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Chapter 18

Smart Diagnostic AI in Parkinsonism – Early Detection, Digital Biomarkers, and Precision Management

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Abstract: Parkinson's disease (PD) and related parkinsonian syndromes represent a major global health burden, affecting more than 10 million people worldwide. Traditional diagnostic approaches mainly rely on clinical observation of motor symptoms and expert interpretation, which are often subjective and may fail to detect early disease manifestations. Consequently, delayed or inaccurate diagnoses are common, limiting opportunities for timely intervention and improved patient outcomes. The slow progression and heterogeneous nature of PD further emphasize the need for more sensitive and objective diagnostic methods capable of identifying subtle dysfunction before the onset of classical motor symptoms. Recent advancements in artificial intelligence (AI), particularly machine learning (ML) and deep learning (DL), have created new opportunities for early diagnosis, digital biomarker discovery, and precision management of parkinsonism. AI-based analyses of motor features including eye movements, facial expressions, speech patterns, handwriting dynamics, finger tapping, and gait characteristics have demonstrated greater sensitivity in detecting early disease-related changes compared with traditional clinical evaluations. Evidence suggests that these measurable motor signatures may appear years before clinical diagnosis, enabling potential presymptomatic screening. This review summarizes recent progress in AI-driven diagnostic technologies for PD and atypical parkinsonian disorders. It highlights computational frameworks that integrate multimodal data, sensor-based monitoring, and real-time clinical decision support systems, supporting the development of personalized diagnosis and management strategies for improved patient care.

Keywords: Parkinson's disease, Artificial intelligence, Machine learning, Deep learning, Digital biomarkers, Early diagnosis, Motor symptom analysis, Precision medicine.

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1. Introduction

Parkinson's disease (PD) and parkinsonian syndromes (PSD) Overall, Parkinson's disease (PD), along with dementia, have raised pandemics concerns with >10 million cases worldwide [1]. Conventional diagnostic approaches are heavily dependent on clinicians' visual observations and trained expert judgments by movement disorder specialists, which frequently result in late or mistaken diagnosis. The gradual course of PD, combined with its diverse array of presentation, calls for a transition towards early diagnosis and better patient care. Artificial intelligence ((AI)), and in particular machine learning (ML) and deep learning (DL) approaches, emerged as a disruptive method for tackling these diagnostic and management challenges [2]. Here, we summarize the recent progress of AI-based diagnostic techniques for parkinsonism. It covers early detection approaches, discovery of digital biomarkers, and precision management that has changed the landscape of clinical practice.

2. Motor Symptom-Based Early Detection

2.1 Automated Analysis of Motor Features using AI

Motor deficits are a class of symptoms that reflect the core clinical features of PD and can be observed in specific classes of impairments covering eye movement, facial expression, speech production-related patterns, handwriting dynamic, finger tapping and gait disturbances. Before the onset of clear motoric symptoms, patients usually show mild and measurable types of motor abnormalities that can also be captured using AI–based analysis. Recent comprehensive reviews have shown that before the apparent onset of clinical symptoms PD patients present a broad spectrum of detectable motor abnormalities [3]. This discovery paves the way for early, pre-symptomatic diagnosis using advanced computational methods.

2.2 Smartphone-Based Drawing Assessments

Another realist perspective would be the recent hand drawing testing software for smart phones. A new mixed deep learning model of one-dimensional convolutional neuralised networks and the bidirectional gated recurrent unit has achieved a stable diagnostic ability to analyze the motion data induced by finger drawing on the smartphone screen. The classification accuracy of spiral drawings was 87.93% for cross-validation and for wave drawings, it was 87.24%, with a combined scoring accuracy of 91.20% when mixed assessments were present [4]. Combining spiral and wave tasks resulted in the best performance with 95% confidence intervals, highlighting the value of multimodal motor tests. Most importantly, this telemedicine-ready approach also relies on bare-finger manipulation for consumer-level smartphones37, 54, thus providing operator-independent diagnosis and is ready to allow low-cost and easy PD testing in various remote healthcare practice scenarios or resource-poor settings.

