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ORIGINAL PAPER

Multimodal machine learning for Parkinson's disease diagnosis and genetic subtyping

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Abstract

Purpose Parkinson's disease (PD) is a complex neurodegenerative disorder influenced by genetic, clinical, and lifestyle factors. While machine learning (ML) has demonstrated potential in supporting PD diagnosis, existing approaches often rely on single-modality data and lack interpretability for individualized risk estimation. This study aimed to develop and validate an interpretable multimodal ML framework that enhances PD diagnosis and genetic subtype classification, supporting precision health and clinical decision-making.

Methods We integrated clinical assessments, voice-derived acoustic features, and genetic variant data to construct a multimodal prediction framework. Random Forest, XGBoost, and LightGBM models were trained on clinical and voice data, while a separate classifier was trained on genetic variants for subtype identification. Stacked generalization was employed using logistic regression and support vector machine (SVM) as meta-learners. Final predictions were aggregated using weighted ensemble stacking, with AUC-informed contributions. Hierarchical clustering was applied to genetic data to explore subtype patterns. Model interpretability was examined using SHAP analysis.

Results The proposed ensemble model achieved strong predictive performance, with AUCs exceeding 0.96 for PD diagnosis. SHAP analysis highlighted clinically relevant predictors including UPDRS scores, tremor severity, and voice frequency features. Genetic clustering revealed subtype-specific variants, including GBA1 and SNCA (linked to cognitive decline) and LRRK2 (associated with early-onset PD).

Conclusions This interpretable and integrative framework provides accurate PD prediction and meaningful genetic subtype classification. It offers a practical foundation for AI-driven clinical decision support, aligning with personalized care initiatives and advancing the role of health technology in neurodegenerative disease management.

Keywords Parkinson's disease · Multimodal machine learning · Genetic subtyping · Biomedical decision support · Precision neurology · Clinical informatics

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1 Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily affects motor function due to the degeneration of dopamine-producing neurons in the brain. It is the second most common neurodegenerative disease worldwide, following Alzheimer's disease, and affects millions of individuals globally [1]. The global prevalence of PD is estimated at approximately 0.3% of the general population, increasing to over 3% among individuals aged 80 years and older. In 2016, an estimated 6.1 million people were living with PD—more than double the number reported in 1990 [2]. Prevalence increases significantly with age: 41 per 100,000 individuals aged 40–49; 107 per 100,000 for ages 50–59; 428 for ages 60–69; and up to 1,903 per 100,000

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in those over 80. PD is also more common in males than females [3]. With global population aging, the burden of PD is expected to rise sharply. By 2050, it is projected that 25.2 million people will be living with PD worldwide, representing a 112% increase from 2021, with a projected prevalence of 267 cases per 100,000 individuals [4].

PD is a multifactorial disorder influenced by genetic, environmental, and lifestyle factors. Genetic risks are largely driven by mutations and polymorphisms in genes such as *SNCA*, *LRRK2*, *Parkin*, and *PINK1*. Among these, mutations in the *GBA1* gene—also implicated in Gaucher disease—currently represent the strongest known genetic risk factor for PD. Genome-wide association studies (GWAS) have identified over 40 additional polymorphisms associated with increased PD susceptibility [5]. These genetic determinants also contribute to PD subtypes, influencing age of onset and symptom severity. For example, *GBA1* mutations are associated with earlier onset and more aggressive disease progression [6], while the *A340T* variant in *PINK1* has been linked to late-onset PD, reflecting a genetic basis for age-related phenotypes [7].

Beyond genetics, lifestyle factors such as tobacco use, caffeine consumption, physical activity, and diet significantly influence PD risk [8, 9]. Environmental exposures—including pesticides, heavy metals, solvents, and traumatic brain injury—have also been implicated in PD pathogenesis [10].

Recent advances in machine learning (ML) have significantly enhanced diagnostic accuracy and subtype classification in PD. ML models have been successfully applied to diverse data types including speech patterns, gait dynamics, handwriting, clinical assessments, and imaging modalities, often outperforming traditional diagnostic approaches [11–13]. In particular, voice-based ML models have shown promise in differentiating PD patients from healthy controls by extracting relevant acoustic biomarkers [14, 15]. These innovations support earlier detection, subtype stratification, and personalized disease monitoring.

