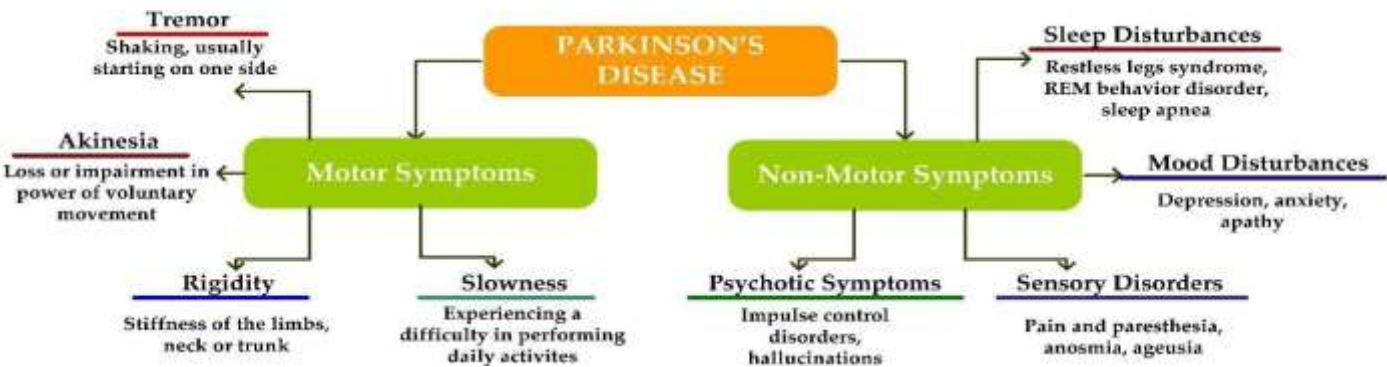


Figure.4 Parkinson's disease classification.

IV.METHODOLOGY

The methodology for this comprehensive review on artificial intelligence (AI) applications in Parkinson's Disease (PD) detection is structured to systematically identify, evaluate, and synthesize the growing body of literature on machine learning (ML) and deep learning (DL) techniques in this field. This methodology ensures a balanced and in-depth analysis of how AI contributes to early detection, classification, and progression prediction in PD, highlighting advancements and identifying gaps in current research [25].

The initial phase involved a rigorous literature search across several reputable academic databases, including IEEE Xplore, SpringerLink, ScienceDirect, Wiley Online Library, Scopus, Web of Science Google Scholar, and the ACM Digital Library show in figure.5. The aim was to capture a broad array of studies encompassing both machine learning and deep learning applications in PD detection. The search terms used were strategically chosen to maximize relevant study retrieval and included combinations of “Parkinson’s Disease,” “machine learning,” “deep learning,” “artificial intelligence,” “early detection,” “diagnostic tools,” and “biomarkers.” Boolean operators (AND, OR) were employed to refine search results, targeting studies that fall at the intersection of AI and PD[27].

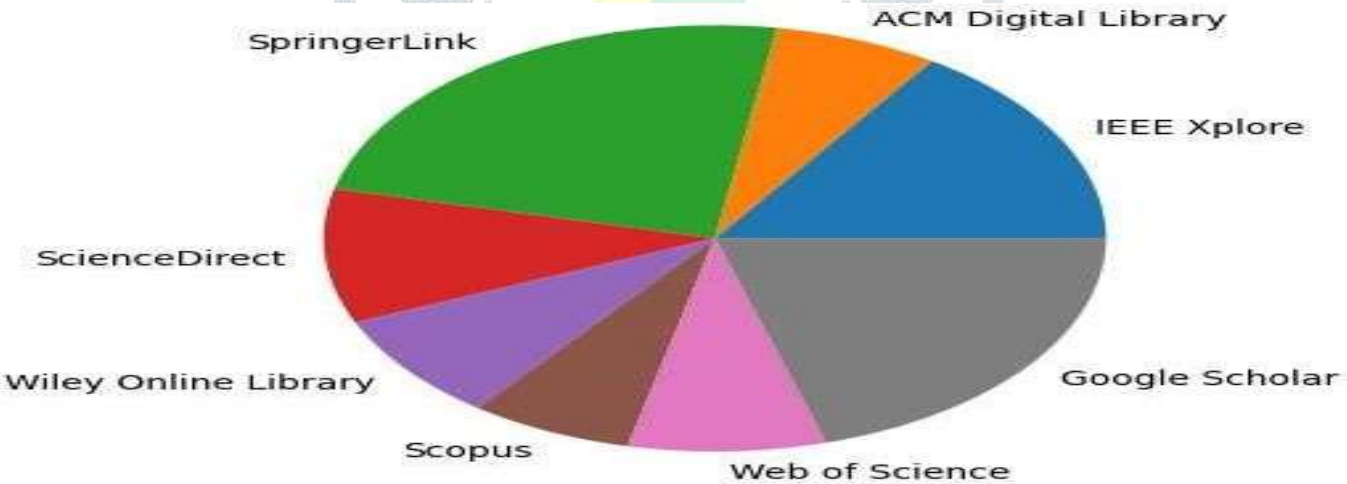


Figure.5 Reputable academic databases

To ensure that the review captured relevant and recent research contributions, inclusion and exclusion criteria were applied rigorously. Studies were considered if they had been published within the last decade, with a particular focus on those providing quantitative performance metrics—such as accuracy, sensitivity, specificity, and AUC scores—that evaluate the efficacy of AI models. Additionally, only studies focusing explicitly on PD were included, whether the methods utilized imaging, genetic, clinical, or voice-based biomarkers to aid detection and classification.