2.3 Analysis of Facial Expressions and Eye Movements

With the advance of computer vision techniques, automatic analysis of facial expressions and eye motions as digital biomarkers for PD detection have become possible. Hypomimia, decline in facial expression is one of the earliest motor symptoms observed in Parkinson's disease. CNNs applied on static facial images have achieved state-of-the-art accuracy for early to mid-stage PD detection. The best performer was ResNet18, with F1 scores of 99.67%, followed by MobileNetV3, which excelled in recall

(99.00%); these results indicate the potential for high-sensitivity screening applications [5]. When inspecting Grad-CAM visualization analysis findings, we observed that the most predictive facial regions across these models circled eyes, lips and nose - specific anatomical locations linked to characteristic PD-related hypomimia. This indicates that facial changes specific to disease can be detected automatically, which is related to traditional presentation.

2.4 Speech and Acoustic/Speech Analysis as Digital Biomarkers

Vocal dysfunction is the first and most common non-motor symptom of Parkinson's disease. In the last few years, voice-based machine learning and deep learning has become quite promising for non-invasive detection of early PD. A thorough study on detection of PD from voice using 69 studies reported that classical models like Support Vector Machine and Random Forest have shown to achieve above average performance for small, homogeneous datasets while deep learning based architectures including CNNs (Convolution Neural Networks), RNNs (Recurrent Neural Networks) and Transformer-based foundation models gained more robust and scalable in different languages and recording environment [6].

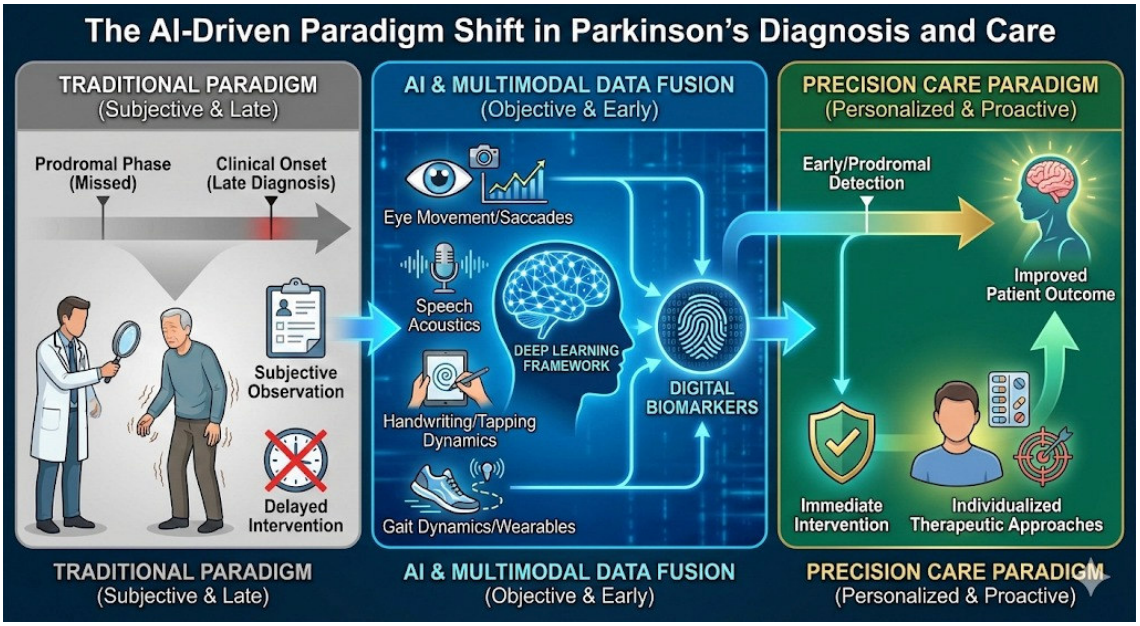
Novel acoustic analysis models have obtained attractive diagnostic results. A multi-modal decentralized hybrid learning model fusing weighted attention mechanism with contrastive speech embeddings (pre-trained by Wav2Vec 2.0) from voice biomarkers attained an accuracy of 96.2% and AUC (area under receiver operating characteristic curve) score of 97.1%, which significantly outperformed individual modality-based method and baseline fusion methods [7]. These findings emphasize the potential of voice-based ML tools for early PD detection, and advocate their utilization in clinical workflows and telehealth diagnostic solutions. Furthermore, voice biomarkers have been found to hold prognostic significance independently of diagnosis. Machine learning algorithms trained on vocal features and evaluated with depression severity scales have reached accuracies up to 0.77 in distinguishing depressed from non-depressed PD individuals [8], indicating that voice analysis is able to capture both motor and NM aspects of the disease.