Despite this progress, existing ML models often rely on single-modality data, limiting their generalizability and clinical utility. A key advancement lies in the integration of multimodal data—such as genetic profiles, neuroimaging, and clinical assessments—which has the potential to improve diagnostic performance. However, multimodal integration introduces challenges related to data heterogeneity, varying formats and scales, and increased dimensionality. These issues can impair model training and lead to overfitting, even when dimensionality reduction techniques are applied [16, 17]. Moreover, many current ML algorithms struggle to capture the complex relationships among different data types, resulting in suboptimal predictive performance. Although recent deep learning methods designed for multimodal inputs show promise [18], they remain under development and require broader validation [19].

Notably, many current multimodal ML frameworks emphasize predictive performance while offering limited transparency, making them difficult to translate into clinical workflows [20–22]. Few explicitly address the challenges of heterogeneous data integration, interpretability, and generalizability, leaving a gap in the development of clinically applicable, explainable artificial intelligence (AI) for PD.

To address these limitations, we propose an interpretable multimodal ML framework that integrates clinical assessments, voice-derived acoustic features, and genetic variants for PD diagnosis and genetic subtype classification. Our approach employs stacked and weighted ensemble learning combined with SHapley Additive exPlanations (SHAP)-based interpretability [23], thereby balancing high predictive performance with transparent, clinician-friendly insights. Beyond accurate classification, the framework provides individualized risk estimates and supports personalized clinical management, advancing the goal of AI-enabled precision neurology.

2 Materials and methods

This study developed a multimodal ML framework for PD prediction and genetic subtype classification by integrating clinical, voice, and genetic data. The clinical dataset was curated from publicly available hospital repositories and electronic health records (EHRs), containing structured information such as patient demographics, medical history, and clinical assessments. Standardized evaluation tools—including the Montreal Cognitive Assessment (MoCA) [24] and the Unified Parkinson's Disease Rating Scale (UPDRS) [25]—were incorporated to capture cognitive and motor function.

Voice-derived features were obtained from a publicly accessible dataset hosted on the University of California Irvine (UCI) repository. These features included key acoustic biomarkers such as average, maximum, and minimum fundamental frequencies, jitter, shimmer, and noise-to-harmonic ratio (NHR), all of which have demonstrated relevance in PD-related vocal impairment. Genetic data were curated from trusted resources such as the National Institutes of Health (NIH) and provided in Variant Call Format (VCF), encompassing annotated information on mutations and polymorphisms associated with PD. These included chromosomal positions, gene symbols, and clinical significance based on GRCh37/GRCh38 genome builds. To enhance clarity, a glossary of the multimodal datasets—including their sources and representative features—is presented in Table 1.

Table 1 Overview of data modalities included in the multimodal framework. This glossary clarifies the source and representative features of the clinical, voice, and genetic datasets

Modality	Source	Representative features
Clinical dataset	Hospital repositories and electronic health records (EHRs)	Demographics, medical history, UPDRS, MoCA, Tremor, Rigidity, SleepQuality, PhysicalActivity, lipid profile
Voice dataset	Publicly accessible UCI repository (acoustic features)	Fundamental frequency (F0), jitter, shimmer, noise-to-harmonic ratio (NHR), spread1, PPE, MDVP: FhiHz, MDVP: FoHz
Genetic dataset	NIH repositories, Variant Call Format (VCF) records, GRCh37/38 genome builds	PD-associated variants (e.g., GBA1, SNCA, LRRK2, PINK1), chromosomal positions, pathogenicity, clinical impact

To ensure data integrity and cross-modality compatibility, a comprehensive preprocessing pipeline was implemented. Missing values were imputed using domain-informed strategies tailored to both Missing at Random (MAR) and Missing Not at Random (MNAR) patterns. To address class imbalance in the voice dataset—where PD samples outnumbered controls—the Synthetic Minority Over-sampling Technique (SMOTE) [26] was applied, resulting in a more balanced training set. Continuous variables were standardized using z-score normalization, while categorical variables, including genetic subtype annotations, were harmonized using established biomedical ontologies such as HL7, ICD-10, and Ensembl gene nomenclature.

