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Enhancing Parkinson's Disease Prediction and Further Research Using Machine Learning Techniques

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Abstract

The nerve cells that are found inside the human body are permanently damaged by a neuron-degenerative illness. Parkinson's and Alzheimer's, on nerve cells. In Parkinson's disease, the loss of dopamine neurons in the brain leads to disruptions in smooth coordination and communication with other nerve cells, resulting in characteristic motor symptoms such as tremors, stiffness, and impaired balance. This loss of coordination underscores the importance of dopamine in regulating movement and highlights one of the key pathological features of Parkinson's disease.Dopamine neuron deficit has an impact on both motor and non-motor symptoms. Physicians and other healthcare professionals still manually check patients' symptoms to diagnose Parkinson's disease. Numerous methods have been presented by researchers to identify Parkinson's disease. These methods make use of a variety of modalities, including voice signals, handwriting traces, PET and SPECT scans, MRIs, and finger tapping tests. These methods are discussed in this publication along with the difficulties that researchers are currently facing in diagnosing Parkinson's disease. Although a cure for Parkinson's disease is still a long way off, advances in recent years have substantially increased our knowledge of the illness's processes as well as its paraclinical and re-motor early signs. Although a proven disease-modifying medication has not yet been found, afflicted patients now have better options for symptomatic care. This includes invasive methods like continuous device-aided medication delivery and deep brain stimulation for patients with motor difficulties. The various aspects of non-motor issues that patients encounter have now been thoroughly identified and are the focus of non-pharmacological methods as well as therapy trials.

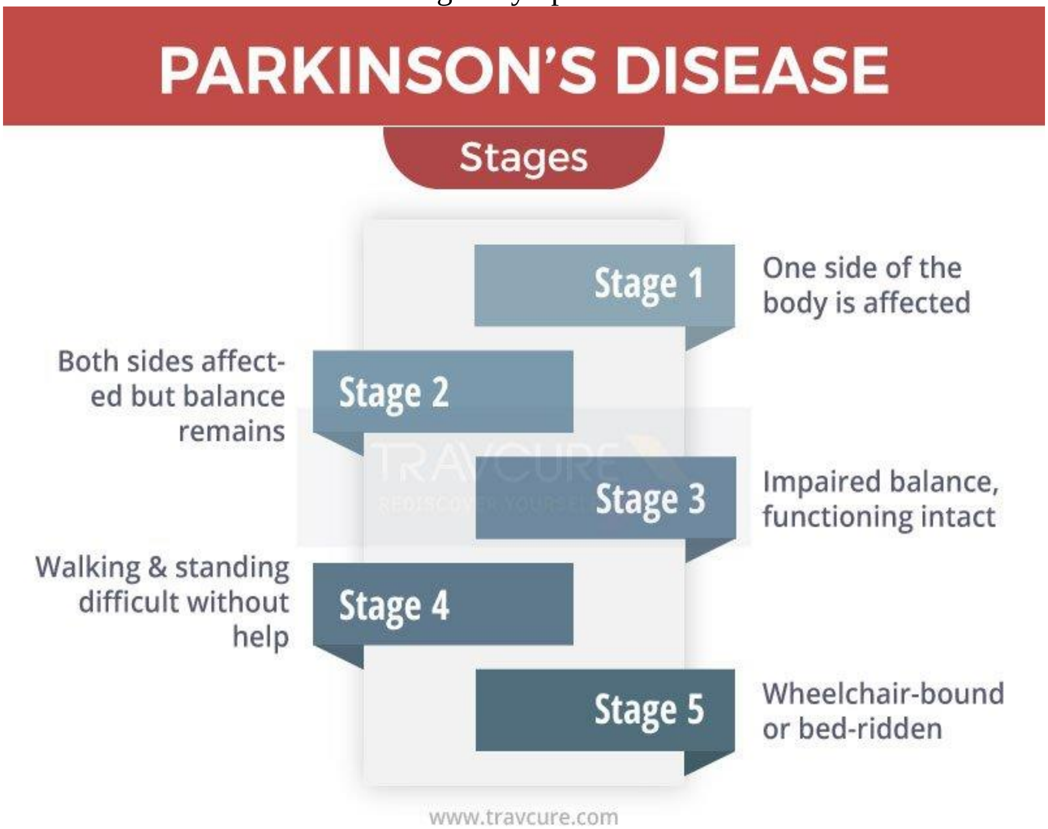
Keywords*: Parkinson Disease (PD), Detection, PET image, SPECT scan, MRI*