2.5 Gait and Disorders of Movement

Gait dysfunction is a cardinal motor symptom of advanced Parkinson's disease and contributes significantly to falls and decreased quality of life. Quantitative gait analyses have become widely used in computer vision technologies. A systematic review on the use of computer vision in Parkinson's disease reported gait was the most investigated parameter (42% of papers), with results being obtained using OpenPose and custom computer vision at around 36% each [9]. In multiple applications, computer visions pipelines demonstrated diagnostic discrimination and tracking (eg., severity) highly aligned with expert assigned clinical ratings. This non-contact methodology provides objective motor deficit quantification with the promise of diagnostic and longitudinal use.

So far, phone-based gait information and unsupervised machine learning have been effective in clustering Parkinson's disease by severity. Four distinct gait clusters related to disease severity were identified during analyses of the 8,779 accelerometer recordings obtained from 1,957 participants. The MDS-UPDRS score for balance and walking problems (2.43) was significantly higher in the most severe vs least severe

group, with a freezing episode scores of 8.41 observed in patients who were most severely affected [10]. The benefit of these unsupervised methods is their ability to reveal latent patterns without the prevision such a group allocation so that specific motor phenotypes can be identified.



3. Multimodal Digital Biomarkers and Its Holistic Detection

3.1 Integrating Multiple Data Modalities

Although single motor evaluations offer useful diagnostics, incorporation of several data domains improves the sensitivity and specificity for PD diagnosis. Heterogeneous integration of digital biomarkers has outperformed single modality approaches. Deep learning models, which leveraged tapping, gait and voice data simultaneously, had an AUC over 0.944 in discriminating PD from control subjects among 6,418 participants — clearly superior to the single modality model [11]. Importantly, these combined models not only were strongly correlated with but also surpassed patient self-reported symptom scores for PD diagnosis, indicating that the dimensions of disease being captured by objective digital measures are distinct from those perceived subjectively by a patient.

3.2. Wearable Sensing and Remote Monitoring

Smart wrist products, consisting of smartwatches and wristbands, are a highly promising technology that can be used for continuous non-invasive PD monitoring. A recent systematic review found 130 papers concerning smart wrist devices for movement disorders, most of them addressed to Parkinson's disease [12]. These sensors are cheaper, easy to use and cause minimal trauma compared with other types of sensors making patients willing to accept them for long term monitoring.

Data obtained from smartwatches has achieved promising performance on Parkinson's disease recognition. A digital risk score generated from multi-year smartwatch monitoring (mean, 485 days) of sleep, vital signs and physical activity data discriminated PD patients from matched healthy controls with an area under the

precision-recall curve of 0.96 [13]. When tested relative to gold-standard biological markers such as dopamine transporter imaging and cerebrospinal fluid (CSF) alpha-synuclein seed amplification assays, the digital risk score was more strongly associated with DaTscan putamen binding compared to clinical prodromal PD criteria, potentially providing additive diagnostic information. of note, the digital risk score outperformed the Movement Disorder Society prodromal PD score for sensitivity (0.59 vs 0.35 to identify synucleinopathy or neurodegeneration), but with lower precision. "We recommend that DRS be sensitive screening, while providing an early warning and then proceed to a more specific confirmatory test.