To reduce dimensionality and enhance model interpretability, we employed a combination of Recursive Feature Elimination (RFE) and domain-specific filtering. Clinical and voice datasets were transformed into structured tabular formats (CSV), while genetic variants were retained in their standardized genomic representations. Due to the absence of record-level linkage between the clinical, voice, and genetic datasets, integration was performed at the model level rather than the patient level. Each modality contributed to its own base classifier, with outputs combined through ensemble learning. Although this approach enables robust multimodal prediction, it represents a methodological compromise, as patient-level integration would allow direct modeling of cross-modal interactions. This limitation underscores the need for future work with longitudinal, patient-specific multimodal datasets.

A multi-stage ML pipeline was implemented to facilitate both PD diagnosis and genetic subtype classification (Fig. 1). Initially, base classifiers were independently trained on the clinical and voice datasets using a diverse set of algorithms: Random Forest (RF), eXtreme Gradient Boosting (XGBoost), CatBoost, Light Gradient Boosting Machine (LightGBM), K-Nearest Neighbors (KNN), Naive Bayes, Support Vector Machines (SVM), and Multilayer Perceptron (MLP). Only models achieving greater than 90% accuracy under k-fold cross-validation were selected for downstream ensemble construction.

Two stacking-based ensemble models were developed. The first ensemble integrated predictions from the clinical and voice classifiers, with Logistic Regression serving as the meta-learner. The second ensemble, trained exclusively on genetic variant features, employed SVM as the meta-learner due to its robustness in handling high-dimensional genomic inputs. Both ensembles were trained using five-fold cross-validation and evaluated using accuracy, F1-score, and area under the receiver operating characteristic curve (AUC) [27].

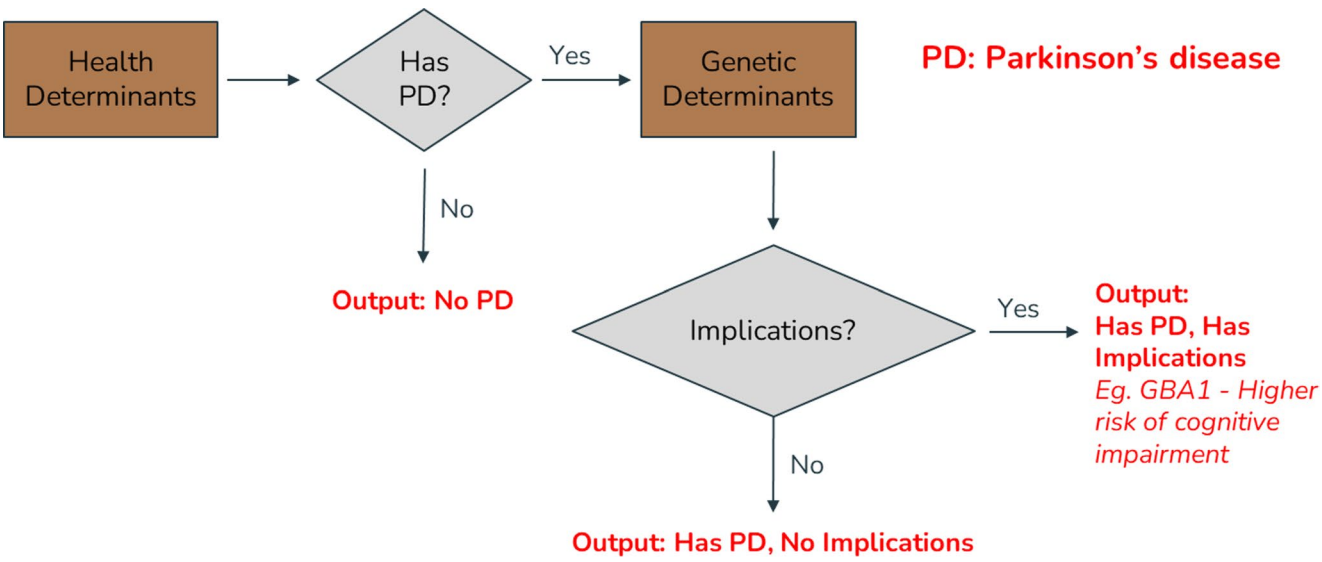

Fig. 1 Flowchart of study

To derive a unified prediction, we implemented a weighted stacking strategy. Model weights were determined based on AUC performance, allowing proportional integration of prediction probabilities. For instance, if the clinical-voice ensemble achieved an AUC of 0.9678 and the genetic ensemble 0.9813, their respective weights were computed as 0.4965 and 0.5035. The final diagnostic probability was calculated as the weighted average of the ensemble outputs, effectively synthesizing phenotypic and genotypic information.