Studies lacking substantial quantitative data or those that did not contribute novel findings (such as review articles) were excluded. Moreover, while studies on neurodegenerative diseases were reviewed, only those specifically addressing PD or employing methodologies directly applicable to PD detection were selected.

The data extraction process involved compiling critical information from each study, including the type of AI model used, dataset characteristics, feature selection methods, performance metrics, and any observed limitations or challenges. Studies were then categorized based on the type of AI model applied—machine learning or deep learning—and further analyzed within subcategories, such as supervised and unsupervised learning, recurrent and convolutional neural networks, or hybrid approaches combining multiple techniques.

Following data extraction, a comparative analysis was conducted to evaluate the efficacy of various ML and DL techniques in PD detection and classification. This comparison provided insights into the relative strengths and weaknesses of each approach, especially in terms of accuracy, reliability, and computational efficiency. The methodology concludes with a synthesis of emerging trends, best practices, and potential areas for future research, based on the insights gleaned from this comparative analysis.

V. DISCUSSIONS – CHALLENGES & RECOMMENDATIONS:

Despite the absence of a known cure for Parkinson's disease, its development can be mitigated and managed through a precise and timely diagnosis. AI is a viable alternative to conventional PD detection methods for the detection of early-stage PD. Using artificial intelligence (AI) can facilitate global Patient symptom monitoring and epidemiology initiatives. Regardless of the level of stimulation these It is crucial to evaluate the prospective limitations and value of technologies, these innovative analytical methods. The most promising applications of AI are yet to be discovered futuristic [30]. In this section, we have provided a concise summary of the current obstacles and constraints and have proposed potential recommendations for the future that could result in the development of efficient AI and machine learning techniques to resolve the concerns.

4.1 Current Limitations and Challenges

At present, DL-based CAD systems are typically employed as educational tools or as diagnostic aides [29]. A program can now be developed in the actual world to diagnose Parkinson's disease using MRI modalities, thanks to the assistance of valuable research. However, investigators continue to encounter the following obstacles:

4.1.1 Challenges associated with multimodality datasets for the detection of Parkinson's disease

Researchers face an additional challenge in diagnosing Parkinson's disease: the absence of multimodal imaging datasets. Multimodality neuroimaging information frequently facilitates the identification of brain disorders, such as schizophrenia (SZ), Alzheimer's disease (AD), and Parkinson's disease (PD) [184]. The reliable detection of PD has been described in a variety of clinical investigations using a combination of neuroimaging modalities, including EEG-fMRI [25], MRI-PET [26], fMRI-MEG [27], and fMRI-sMRI [28]. The diagnosis of Parkinson's disease using multimodality neuroimaging data is a complex and time-consuming process for physicians, despite the numerous benefits. The absence of multi-modality neuroimaging datasets for the detection of Parkinson's disease has been a substantial challenge for researchers. The availability of multimodality neuroimaging datasets could lead to substantial research on the diagnosis of Parkinson's disease using AI methods.

4.1.2 Problems with Clinical Validation

Standard ML parameters, such as precision, specificity, and sensitivity and/or the area under the curve of a receiver operating characteristic curve, are primarily used to assess the efficacy of deep learning algorithms in the detection of Parkinson's disease. The clinical efficacy and expected beneficial changes to patient care may not be accurately represented by these measures. In addition, physicians must undergo training on the proper use of AI-powered diagnostic tools prior to their implementation in the clinic, as certain metrics are challenging to interpret [29]. In order to substantiate the validity of the proposed DL framework for PD diagnosis, the most recent research that addressed this issue conducted an against one another assessment of the system's efficiency with a team of neurologists and also connected model predictions with neuropathological data. It is crucial to conduct clinical validation to ensure that the imaging-specific features are comparable with the intended clinical adoption, as a result of data inconsistencies. By means of clinical adoption [30], a CAD system must be adapted to a new community, necessitating the participation of particular members of the deploying population's planned demographic of interest.

VI. CONCLUSION:

In sum, the integration of artificial intelligence in Parkinson's disease detection marks a transformative shift in the medical approach to this complex neurological disorder. Machine learning and deep learning techniques have made it possible to analyze intricate patterns within large-scale clinical, genetic, and imaging datasets, enabling earlier and more accurate identification of Parkinson's symptoms. These models can reveal underlying patterns in speech, gait, and brain imaging that may go undetected through traditional methods, promising more timely intervention and targeted treatment plans.

The convergence of AI with Parkinson's disease research also reflects a broader evolution in healthcare, where predictive, data-driven models are helping bridge the gaps in diagnostic precision and disease monitoring. However, challenges remain—particularly in ensuring that these advanced models are interpretable, ethically sound, and standardized for clinical application. Further research, coupled with robust collaborations among neurologists, data scientists, and AI researchers, is essential to bring AI

solutions from the lab to bedside. By doing so, we can not only improve diagnostic accuracy but also deepen our understanding of Parkinson's disease, paving the way toward more personalized and impactful care for patients.

VII. FUTURE SCOPE:

The future scope of artificial intelligence in Parkinson's disease detection holds great promise as advancements in machine learning and deep learning continue to unfold. As more high-quality, diverse datasets become accessible, AI models can evolve to capture even finer details in patients' physiological, genetic, and behavioral data, making early diagnosis more precise and personalized. Enhanced computational power will further allow these models to process complex, multimodal data sources, such as combining imaging with speech and motor data, to provide a more holistic view of the disease's onset and progression.

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