3.3 Electrocardiogram-Based Detection

It has recently been suggested that the development of electrocardiographic changes may be a possible early indicator of risk for Parkinson's disease. A deep neural network model that used standard 10-sec 12-lead electrocardiograms was created to predict the PD risk at prodromal phase. This 1D-CNN model was developed in 131 cases and 1,058 controls and externally validated by an independent cohort comprising of 29 cases and 165 controls [14]. Model extrernal validation AUC= 0.67 in predicting future PD any time between 6 months to 5 years from the ECG, and higher sensitivity close to prediction (AUC:6months-1year=0.74). Therefore, routine ECGs could help to identify subjects with prodromal PD who could be included in cost-effective population-based detecting early activities and enrolled into studies on disease-modifying therapies.

3.4 Ophthalmic Imaging and Retinal Biomarkers

The technique ophthalmic imaging has become increasingly established in metabolic phenotyping. AI assisted ophthalmic imaging is an emerging domain for non-invasive early diseases detection. With AI algorithms several studies analysing OCT and fundus images have reached impressive diagnostic performances, with low extremes of AUCs being 0.9185 in PD detection, sensitivities ranging from 80% to 100%, specificities as high up to 85% [15]. Because AI-assisted analysis of optical coherence tomography angiography can detect retinal vascular changes, the eye provides a window to neurodegeneration. This multimodal neuroimaging technique underscores the complementary nature of different imaging modalities for an overall PD assessment.

4. Molecular and Proteomic Biomarkers

4.1 Prodromal Detection Using Plasma Proteomics

Plasma proteomics and blood biomarkers one of the most exciting discoveries in early detection of PD is that plasma-based biomarkers can be selected for at a very early stage using blood-based proteomics. It was recently discovered in a targeted multiplexed mass spectrometry assay that a panel of eight proteins could identify Parkinson's disease patients and even diagnose 79% of pre-motor isolated REM sleep behavior disorder up to 7 years before motor dysfunction signs appeared [16]. Such biomarkers are Granulin precursor, Mannan-binding-lectin-serine-peptidase-2, Endoplasmic-reticulum-chaperone-BiP, Prostaglandin-H2-D-isomerase, Intercellular-adhesion-molecule-1, Complement C3, Dickkopf-WNT-signaling pathway-inhibitor-3 and Plasma-protease-C1-inhibitor. This blood panel shows both clinical effectiveness for population-based early detection and association with severity of symptoms, supporting biological relevance to disease progression.

4.2 Extracellular Vesicle Biomarkers

Extracellular vesicles in blood plasma as potential innovative platform for diagnosis of Parkinson's disease. These vesicles are membranous and can cross the blood-brain barrier, transporting proteins associated with pathology such as alpha-synuclein and tau. In a recent comprehensive profiling of the exosome-proteome, and lipidome found age-independent and age-dependent EV biomarkers associated with prodromal PD [17]. Functional studies demonstrated that protein lipid interactions are involved in PD pathogenesis, amongst them the role of lipids and the modulation of APOE signaling on it. Machine learning models incorporating presumptive EV proteins provided strong age-discrimination across the groups, suggesting that molecules in EVs could also be used as diagnostic for early disease and discovery efforts to implement the mechanisms underlying PD pathology.

Extracellular vesicle microRNA profiles have also been indicated in biomarker discovery. EV small RNA sequencing established specific miRNA profiles capable of differentiating between iRBD (AUC 0.969) and PD patients (AUC 0.916) compared to HC [18]. Four miRNAs associated with iRBD conversion to PD were identified, serving as a molecular window of progression trajectories. These observations support the sensitivity and specificity of EV-derived miRNA panel as early diagnostic and conversion predictive biomarkers.