In addition to classification, the framework included an unsupervised genetic subtype discovery module. Hierarchical clustering was applied to the genetic variant dataset, using features such as chromosomal location, germline pathogenicity, and clinical impact scores. Known PD-associated mutations in genes such as *GBA1* and *SNCA* were used as internal validation anchors. This approach enabled the identification of biologically meaningful genetic subgroups, with potential implications for personalized clinical decision-making and targeted intervention strategies.

3 Results

The clinical and voice-based ML models demonstrated strong predictive capabilities for PD diagnosis. Among individual classifiers, RF and XGBoost consistently achieved accuracy levels above 90%, underscoring the discriminative power of behavioral and clinical features. When combined via a stacking ensemble with logistic regression as the meta-learner, the integrated model exhibited enhanced robustness and generalizability across cross-validation folds. This ensemble outperformed most base models in terms of both accuracy and AUC, confirming the synergistic value of multimodal integration.

To interpret model predictions and elucidate feature contributions, SHAP analysis [23] was conducted on both the clinical-voice and clinical-behavioral datasets. As shown in Fig. 2, the most influential voice-based features included *spread1*, *PPE*, *MDVP: FhiHz*, and *MDVP: FoHz*, highlighting the relevance of vocal pitch variability and amplitude instability in PD detection. Elevated values for these