I. Introduction

A neuron-degenerative illness destroys the nerve cells that make up the human body permanently Alzheimer's disease is characterized by the accumulation of abnormal protein aggregates, including beta-amyloid plaques and tau tangles, in the brain. These protein aggregates lead to neuronal dysfunction and eventual cell death, particularly in regions responsible for memory and cognitive function, such as the hippocampus and cerebral cortex. Both motor and non-motor symptoms are impacted by dopamine neuron deficit. Parkinson's disease is still identified by physicians and other healthcare professionals manually examining patients' symptoms. Numerous methods for identifying Parkinson's disease have been developed by researchers. A variety of modalities, including speech signals, handwriting traces Fig.1. , PET and SPECT scans, MRIs, and finger tapping tests, are used in these procedures. These methods, together with the current difficulties faced by researchers in the identification of Parkinson's disease, are presented in this publication.

The nerve cells that are found inside the human body are permanently damaged by a neuron-degenerative illness. Parkinson's disease and Alzheimer's disease are the two most prevalent neuron-degenerative illnesses. Parkinson's disease results in the loss of dopamine neurons in the brain. These neurons are in charge of coordinating smooth coordination by corresponding with other nerve cells. Dopamine neuron deficit has an impact on both motor and non-motor symptoms. Physicians and other healthcare professionals still manually check patients' symptoms to diagnose Parkinson's disease. Numerous methods have been presented by researchers to identify Parkinson's disease. These methods make use of a variety of modalities, including voice signals, handwriting traces, PET and SPECT scans, MRIs, and finger tapping tests. These methods are discussed in this publication along with the difficulties that researchers are currently facing in diagnosing Parkinson's disease.

. Fig 1. Symptoms of Parkinson



II. Methodology Modalities for Parkinson's Detection

A growing amount of research suggests that aberrant folded proteins may be seeded by prion like mechanisms, which could then expand the neuron degeneration process. It has been demonstrated that soluble endogenous alpha-syncline is recruited into Levy body-like inclusion bodies by fibrils originating from recombination alpha-syncline, which causes neuronal death [27]. Recent research has confirmed that alpha-syncline is pathogenic. After being extracted from the post-mortem brains of Parkinson's disease patients, levy body-enriched fractions containing alpha-syncline were injected into a significant number of macaque monkeys and wild-type mice [18]. When Levy body-derived human alpha-syncline was given to control animals, it did not internalize into host neurons, collect within integral neurons, or disseminate to interconnected locations like it did when non-Levy body alpha-syncline was given to the same patients.

. This led to the gradual degradation of neurons and the abnormal conversion of endogenous alpha-syncline. Therefore, it seems that the development of PD is significantly influenced by the expansion of abnormal alpha-syncline, and Levy bodies probably serve as a defense mechanism. Evidence from animal models of multiple system atrophy (MSA) points to a similar process, which further supports this idea [26].

Because Parkinson's causes structural abnormalities in the brain, visual imaging such as MRIs, PET scans, and SPECT scans may be useful in diagnosing Parkinson's disease. The PET/SPECT scans are intrusive, meaning that a radioactive substance must first enter the patient's body in order to perform the scan. The injured organ gathers the radioactive chemical. By looking at the scan, which shows the radioactive tracer as bright red spots, one can determine the extent of organ damage. The PET scan looks at how the brain's movement-related areas are active and functioning. Spectroscopy, however, is mostly used to examine dopamine transporter function. As MRI shows the structure of the brain, it may be able to identify PD shows Fig.2.

Since PD causes structural abnormalities that may be seen on an MRI, it can also be utilized to identify PD patients from DIP. Pseudo Parkinsonism does not appear to be associated with any structural brain abnormalities. Researchers have employed structural MRI (sMRI) and functional MRI (fMRI) MRI sequences to classify Parkinson's disease (PD). There are two types of MRI: T1 weighted MRI and T2 weighted MRI. The duration of the echo and the repetition time throughout the conduct are different for both types. This distinction between CSF appearance in T1 and T2 weighted MRI scans is important for radiologists and clinicians in accurately interpreting brain images and diagnosing various neurological conditions, including Parkinson's disease.