4.3 Inflammatory and Metabolomic Biomarkers

Through merging with machine learning, an analysis of the inflammatory response biomarkers showed that IL18R1, NMUR1, and RELA were three crucial features related to the pathogenesis for PD [19]. These biomarkers were highly associated with many cell types, such as T cells, endothelial cells and excitatory or inhibitory neurons, indicating multiple levels of immunologic events in the pathogenesis of the disease. With interpretable artificial neural network models, to find diseasematter by quantitative mass spectrometry-based metabolomics specific patterns of metabolite s in blood plasma. In a study of the whole metabolomics data, without any specific pre-selection of variables and considering two orders for non-linear terms in neural network, an average AUC of >0.995 was reached for the PD prediction from plasma blood data performed by neural network models which outperformed other machine learning methods [20]. Identified PD-specific markers such as an exogenous polyfluoroalkyl substance and a few endogenous metabolites are backdated to before the clinical diagnosis stage of PD, which is earlier than predictive signals.

5. Neuroimaging and Deep Learning Analysis

5.1 Dopamine Transporter Imaging

Single-photon emission computed tomography imaging of the dopamine transporter is an established marker of nigrostriatal dopaminergic degeneration in Parkinson disease. The clinical utility of these imaging studies has been evolved by deep leaning approaches. A system including convolutional neural network classification with an uncertainty detection module produced accuracy of 98.0\% on internal test data, and there was a per-case accuracy of 99.8\% for cases that were flagged as "certain" [21]. The what uncertainty detection module detected 90% of the misclassified

cases, while only flagging 2.5% of the correctly classified cases, clearly emphasizing scoring confidence as an element for clinical utility. adsad

Combined early and delayed brain imaging with dual-phase 18F-FP-CIT PET enabled greater diagnosis discrimination than single-modality approaches. Combined imaging had a 90% agreement with clinical diagnosis in all diagnostic categories, and was superior to either alone [22]. This combination of modality demonstrates the value in combining complementary physiologic data to improve diagnostic acuity.

5.2 MRI Radiomics and Structural Analysis

The structural magnetic resonance image in combination with radiomics features showed high accuracy for discriminating PD subtypes, and disease progression. Another support vector machine model using fusion radiomics features of deep brain nuclei obtained AUCs of 0.988 in training and 0.976 in external testing for PD diagnosis [23]. Within 1 min, the fully automatic classifier was able to differentiate PD from healthy controls, significantly enhancing diagnostic efficiency and having a potential large added-value for daily clinical practice.

For the latter purpose, a boosted decision tree model on MRI radiomics features in eight subcortical nuclei reached 1.000 AUC for motor subtype differentiation regarding tremor-dominant versus postural instability/gait difficulty]. Clinical net benefit analysis showed positive clinical net benefits across a broad range of probabilities, which suggested that this fully automatic motor subtype classification is clinically useful.

5.3 Multimodal Neuroimaging Integration

Advanced machine learning methods combining different neuroimaging modalities and clinical data have led to improved prediction performance when compared to a single modality. A cross-modal fusion prediction model which incorporated the information of clinical, diffusion tensor imaging and dopamine transporter imaging reached AUC at 77.91% for predictor PD progression [25]. These are 24.48%, 30.78% and 32.7% improvement in AUC over using clinical, DTI or DAT data only, which illustrated the significant gain via multimodal data integration.

A neurodegenerative disease modeling dedicated AI-radiomics network which is integrated with symbolic reasoning, deep learning and multi-modal feature was developed. This model performed with an F1 of 88.90 on AD and 85.43 on PD imaging [26], suggesting that it effectively captures disease patterns in a wide variety of imaging and non-imaging modalities.

6. Acoustic and Speech Signal Processing

6.1 Advanced Feature Extraction Techniques

Recent progress in acoustic feature extraction approaches has improved the discriminative capacity of speech-based PD detection. k-NN exhibited best performance in a comparison of machine learning methods capable of early PD diagnosis by speech biomarkers (accuracy 98.52% and average accuracy is 97.33%) [27]. On average, the artificial neural networks and AdaBoost achieved accuracy rates of 93.15% and 91.77%, respectively, with all models displaying good discriminative performance in a variety of common evaluation metrics.