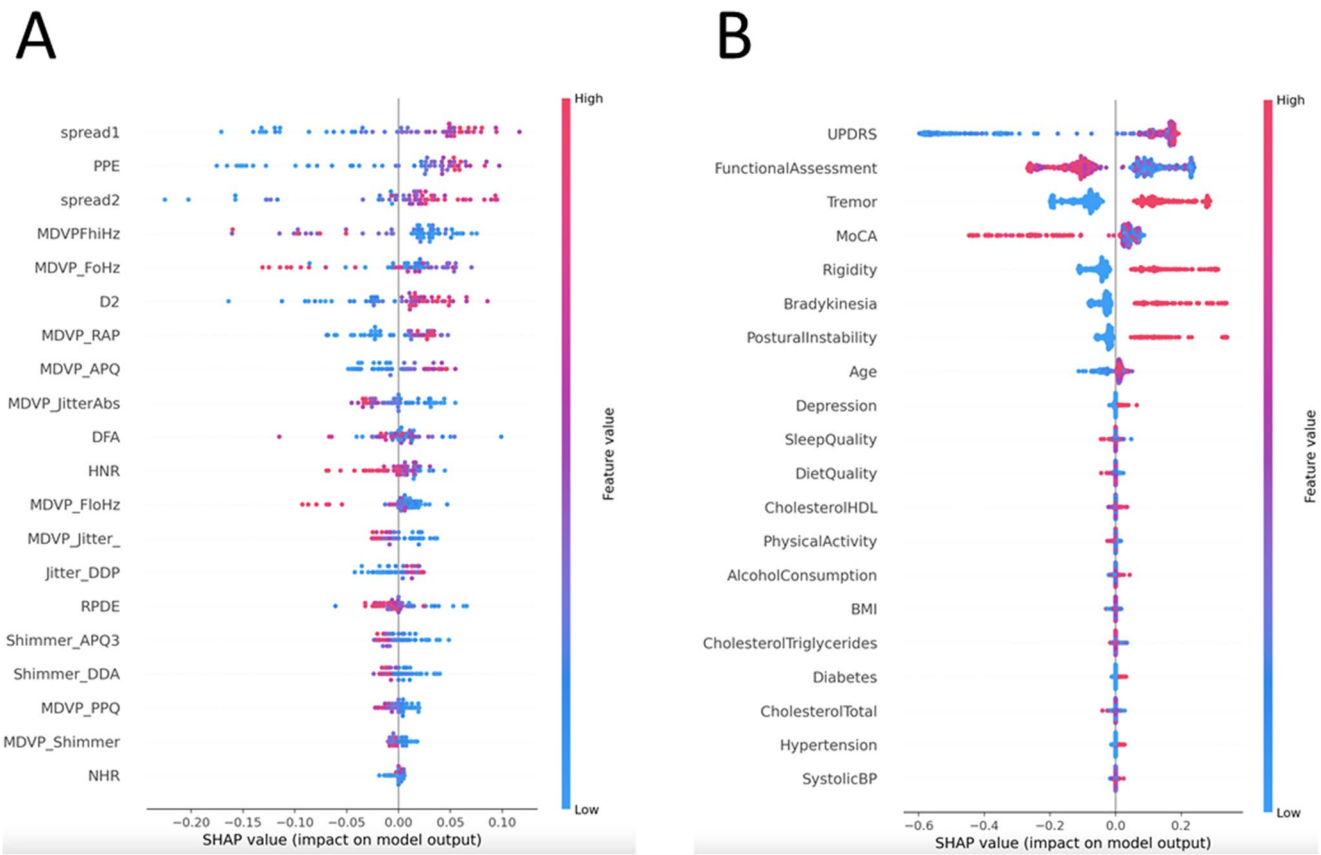

Fig. 2 SHAP analysis on top influence factors. (**A**) voice dataset; (**B**) clinical dataset. Features in red indicate higher values, while blue indicates lower values relative to the cohort mean. For the voice model, elevated *spread1*, *PPE*, and frequency-related features (e.g., *MDVP: FhiHz*, *MDVP: FoHz*) correspond to increased vocal instability, a hallmark of PD-related dysarthria. For the clinical model, higher *UPDRS* and *Tremor* scores strongly increased PD probability, consistent with established neurological assessments. *MoCA* and *Rigidity* also contributed significantly, reflecting cognitive and motor impairments. These findings provide clinically interpretable links between model predictions and patient-relevant features

Table 2 Meta-learner performance for parkinson's disease diagnosis

Dataset	Meta-learner	Mean AUC	Mean accuracy
Clinical (Dataset 1)	Logistic Regression	0.9678	0.9288
Clinical (Dataset 1)	Decision Tree	0.9507	0.9225
Clinical (Dataset 1)	MLP	0.9677	0.9256
Clinical (Dataset 1)	SVM	0.9495	0.9256
Voice (Dataset 2)	Logistic Regression	0.9949	0.9551
Voice (Dataset 2)	Decision Tree	0.8657	0.8652
Voice (Dataset 2)	MLP	0.9944	0.9326
Voice (Dataset 2)	SVM	0.9813	0.9663

MLP: multilayer perceptron; SVM: support vector machine

acoustic biomarkers (indicated in red) were positively associated with PD probability, reinforcing their diagnostic utility.

In the clinical-behavioral dataset, top contributing features included *UPDRS*, *Tremor*, *MoCA*, and *Rigidity*. Higher *UPDRS* and *Tremor* scores were particularly predictive of PD, consistent with standard neurological assessment practices [28]. Additionally, features such as *SleepQuality*, *PhysicalActivity*, and lipid biomarkers (e.g., *Cholesterol-HDL*) contributed moderately to model performance, suggesting their potential utility in personalized risk profiling [29].

The genetic model, trained on curated variant data, effectively identified molecular signatures associated with PD subtypes. Beyond classifying PD status, it facilitated meaningful stratification based on genotype. Hierarchical clustering of genetic variants revealed biologically coherent subgroups. For instance, mutations in *GBA1* and *SNCA*—frequently associated with cognitive impairment in PD [30]— clustered together, while variants in *LRRK2* and *PINK1* formed a distinct group linked to early-onset PD [31]. These results validated the model's ability to delineate clinically relevant genetic subtypes.