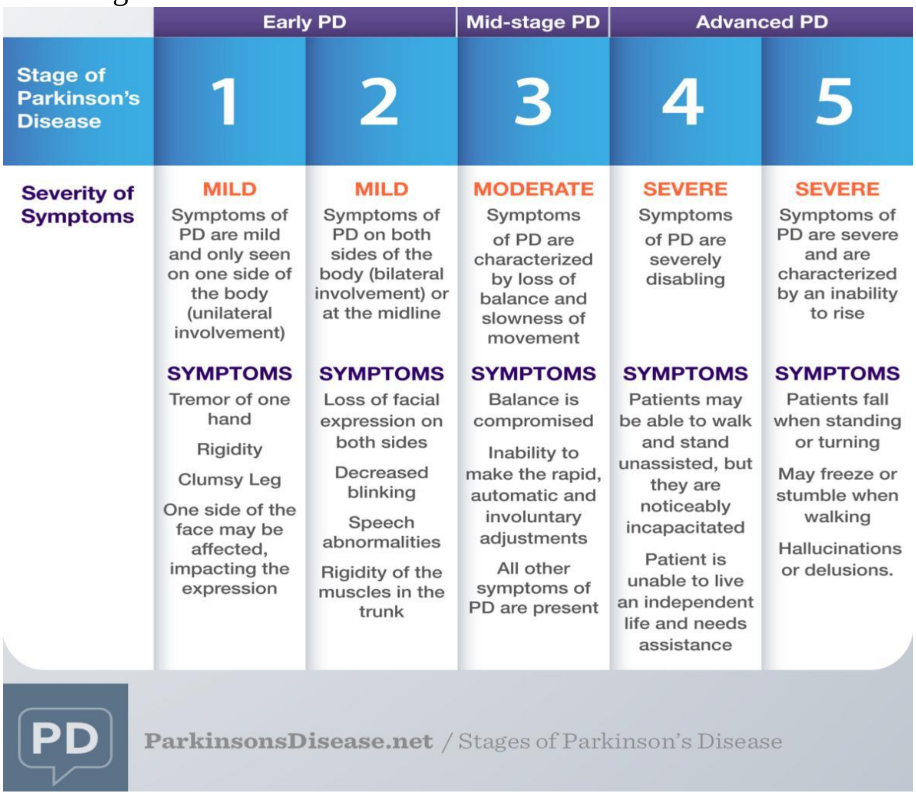


Fig.2 Detection Modalities of Parkinson

III. Proposed Methodology

The suggested approach gathers audio data regarding the vocal modulations of Parkinson's patients from a variety of age groups Fig.4. The data collection includes information on vowel patination MDVP, shimmer, and jitters. Prepossessed, processed, and displayed data allows for a comprehensive comprehension of the properties. 75 percent of the data is used to train four models: K nearest neighbors, Random Forest Regression, SVM, and Logistic Regression. Based on changes in frequency, models are trained to categorize audio data into two groups: PD and healthy. Models are assessed using 25% of the data and are graded according to their sensitivity, accuracy, precision, and confusion matrix score for men and women.