Analysis of voice spectra has been most revealing. The outcomes produced by Mel-frequency cepstral coefficients (MFCCs), Mel spectrogram and waveform capture essential vocal aspects of PD, such as reduced vocal range, weak harmonics, increased spectral entropy and damaged formant structures [28]. Deep learning based on combined convolutional neural networks and long short-term memory and gated recurrent units achieved best results, with a bidirectional LSTM model achieving 97% accuracy and an AUC of 0.95 for voice classification tasks.

6.2 Beyond Acoustics: Speech Content Analysis

In addition to acoustic characteristics, the linguistic content of speech has appeared as a useful diagnostic indicator. Characterization of word properties in the digital space: A prognosis on cognitive symptom severity in PD and differentiation of PD with vs. without CV impairment (hence, cognitive phenotypes of PD). Semantic variability, granularity, concreteness and word length all had strong relationships with cognitive status [29]. Machine learning classification between patients with and without mild cognitive impairment yielded area under the receiver operating characteristic curve = 0.76 in validation data, and generalizes well to out-of-sample pre-surgical and post-surgical samples.

The speech patterns in neurodegenerative diseases are quite different for various causes of these disorders. An elastic net machine learning model built on 12 speech features extracted from the Rainbow Passage reached a balanced accuracy rate of 77% in separating five diagnostic groups, with group-wise sensitivities as follows: progressive supranuclear palsy (76%), Parkinson's disease (67%), Huntington's disease (83%) and amyotrophic lateral sclerosis (73%) [30]. These results thus indicate that digital speech analysis can help in a multimodal differential diagnosis of neurodegenerative disorders.

7. Precision Phenotyping and Disease Subtypes

7.1 Machine Learning-Based Subtype Identification

Parkinson's disease (PD) shows considerable clinical heterogeneity, natural history and progression form different symptomatic profiles and rates of dissemination. Machine learning analysis of multimodal data (comprising clinical, physical function, gait and (when wearable are included) body-worn sensor data) identified three PD subtypes of severity associated with different trajectories [31]. Of all assessed modalities, wearable sensor-derived gait features were determined to be the most correlated descriptors of PD disease severity. Model using the first principal component of left/right ankle data was able to perfectly classify these clinically severe vs. mild PD subtypes with an area under curve (AUC) = 1.0.

Combining gait data with metabolomics and clinical information also improved the accuracy of predicting disease complications. Models that integrated digital gait sensor data with metabolomics and clinical measures achieved AUC of 83–92% for PD vs. control differentiation and our best performing models reached up to 75% of accuracy in motor severity classification [32]. The inclusion of gait alongside metabolomic and clinical data enhances disease prediction in the more difficult-to-discriminate comorbidities, hallucinations, and illustrates the complimentary information provided by multimodal integration for holistic description of disease.

7.2 Speech-Driven Motor Phenotype Clustering

New clustering algorithms have been used for acoustic speech data and thus far, limited numbers of discrete speech-based PD subtypes correlated with various motor symptom profiles are identified. There were three such clusters, namely: mild (n=49), moderate (n=13) and severe clusters (n=29) [33]. Tremor and postural-gait stability subscores in clusters were significantly different, with the severe cluster showing a more bothersome tremor and worse postural-gait instability compared to the mild cluster.

7.3 Integrative Multi-Omics Approaches

A comprehensive integrated analysis of genetic, transcriptomic and clinical data have identified separate PD pace subtypes showing diverse progression paths. Three subtypes were defined - Inching Pace: mild baseline severity and slow rate of progression, Moderate Pace: mild starting severity but moderate progression, and Rapid Pace: most rapid progression [34]. These subtypes were characterized by the Cerebrospinal fluid phosphorylated tau to alpha-synuclein ratio and brain atrophy patterns in localized regions. Network-based analyses uncovered molecular driver genes and pathways linked to each subtype, with fast-pace-specific modules suggesting neuroinflammation, oxidative stress, and metabolic reprogramming as drivers of accelerated disease progression.