The final decision-support model, constructed via a weighted stacking strategy, demonstrated improved diagnostic performance by integrating outputs from both the clinical-voice and genetic ensembles. AUC-derived weights (0.4965 for the clinical-voice model and 0.5035 for the genetic model) enabled proportional fusion of prediction probabilities (Table 2). For example, in a representative case where the clinical-voice model yielded a PD probability of 90% and the genetic model output was 80%, the final fused probability was 84.97%. This approach provides a refined and balanced risk estimation, synthesizing phenotypic and genotypic insights.

Altogether, the multimodal ensemble framework supports comprehensive risk stratification and offers actionable, individualized predictions. These findings lay a strong foundation for integrating AI-based decision support into clinical workflows for precision neurology.

4 Discussions

This study presents a novel multimodal ML framework that significantly improves diagnostic precision and enables genetic subtype classification in PD. Unlike conventional approaches that rely on a single data modality—such as clinical assessments or genetic profiling—our framework integrates heterogeneous inputs spanning demographic, behavioral, clinical, and molecular features. This comprehensive data fusion supports a more accurate and holistic characterization of PD, advancing the field toward precision neurology and individualized therapeutic strategies.

The use of stacked and weighted ensemble learning contributed to improved predictive performance while maintaining model interpretability. By quantifying the relative contributions of each modality, the framework offers a modular and transparent structure, allowing clinicians to understand the rationale behind predictions and tailor management accordingly. In addition, hierarchical clustering applied to genetic variant data enabled the discovery of clinically meaningful subtypes. For example, the clustering of *GBA1* and *SNCA* mutations—both associated with cognitive impairment—supports the case for targeted cognitive monitoring [30]. Similarly, variants in *LRRK2* and *PINK1* were grouped into a cluster linked to early-onset PD, providing insights for proactive surveillance and intervention [31].

Interpretability was further enhanced through SHAP analysis [23], which elucidated feature-specific influences on prediction outcomes. In the voice-based model, acoustic markers such as *spread1* and *PPE*—which reflect variations in voice amplitude and pitch—emerged as dominant contributors, consistent with known vocal impairments in PD. In the clinical-behavioral model, established neurological scores such as *UPDRS*, *Tremor*, and *MoCA* were the most influential features, reinforcing their diagnostic relevance [28]. Notably, non-motor features—including *Depression*, *DietQuality*, and *SleepQuality*—also demonstrated predictive utility, underscoring the multifactorial and systemic nature of PD [32]. These results highlight the value of explainable AI in supporting transparent, clinician-friendly decision-making.

Several limitations should be noted. First, genetic data were drawn from public repositories and may not capture rare or population-specific variants, limiting generalizability. Second, despite extensive preprocessing, differences in data collection and annotation introduced integration challenges. Third, although the framework achieved excellent

cross-validation performance (AUC > 0.96), the absence of external validation remains a major limitation. Future work will involve testing on independent hospital cohorts and multi-center datasets to establish robustness. Additionally, integration was performed at the model level rather than at the patient level due to the lack of record-linked multimodal datasets. While this enabled the use of diverse data sources, it restricted modeling of direct cross-modal interactions within individuals. Incorporating patient-level multimodal records from EHRs and genomics will be critical for translational validity.

For clinical adoption, the framework must ultimately be deployed within operational decision support systems and evaluated across diverse healthcare settings. Ethical and privacy considerations are also essential. Given the sensitivity of genetic and clinical data, strict adherence to anonymization, secure storage, and governance protocols is required. Future applications should explore privacy-preserving ML strategies, such as federated learning and differential privacy, to ensure responsible use of multimodal health data in real-world environments.

5 Conclusion

This study introduces a validated multimodal ML framework that integrates clinical, behavioral, and genetic data to enhance the prediction of PD and enable meaningful genetic subtype classification. By employing stacked and weighted ensemble learning techniques, the model achieved high diagnostic accuracy while offering interpretable, subtype-specific insights to support personalized treatment strategies.

By jointly modeling phenotypic and genotypic information, the proposed approach illustrates the potential of AI to advance precision medicine in the domain of neurodegenerative disorders. Beyond accurate diagnosis, the framework supports individualized risk stratification and clinical decision-making, bridging the gap between data-driven prediction and actionable care. This work lays a strong foundation for future translational applications, including real-world deployment in clinical decision support systems and personalized care planning for patients with PD.