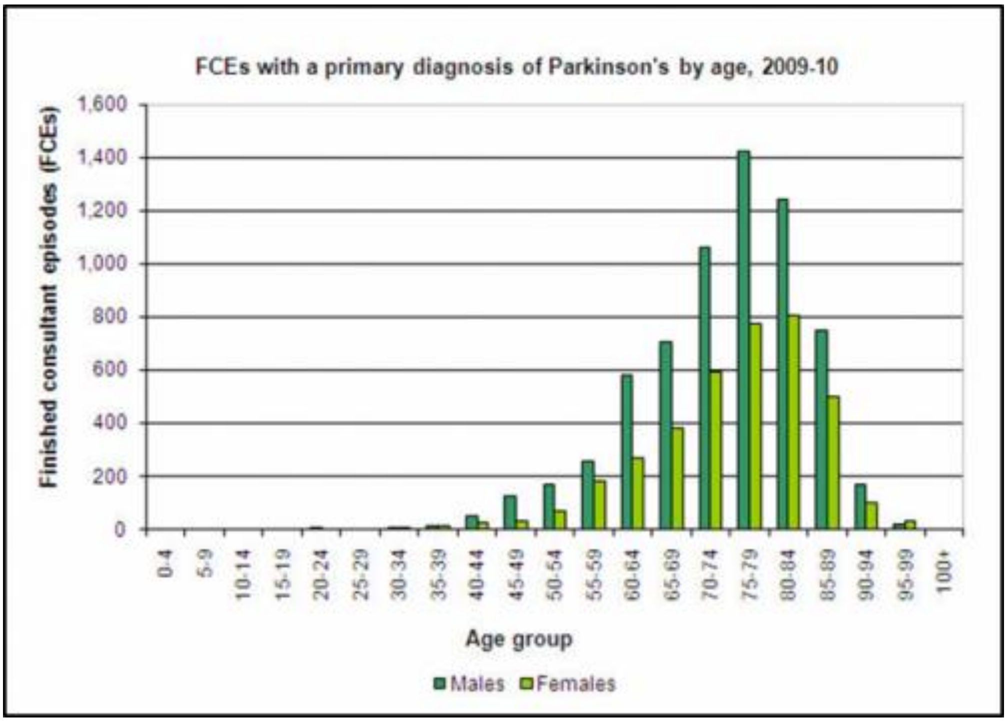


Fig.4. Parkinson's patients from a variety of age group

IV. Longitudinal Study in PD Cognitive

Clinical trials involving people with Parkinson's disease (PD) and cognitive impairment present many difficulties. First, there is a deficiency of a solid understanding of pathophysiologic pathways to direct the development of interventions. Additionally, it's probable that multiple treatment modalities will be required for effective therapy, such as pharmacologic cognitive therapies in addition to exercise. Present research occasionally mixes populations from the standpoint of study design.

V . Literature Survey:

In the paper by Almeida J.S. et al. titled "Detecting Parkinson's disease with sustained phonation and speech signals using machine learning techniques" published in Pattern Recognition Letters (2019), the authors proposed a method for diagnosing Parkinson's disease. They utilized sustained phonation and speech signals along with machine learning techniques, specifically employing linear discriminant analysis and classification algorithms.

The article explores the extraction of valuable information from processed documents and delivering useful insights, as presented by ChenH.-L. et al. in their paper titled "An efficient diagnosis system for detecting Parkinson's disease using a fuzzy k-nearest neighbor approach" published in Expert Systems with Applications (2013). The focus is on aiding physicians and patients in the diagnosis process.

The paper discusses the correlation between the increasing world population and the rise in nervous diseases, highlighting the strain it puts on hospitals and its potential impact on mortality rates due to lack of available beds. To address these challenges, the paper proposes solutions involving physiotherapists, nanoelectronics, and machine learning technologies.

Physicians can remotely access patient reports, facilitated by machine learning algorithms and IoT (Internet of Things) integration. Medical devices leveraging machine learning and

IoT capabilities have been developed for intelligent decision-making, monitoring, and control purposes, as exemplified by CampsJ. et al.'s work on deep learning for freezing of gait detection in Parkinson’s disease patients using a waist-worn inertial measurement unit (Knowledge-Based Systems, 2018). This integration of machine learning and IoT is aimed at reducing costs while improving patient care and accessibility to medical services.

The paper explores a domain model that integrates Attribute-Based Access Control (ABAC) with the detection of Parkinson’s disease using shifted one-dimensional local binary patterns from gait data. This model, as proposed by ErtuğrulO.F. et al., combines aspects of access control with the analysis of gait patterns for diagnosing Parkinson’s disease. The integration of ABAC with gait analysis enhances the security and precision of access control systems while also Increasing awareness among healthcare professionals and the general public about the early signs and symptoms of PD is essential

The paper introduces a continuous learning process aimed at calculating frequencies, probabilities, and dependencies to construct a predictive process model. This model, developed by GroverS. et al., focuses on improving economic factors and enhancing performance. Furthermore, the study delves into predicting the severity of Parkinson’s disease using deep learning techniques. By employing deep learning algorithms, the research aims to enhance the accuracy of predicting the severity of Parkinson’s disease, ultimately contributing to more effective management and treatment strategies.

The paper explores the utilization of the c-means clustering algorithm and Hadoop technology for analyzing data to tailor drug prescriptions for individual patients. Authored by ChoiH. et al., the study focuses on refining the diagnosis of Parkinson’s disease through the deep learning-based interpretation of dopamine transporter imaging. By employing advanced clustering algorithms and big data processing technologies, the research aims to improve the accuracy and effectiveness of diagnosing Parkinson’s disease, leading to more personalized and efficient treatment strategies.