8. Cognitive Impairment Detection and Monitoring

8.1 Early detection of MCI

Cognitive impairment is a major comorbidity in Parkinson's disease with an impact in patient quality of life and disease course. Machine learning algorithms, integrating clinical examination, cerebrospinal fluid biomarkers and imaging data have shown excellent predictive accuracy for cognitive impairment. In predicting continuous cognitive decline in early PD patients, a multimodal machine learning model performed well for models that used baseline cognition, CSF phosphorylated tau, total tau, amyloid- beta and geriatric depression scale scores and anxiety scores [35]. Tau and amyloid-beta pathology may have predictive value for cognitive impairment in PD, similar to those observed in Alzheimer's disease, likely indicating common pathogenic mechanisms.

Age at onset and visuospatial function were major predictive factors for the cognitive impairment, and there were sex differences [36]. Multi-cohort models had better stability of performance than single-cohort models and found men to have a higher likelihood of subjective cognitive decline when compared to women, underlining that sex-specific considerations affect cognitive assessment.

Machine learning models using clinical routine parameters performed as well as advanced neuroimaging with regard to diagnostic accuracy. A machine learning model with only commonly measured clinical covariates reached an AUC of 0.83 in discovery cohort and retained the accuracy of 71.57% in external set [37]. SHAP interpretability analysis demonstrated age, neutrophil to lymphocyte ratio (N/L), and serum uric acid were important predictors, displaying cooperative risks between the elevation of inflammatory markers and the decrease of antioxidant status.

8.2 Digital Measures for Cognitive Phenotyping

Digital assessment of cognitive function based on voice patterns has improved not only diagnostics, but also psychosomatic testing. Linguistic and acoustic markers extracted from monologue recordings Discriminated mild cognitive impairment across neurodegenerative disease [38]. According to the machine learning models, the addition of speech biomarkers significant obtained better classification performance compared to that using clinical scores alone and results predict Montreal Cognitive Assessment (MoCA) scores with a normalized error of 10%.

9. Challenges and Constraints in Clinic Translational Perspectives

9.1 Heterogeneity of the dataset and validation concerns

Driven by tremendous effort however, there are still great challenges to translate AI research into practice. An exhaustive systematic review on machine learning for Parkinson's disease extracted 133 articles from between 2021 and April 2024, and classified research derived from into acoustic data, biomarkers, medical imaging, movement data, and multimodal datasets [39]. The review emphasized ongoing challenges, such as dataset heterogeneity, class imbalance and inconsistent validation strategies that prevent adequate reproducibility and clinical translation.

Research of voice-based PD detection is a case in point. Although traditional machine learning methods offered high accuracy on small, homogeneous datasets and deep learning-based architectures showed greater universality, several challenges such as heterogeneity of datasets, longitudinal class imbalance, and lack of uniformity in validation practices resulted in poor reproducibility and limited clinical translation [6]. The field is also seeing a shift away from hand-designed feature-based pipelines in favor of self-supervised, representation-learning approaches that promise greater generalization, necessitating new benchmarks in the form of large-scale multilingual and publicly-available dataset with standardized evaluation protocols.

9.2 Model Interpretability and Explainability

A major bottleneck for the translation of AI models into a clinical setting is their limited explainability, which is commonly referred to as "black box". Interpretable artificial intelligence techniques, such as SHAP and LIME are gaining popularity to improve the model interpretability. A hybrid model consisting of keystroke dynamics and explainable AI found that the most sensitive pathophysiological biomarkers for detecting PD included latency time, inter-key coordination dysfunction, and motion smoothness reduction [40]. Model ensembles decreased false positives rates by 42% compared to single models and remained interpretable with feature importance analysis.

9.3 Regulatory and clinical integration barriers

Technical challenges aside, even incorporation of digital health technologies into regulatory and clinical frameworks is fraught with complications. A single case study of Parkinson's disease demonstrated the tangled web of regulatory requirements for digital health technologies in a drug-specific context [41]. Precompetitive public-private partnerships were called out as critical to further regulatory maturity of digital health technology measurements for clinical trials, such as standardized data-collection protocols and strong analysis methods robust to residual variability.