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Code Availability Not applicable.

Declarations

Ethics approval Not applicable.

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References

1. Chou KL, Martello J, Atem J, Elrod M, Foster ER, Freshwater K, Gunzler SA, Kim H, Mahajan A, Sarva H, Stebbins GT, Lee E, Yang L. Quality improvement in neurology: 2020 Parkinson disease quality measurement set update. Neurology. 2021;97(5):239–45.
2. Ternák G, Németh M, Rozanovic M, Márovics G, Bogár L. Antibiotic consumption patterns in European countries are associated with the prevalence of Parkinson's disease; the possible augmenting role of the narrow-spectrum penicillin. Antibiotics. 2022. https://doi.org/10.3390/antibiotics11091145.
3. Pringsheim T, Jette N, Frolkis A, Steeves TDL. The prevalence of Parkinson's disease: a systematic review and meta-analysis. Mov Disord. 2014;29(13):1583–90.
4. Su D, Cui Y, He C, Yin P, Bai R, Zhu J, et al. Projections for prevalence of Parkinson's disease and its driving factors in 195 countries and territories to 2050: modelling study of global burden of disease study 2021. BMJ. 2025;388:e080952.
5. Belbasis L, Bellou V, Evangelou E. Environmental and genetic risk factors for Parkinson's disease, in Diagnosis and Management in Parkinson's Disease: The Neuroscience of Parkinson's Disease, Volume 1. 2020. pp. 57–71.
6. Skrahin A, Horowitz M, Istaiti M, Skrahina V, Lukas J, Yahalom G, et al. GBA1-associated parkinson's disease is a distinct entity. Int J Mol Sci. 2024. https://doi.org/10.3390/ijms25137102.
7. Wang F, Feng X, Ma J, Zou H, Chan P. A common A340T variant in PINK1 gene associated with late-onset parkinson's disease in Chinese. Neurosci Lett. 2006;410(2):121–5.
8. Paul KC, Chuang YH, Shih IF, Keener A, Bordelon Y, Bronstein JM, et al. The association between lifestyle factors and Parkinson's disease progression and mortality. Mov Disord. 2019;34(1):58–66.
9. Kyrozis A, Ghika A, Stathopoulos P, Vassilopoulos D, Trichopoulos D, Trichopoulou A. Dietary and lifestyle variables in relation to incidence of Parkinson's disease in Greece. Eur J Epidemiol. 2013;28(1):67–77.
10. Lo RY, Tanner CM. Parkinson's Disease; Epidemiology, in Encyclopedia of the Neurological Sciences. 2014. pp. 833–839.
11. Zhang J. Mining imaging and clinical data with machine learning approaches for the diagnosis and early detection of Parkinson's disease. NPJ Parkinsons Dis. 2022;8:1.
12. Dennis A-GP, Strafella AP. The role of AI and machine learning in the diagnosis of Parkinson's disease and atypical parkinsonisms. Parkinsonism Relat Disord. 2024;126:106986.
13. Shokrpour S, MoghadamFarid A, Bazzaz Abkenar S, Haghi Kashani M, Akbari M, Sarvizadeh M. Machine learning for Parkinson's disease: a comprehensive review of datasets, algorithms, and challenges. NPJ Parkinsons Dis. 2025;11(1):187.
14. Mohammed MA, Elhoseny M, Abdulkareem KH, Mostafa SA, Maashi MS. A Multi-agent Feature Selection and Hybrid Classification Model for Parkinson's Disease Diagnosis. ACM