The paper employs an empirical dataset to classify real-world tickets using machine learning analytical techniques, with the aim of enhancing business processes. Authored by DaliriM.R.,Utilizing a machine learning approach for diagnosing Parkinson's disease by analyzing gait patterns with the Chi-square distance kernel is an innovative and promising strategy. Gait analysis has gained attention as a non-invasive and cost-effective method for detecting early signs of neurological disorders, including Parkinson's diseaseThe paper suggests the use of medical sensors to gather patient health data, which is then transmitted to the cloud via machine learning techniques. Authored by JaegerH. et al., the study proposes a cloud-based framework for machine learning in the healthcare domain. Specifically, it tests this framework by applying it to ECG monitoring and the detection of abnormality reports. By leveraging machine learning algorithms and cloud computing infrastructure, the research aims to optimize the analysis of health data and enhance the accuracy of detecting abnormalities in ECG signals.

The paper describes an experiment conducted using real health data to identify patients at risk, focusing on Parkinson's disease. Authored by El MaachiI. et al., the study applies clustering algorithms and machine learning techniques to analyze gait patterns. Specifically, a Deep 1D-Convnet model is utilized for accurate detection of Parkinson's disease and prediction of its severity. By leveraging advanced machine learning methods, the research aims to improve the precision of identifying individuals at risk for Parkinson's disease and predicting the severity of their condition based on gait data.

The science does not track attempts to enhance PD patients' quality of life [7], [8], [9], or [10]. In an effort to improve outcomes for both treatment and diagnosis assistance, computer-aided detection and diagnosis systems based on image processing, neural networks, and other approaches have been widely used [11]. One of the driving forces for the creation of these tools is the possibility that pattern recognition and other methods can identify minute symptoms of Parkinson's disease (PD) that a human would miss. They might also offer some pertinent data to back up the final diagnosis. For example, the automatic PD recognition using the Optimum-Path Forest (OPF) [13], [14] classifier was proposed by Spadotto et al. [12].

The majority of studies focused on automatic Parkinson's disease (PD) detection have primarily utilized voice-based data. However, analyzing periodicity and regularity in voice signals is often limited to voiced regions, necessitating methods to distinguish between voiced and unvoiced (silent) intervals for evaluating continuous speech samples. To diagnose PD, Das conducted a study employing various classification techniques such as neural networks, decision trees, and regression. The dataset comprised 31 individuals, 23 of whom had PD and 8 who were healthy. Through testing multiple strategies, neural networks yielded the highest performance, achieving an accuracy of approximately 92.9%.
The review encompasses papers covering a range of modalities, including voice-based data analysis and other methods for PD classification. Researchers examined studies employing diverse techniques to distinguish between PD patients and healthy individuals.

Clinical Trials and Research for PD-MCI

The update from the 2019 Movement Disorders Society (MDS) regarding evidence-based care for Parkinson's disease (PD) non-motor symptoms highlighted the challenges in addressing non-dementia cognitive impairment in PD. Specifically, the review indicated that there was inadequate evidence to support the use of certain pharmacologic and non-pharmacologic treatments for cognitive impairment in PD. Here's a breakdown of the findings.

Every method under review had the term "investigation" on it [47]. Nonetheless, studies indicate that in PD patients without dementia, physical activity and treatment may be helpful in achieving desired cognitive goals [32]. Global cognition was enhanced by intense physical treatment, but executive function was not improved by aerobic exercise (such as riding a recumbent bicycle or treadmill). To target PD-MCI, more study is required to determine both pharmacologic and non-pharmacologic techniques, as well as combination approaches Fig.3. Meanwhile, especially in light of the growing body of evidence demonstrating the advantages of exercise for Parkinson's disease.