10. Future Directions and Emerging Technologies

10.1 Wearable Sensor-Based Continuous Monitoring

The combination of wearable sensors and sophisticated machine learning now offers the opportunity to monitor disease longitudinally in the free living. Digital biomarkers developed for bradykinesia and resting tremor from wrist-worn accelerometer correlated well to strongly with clinically-assessed symptom severity, and were able to discriminate changes in motor state associated with treatment [42]. Further work will extend these capabilities for continuous monitoring of other motor and non-motor features with real-time feedback and treatment optimization.

10.2 Large Language Models and NLP

Novel, large language models combined with natural language processing provide new possibilities for cognitive testing and clinical decision support. Large language models showed the potential to recognise cognitive decline in EHRs as an ensemble of large language models and locally trained machine learning models obtained precision of 90.3%, recall of 94.2% and F1-score of 92.2% [43]. These complementary strategies based on different error profiles indicate potential hybrid systems in future which are combined with more than one analytical framework.

10.3 Personalized Treatment Strategies and Precision Medicine

Combining precision personalized medicine with music therapy is one of the innovative tools we can use for holistic, patient-centered management of PD. Personalized medicine utilizing gene targeted therapies along with digital biomarkers and wearable sensors led to increased precision and individualization of therapy regimens [44]. Future implementation efforts should target the reduction of access block and the demonstration that “big longitudinal” studies can be done, and work across diagnostic groups is needed to develop organised treatment plans, integrating genetic markers with individualised neuromodulation.

10.4 Closed-Loop Sensor-AI-Robot Frameworks

Towards this ambitious vision, a human-AI-robot collaboration model has been proposed with closed-loop sensor-intelligence-actuator systems in the multimodal sensing and AI applications [45]. Such systems would provide ongoing patient-specific guidance via AI agents built on top of robotic and wearable foundation models, reinforcement and continuous learning, serving as a foundation for evolving digital twins of PD patients.

Conclusion

Artificial intelligence (AI) has become a paradigm-shifting platform for the early diagnosis, phenotyping and personalized treatment of Parkinson's disease and parkinsonian syndromes. By examining the broad range of motor and non-motor phenotypes that can be captured through smartphone, wearable sensor, and multimodal neuroimaging data, AI allows the recognition of disease at increasingly earlier stages including in prodromal or pre-symptomatic phases. Machine learning combinatorial profiling of among-across modals ranging from acoustic biomarkers and motor assessments to blood-based proteomic markers and advanced neuroimaging yield synergetic accuracy gains in diagnosis and prognostication beyond any single modality.

Blood-borne biomarkers derived from plasma proteomics and extracellular vesicle profiling have reached impressive sensitivity for de novo PD detection up to seven years prior the onset of motor symptoms, establishing unprecedented possibilities for neuroprotective early intervention. High-resolution phenotyping using integrated multi-omics analysis have uncovered unique disease subtypes with disparate progressions trajectories and pathological drivers, that may benefit from individualized therapeutic approaches.

However, formidable barriers remain associated for their clinical translation. Heterogeneity of data sets, inconsistency in validation methodology, interpretability issues with the models and regulatory impediments are barriers to universal adoption. Solving these problems needs collective commitment from researchers, clinicians, technologists and regulators in forming standardized data collection protocols, validation structure and clinical adoption pathways.

The next stage in treating PD will emerge through the convergence of several technology platforms – wearable sensors, smartphone as companions, AI guided analytics and precision therapeutics – into integrated systems that could monitor continuously, detect early, and intervene personally. As these approaches further develop and gain support with long-term clinical validation and practical roll-out, AI-based strategies offer the potential to disrupt the paradigm of Parkinson's disease care in which patients are managed according to their symptoms rather than through evidence-based prevention and early intervention.

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