Transactions on Multimedia Computing, Communications and Applications, 2021. 17(2s).
15. Liu Y, Li L, Rao Y, Cao H, Tan X, Li Y. Multi-source sparse broad transfer learning for parkinson's disease diagnosis via speech. Medical & Biological Engineering & Computing, 2025.
16. Ganeshnath R, Meenakshy Pillai VJ, Kunju N. A Class Imbalance Learning Approach to Build an Efficient Machine Learning Model for the Diagnosis of Parkinson's Disease. in 2024 1st International Conference on Trends in Engineering Systems and Technologies, ICTEST 2024. 2024.
17. Souza R, Stanley EAM, Camacho M, Wilms M, Forkert ND. An analysis of intensity harmonization techniques for Parkinson's multi-site MRI datasets. in Progress in Biomedical Optics and Imaging - Proceedings of SPIE. 2023.
18. Sua JN, Lim SY, Yulius MH, Su X, Yapp EKY, Le NQK, et al. Incorporating convolutional neural networks and sequence graph transform for identifying multilabel protein lysine PTM sites. Chemometr Intell Lab Syst. 2020;206:104171.
19. Dadu A, Satone V, Kaur R, Hashemi SH, Leonard H, Iwaki H, Makarious MB, Billingsley KJ, Bandres-Ciga S, Sargent LJ, Noyce AJ, Daneshmand A, Blauwendraat C, Marek K, Scholz SW, Singleton AB, Nalls MA, Campbell RH, Faghri F. Identification and prediction of parkinson's disease subtypes and progression using machine learning in two cohorts. Volume 8. NPJ Parkinson's Dis.; 2022. 1.
20. Makarious MB, Leonard HL, Vitale D, Iwaki H, Sargent L, Dadu A, Violich I, Hutchins E, Saffo D, Bandres-Ciga S, Kim JJ, Song Y, Maleknia M, Bookman M, Nojopranoto W, Campbell RH, Hashemi SH, Botia JA, Carter JF, Craig DW, Van Keuren-Jensen K, Morris HR, Hardy JA, Blauwendraat C, Singleton AB, Faghri F, Nalls MA. Multi-modality machine learning predicting parkinson's disease. Volume 8. npj Parkinson's Disease; 2022. p. 35. 1.
21. Park H, Youm C, Cheon S-M, Kim B, Choi H, Hwang J, et al. Using machine learning to identify Parkinson's disease severity subtypes with multimodal data. J Neuroeng Rehabil. 2025;22(1):126.
22. Chang Y, Liu J, Sun S, Chen T, Wang R. Deep learning for Parkinson's disease classification using multimodal and multi-sequences PET/MR images. EJNMMI Res. 2025;15(1):55.
23. Lundberg SM, Lee S-I. A unified approach to interpreting model predictions. Adv Neural Inf Process Syst, 2017. 30.
24. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53(4):695–9.
25. Martínez-Martín P, Gil-Nagel A, Gracia LM, Gómez JB, Martínez-Sarriés J, Bermejo F. The cooperative Multicentric, *Unified parkinson's disease rating scale characteristics and structure*. Mov Disord. 1994;9(1):76–83.
26. Chawla NV, Bowyer KW, Hall LO, Kegelmeyer WP. SMOTE: synthetic minority over-sampling technique. J Artif Intell Res. 2002;16:321–57.
27. Le N-Q-K, Ou Y-Y. Incorporating efficient radial basis function networks and significant amino acid pairs for predicting GTP binding sites in transport proteins. BMC Bioinformatics. 2016;17(19):501.
28. Prime M, McKay JL, Bay AA, Hart AR, Kim C, Abraham A, et al. Differentiating Parkinson disease subtypes using clinical balance measures. J Neurol Phys Ther. 2020. https://doi.org/10.1097/NPT.0000000000000297.
29. Alomari MA, Khalil H, Khabour OF, Alzoubi KH. Lipid profile in Parkinson's disease: the potential role of brain-derived neurotrophic factor. Life Sci. 2022;311:121144.
30. Stojkovska I, Krainc D, Mazzulli JR. Molecular mechanisms of α-synuclein and GBA1 in parkinson's disease. Cell Tissue Res. 2018;373(1):51–60.
31. Hedrich K, Winkler S, Hagenah J, Kabakci K, Kasten M, Schwinger E, Volkmann J, Pramstaller PP, Kostic V, Vieregge P, Klein C. Recurrent LRRK2 (Park8) mutations in early-onset parkinson's disease. Mov Disord. 2006;21(9):1506–10.
32. Dunk D, Mulryan P, Affonso S, O'Keeffe GW, O'Keeffe M, Sullivan AM. Diet quality, sleep and quality of life in Parkinson's disease: a cross-sectional study. Ir J Med Sci (1971 -). 2023;192(3):1371–80.