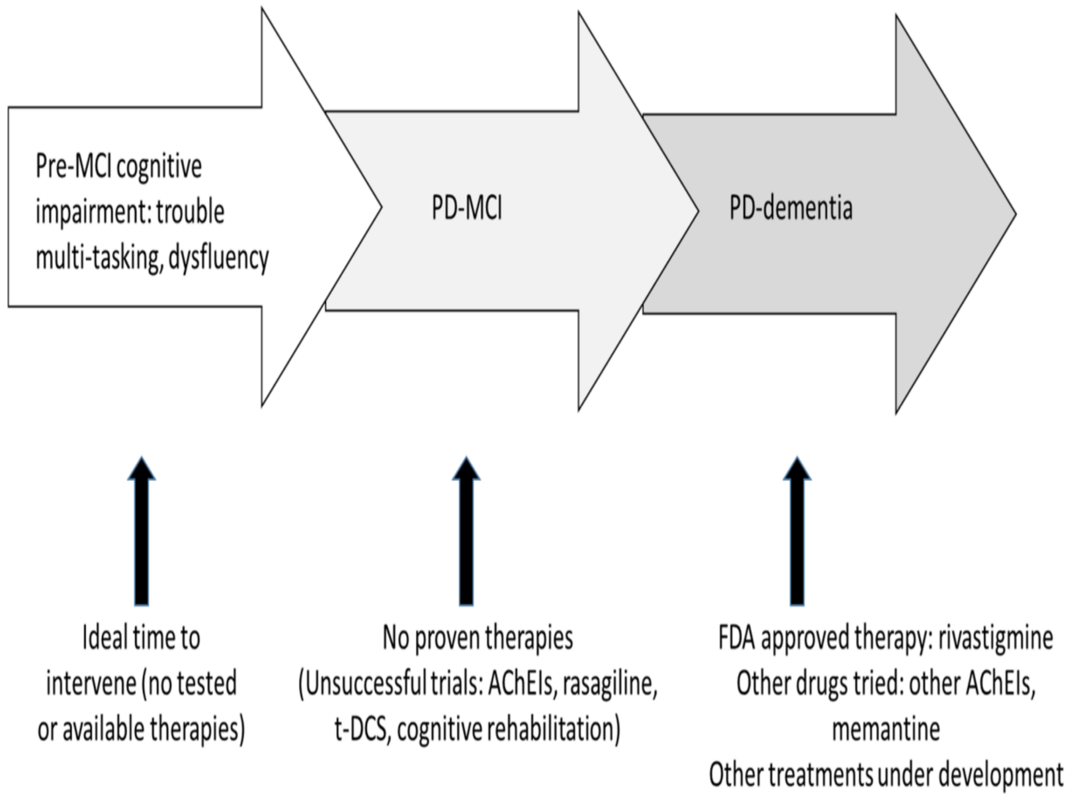


Fig 3. Clinical Approach Parkinson

VI. Discussion and Future Work

The purpose of your study is to identify the most significant characteristics for classifying Parkinson's disease (PD) and to investigate the effects of imbalances in medical data on classification accuracy. This research aims to contribute to the development of more accurate and reliable diagnostic tools for PD. Three methods will be used for PD classification, each based on training on PCA-identified features that are acquired following data set balance, while keeping these needs in mind. The following is a description of each approach's algorithm:

Classification Model Development

Compute the covariance matrix of the scaled data.Perform eigenvalue decomposition or singular value decomposition to obtain the principal components and corresponding eigenvectors.Select the top five principal components based on their explained variance ratios. Identifying variance in each data column, and applying Principal Component Analysis, which includes SVM, logistic regression, random forest, and KNN models. The classification results are then compared using confusion matrix, curve, and accuracy.

VII. Conclusions

It is clear from the literature study that a trustworthy PD detection method is required. For the diagnosis, medical professionals continue to rely on the existence of features. Though they cannot be utilized for the sole purpose of detecting Parkinson's disease (PD), researchers have developed numerous frameworks for its detection using a variety of modalities, including voice signals, SPECT scans, PET images, MRIs, handwritten drawings, and FTT. Every method has its bounds. Imaging tests such as SPECT and PET are intrusive and harmful to people. Voice signals are not very trustworthy, and FTT and scribbled drawings are limited to inspecting deficits of the upper limbs. These days, PD detection is accomplished by researchers using MRI sequences.

VIII. References

[1] B. Heim, F. Krismer , R. D. Marzi , K. Seppi, "Magnetic resonance imaging for the diagnosis of Parkinson's disease", Springer, vol. 124, no. 8, August (2017) pp:915-964.

[2] https://parkinsonsnewstoday.com/parkinsons-disease-statistics/

[3] I. Miyazaki, M. Asanuma, "Dopaminergic neuron-specific oxidative stress caused by dopamine itself", Acta Medica Okayama, vol. 62, no. 3, June (2008), pp. 141-150.

[4] L. V. Kalia and A. E. Lang, "Parkinson's disease", Lancet, vol. 386, August (2015), pp. 896-912.

[5] V. C. Pangman, J Sloan, L Guse, "An Examination of Psychometric Properties of the Mini-Mental Status Examination and the Standardized Mini-Mental Status Examination: Implications for Clinical Practice", Applied Nursing Research, vol. 13, no. 4, , November (2000), pp. 209-213.

[6] Iulian Lancu and Ahikam Olmer, "The Minimental State Examination--An Up-To-Date Review", National Library of Medicine, vol. 145, no. 9, September (2006), pp. 687-690.

[7] H. W. Shin and S. J. Chung, "Drug-Induced Parkinsonism", Journal of clinical Neurology, vol. 8, no. 1, (2012), pp. 15-21.

[8] B Thanvi and S Treadwell, "Drug-induced parkinsonism: a common cause of parkinsonism in older people", BMJ journals, vol. 85, no. 1004, January (2015), pp. 322-326.

[9] A. O. Carvalho, A. S. S. Filho, E. M. Rodriguez, N. B. Rocha, M. G. Carta and S. Machado, "Physical Exercise for Parkinson's Disease: Clinical And Experimental Evidence", US National Library of

[10] P. M. Shah, A. zeb, U. Shafi, S. F. A. Zaidi and M. A. shah, "Detection of Parkinson's Disease in Brain MRI using Convolutional Neural Network", Proceedings of the 24th International Conference on Automation & Computing, Newcastle University, Newcastle upon Tyne, UK, IEEE, (2018), September 6-7.

[11] L. Ali, C. Zhu, N. A. Golilarz, A. Javeed, M. Zhou and Y. Liu, "Reliable Parkinson's Disease Detection by Analyzing Handwritten Drawings: Construction of an Unbiased Cascaded Learning System based on Feature Selection and Adaptive Boosting Model", IEEE Access, vol. 4, (2019), pp. 1- 10.

[12] M. G. Martín, J. M. Montero and R. S. Segundo, "Parkinson's Disease Detection from Drawing Movements Using Convolutional Neural Networks" MDPI, vol. 8, no. 8, August (2019), pp. 907-917.

[13] E. Adeli, F. Shi, L. An, C. Y. Wee, G. Wu, T. Wang, D. Shen, "Joint feature-sample selection and robust diagnosis of Parkinson's disease from MRI data", NeuroImage, vol. 141, May (2016), pp.206-219.

[14] I. A. Illán, J. M. Górriz, J. Ramírez, F. Segovia, J. M. Jiménez-Hoyuela, and S. J. Ortega Lozano, "Automatic assistance to Parkinson's disease diagnosis in DaTSCAN SPECT imaging", The American Association of Physicists in Medicine, vol. 39, no. 10, September (2012), pp. 5971-5980.

[15] B. Rana, A. Juneja, M. Saxena, S. Gudwani, S. S. Kumaran, R. Agrawal, and M. Behari, "Regions-of interest based automated diagnosis of Parkinson's disease using T1-weighted MRI," Expert Systems with Applications, vol. 42, no. 9, (2015), pp. 4506 – 4516.

[16] C. Kotsavasiloglou, N. Kostikis, D. Hristu-Varsakelis, M. Arnaoutoglou,"Machine learning-based classification of simple drawing movements in Parkinson's disease". Biomed. Signal Process. Control, vol. 31, August (2016), pp. 174-180.

[17] T. D. Pham, K. Wårdell, A. Eklund and G. Salerud, "Classification of Short Time Series in Early Parkinson's Disease With Deep Learning of Fuzzy Recurrence Plots", IEEE/CAA Journal of Automatica Sinica, vol. 6, no. 6, (2019), pp. 1306 - 1317.

[18] J. Stamatakis, J. Ambroise, J. Crémers, H. Sharei, V. Delvaux, B. Macq, and G. Garraux, "Finger Tapping Clinimetric Score Prediction in Parkinson's Disease Using Low-Cost Accelerometers", Computational Intelligence and Neuroscience, Hindawi Publishing Corporation, vol. 2013, April (2013), pp. 1-13.

[19] N.K.Ghanad and S.Ahmadi, Combination of PSO Algorithm and Naive Bayesian Classification for Parkinson Disease Diagnosis, Advances in Computer Science: an International Journal, vol. 4, no. 4, July (2015), pp. 119- 125.

[20] Ozkan Cigdem, H. Demirel, D. Unay, "The Performance of Local-Learning Based Clustering Feature Selection Method on the Diagnosis of Parkinson's Disease Using Structural MRI", IEEE International Conference on Systems, Man and Cybernetics (SMC), IEEE, (2019), October 6-9.

[21] Y. Chen, G. Zhu, D. Liu, Y. Liu, T. Yuan, X. Zhang, Y. Jiang, T. Du, J. Zhang, "The morphology of thalamic subnuclei in Parkinson's disease and the effects of machine learning on disease diagnosis and clinical evaluation, Journal of the Neurological Sciences, (2020), April 15.

[22] S Haller, S Badoud , D Nguyen, I Barnaure, M-L Montandon K.O. Lovblad and P.R. Burkhard, "Differentiation between Parkinson's disease and other forms of Parkinsonism using support vector machine analysis of susceptibility-weighted imaging (SWI): initial results." European radiology, vol. 23, no. 1, July (2013), pp: 12-19.

[23] S. Soltaninejad, I. Cheng and A. Basu, "Towards the Identification of Parkinson's Disease Using only T1 MR Images", International Conference on Smart Multimedia Smart Multimedia, ICSM 2018, Springer Nature switzerland AG, vol. 11010, June (2018), pp. 145-156.

[24] S. Sivaranjini and C. M. Sujatha, Deep learning-based diagnosis of Parkinson's disease using convolutional neural network, Multimedia Tools and Applications, vol. 79, March (2019), pp. 15467- 15479.

[25] Athanasios Tagaris, D. Kollia, and A. Stafylopatis, "Assessment of Parkinson's Disease Based on Deep Neural Networks", Springer International Publishing AG, vol. 744, August (2017), pp. 391–403.

26] Niels K. Focke, G. Helms, S. Scheewe, P. M. Pantel, C. G. Bachmann, P. Dechent, J. Ebentheuer, A. Mohr, W. Paulus and C.Trenkwalder, "Individual Voxel-Based Subtype Prediction can Differentiate Progressive Supranuclear Palsy from IdiopathicParkinson Syndrome and Healthy Controls", Human Brain Mapping vol. 32, (2011), pp. 1905–1915.

[27] R. Prashanth, S. D. Roy, P. K. Mandal, and S. Ghosh, "Automatic Classification and Prediction Models for Early Parkinson's Disease Diagnosis from SPECT Imaging", Expert Systems with Applications, vol. 41, no.7, (2014), pp. 3333 – 3342.

[28] H. Fernández, F. J. García-Gómez, D. García-Solís, S. Benítez-Rivero, V. A. Marín-Oyaga, S. Jesús, M. T. Cáceres-Redondo, J. A. Lojo, J. F. Martín- Rodríguez, F. Carrillo and P. Mir, "Machine learning models for the differential diagnosis of vascular parkinsonism and Parkinson's disease using [123I]FP CIT SPECT", Eur J Nucl Med Mol Imaging, Springer, vol. 42, (2015), pp.112–119.

[29] Fermín Segovia, I.A.Illán , J.M.Górriz , J. Ramírez, A. Rominger2 and J. Levin, “ Distinguishing Parkinson’s disease from atypical parkinsonian syndromes using PET data and a computer system based on support vector machines and Bayesian networks”, Frontiers in Computational Neuroscience,vol. 9, November (2015), Article-137.
[30] D. C. Matthews, H. Lerman, A. Lukic, R. D. Andrews, A. Mirelman, M. N. Wernick, N. Giladi, S. C. Strother, K. C. Evans, J. M. Cedarbaum and E. Even-Sapir, “FDG PET Parkinson’s disease-related pattern as a biomarker for clinical trials in early-stage disease”, Elsevier, vol. 20, August (2018), pp. 572–579.
[31] C. Rubbert, C. Mathys, C. Jockwitz, C. J. Hartmann, S. B. Eickhoff, F. Hoffstaedter, S. Caspers, C. R. Eickhoff, B. Sigl, N. A Teichert, M. Südmeyer, B. Turowski, A. Schnitzler and J. Caspers, “Machine learning identifies Parkinson's disease patients based on resting-state between- network functional connectivity”, British Institute of Radiology, vol. 92, no. 1101, May (2019).
[32] C. Zhang, B. Dou, J. Wang, K. Xu, H. Zhang, M. U. Sami, C. Hu, R. Tao, Q. xiao, N. Chen and K. Li, “Dynamic Alterations of Spontaneous Neural Activity in Parkinson's Disease: A Resting-State fMRI Study”, Frontiers in Neurology, vol. 10, September (2019), pp. 1052-1071.

Increasing awareness among healthcare professionals and the general public about the early signs and symptoms of PD is essential. Education campaigns can help individuals recognize subtle motor symptoms such as tremors, rigidity, bradykinesia (slowness of movement), and postural instability, as well as non-motor symptoms like anosmia (loss of smell), constipation, sleep disturbances, and mood changes.