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Artificial intelligence in neurodegenerative disease diagnosis: Advancing Alzheimer's and Parkinson's diseases

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This review article explores the significant advancements of artificial intelligence (AI) as a transformative tool for the early detection of major neurodegenerative diseases, specifically Alzheimer's disease (AD) and Parkinson's disease (PD). Traditional diagnostic techniques, including standardized clinical cognitive assessments, molecular biomarker analysis, and neuroimaging, remain crucial in clinical assessment. However, their utility is often limited by their accessibility, cost, and insufficient sensitivity. In the recent years, AI-driven techniques have emerged as a promising tool in advancing the early detection of AD and PD. These techniques play a crucial role in diagnosis by analyzing complex dataset derived from neuroimaging, integrated wearable sensors, and various digital biomarkers. By integrating multimodal data analysis with digital phenotyping and digital biomarkers discovery, a personalized therapeutic regime can be developed. Challenges, including the need for standardized data acquisition, improving model interpretability, and addressing ethical concerns related to data privacy and equitable access, are also highlighted.

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Introduction

Neurodegenerative diseases represent a burgeoning global health issue characterized by the progressive degeneration of neurons, leading to severe and irreversible loss in specific functions such as motor and cognitive skills [1,2]. Although symptoms associated with certain neurological conditions can manifest early in life, the severity of neurodegenerative diseases generally intensifies with age, creating an immense burden on individuals, families, and healthcare systems. Among various neurodegenerative disorders, Alzheimer's disease (AD) and Parkinson's disease (PD) are most prevalent, owing to their progressive nature and increasing occurrence in aging populations. AD is recognized as a leading contributor to dementia, characterized by the progressive cognitive impairment and significant memory loss. PD is the second most common neurodegenerative disorder globally, following AD, and is responsible for impairments in motor symptoms including postural instability. At their core, both conditions involve a selective and gradual loss of neuronal population, resulting in deficits in memory, movement, and cognitive functions [3]. Thus, early and accurate detection of AD and PD is crucial for improving patient care, enabling timely intervention and prevention [4].

Traditional diagnostic processes for AD and PD primarily rely on comprehensive clinical judgments, functional assessments, and standard neuroimaging techniques like computed tomography scan, magnetic resonance imaging (MRI), and positron emission tomography (PET). While providing invaluable aid in the clinical assessment, these techniques remain limited by their cost and inaccessibility in resource-limited settings [5]. In most cases, diagnoses are made at a later stage after the symptoms are prevalent, missing the window for early diagnosis necessary for timely intervention [6]. Beyond conventional neuroimaging techniques, artificial intelligence (AI) systems are instrumental in facilitating biomarker analysis, speech pattern recognition, and detection of structural changes in the brain (neurodegeneration) associated with AD and PD—changes that often elude the traditional diagnostic methods [7]. This transformative tool not only supports early diagnosis and improves accuracy but also creates a new paradigm for classification of neurodegeneration subtypes, which is crucial for development and implementation of new personalized medicines and medical treatment technologies.

The foundation of these AI-based innovations lies in their capability to learn and extract features from neural imaging and clinical data using deep learning (DL) algorithms. For instance, the ensemble learning approaches provide results with improved accuracy and robustness when combined with multiple algorithms. Similarly, convolutional neural networks (CNNs) are increasingly used to detect structural changes in brain regions affected by AD and PD. Additionally, AI-driven analyses facilitate the identification of digital biomarkers through data stream collected with an aid of wearable sensors and smartphones, a process known as digital phenotyping [8]. These transformative tools not only support early detection and enhance accuracy but also provide refined classification of neurodegenerative disease subtypes, thus paving the way of new personalized therapeutic strategies [9]. However, despite the remarkable and significant applications of AI, several significant challenges exist. Key issues, including standardized data acquisition, model interpretability, data quality, and ethical concerns, are seamless for clinical integration. These limitations highlight the urgent need for noninvasive, scalable tools capable of detecting AD and PD at the early stage. This review particularly aims to discuss the integration of AI with advanced neuroimaging techniques for early detection, highlighting the methodologies, outcomes, and challenges associated with neurodegenerative diseases, particularly AD and PD [10].

Present clinical diagnostic tools for Alzheimer's and Parkinson's diseases

The diagnostics protocols for neurodegenerative diseases, especially AD and PD, are inherently complex. Present clinical tests rely on multimodal approaches that include clinical and cognitive testing, neuroimaging, biomarkers, and molecular analysis. However, while these methods significantly contribute to identifying and monitoring these diseases, they also present challenges with a major impact on early detection and diagnosis, particularly in routine clinical analysis.

Cognitive assessment

Diagnosing cognitive impairments associated with AD and PD often involves standardized cognitive assessment. The Montreal Cognitive Assessment (MoCA) is one of the most widely used tools for both conditions. This 10- to 15-minute assessment evaluates various cognitive domains, including memory, languages, attention, visuospatial abilities, orientation, and executive functions. A recent consensus recognized the MoCA as a suitable diagnostic tool for detecting mild cognitive impairment and early dementia in AD patients [11,12]. The Mini-Mental State Examination (MMSE) also remains a widely used, quick, and simple screening tool for evaluation of their cognitive symptoms, overall mental status over time, and cognitive deficits in both AD and PD. For instance, in PD, the Mattis Dementia Rating Scale Edition-2 is often recommended in addition to the MoCA and MMSE [13]. Additionally, the Symbol Digit Modalities Test is increasingly recognized as a suitable cognitive assessment tool for detecting cognitive dysfunction in PD, particularly as it provides information relation to genetic factors influencing cognitive decline. While the Cambridge Cognitive Assessment-Revised and Alzheimer's Disease Assessment Scale-Cognition are suggested as cognitive assessment tools, they are less commonly utilized in clinical practice than the MoCA and MMSE. Although both AD and PD result in cognitive impairment, application of these assessments can differ slightly due to their unique cognitive profiles. Cognitive changes in PD often manifest as slower information processing (bradyphrenia), often requiring additional assessments that highlight processing speed and executive functions [14]. On the other hand, assessment for AD particularly focuses on orientation and memory, reflecting common cognitive decline in these conditions.

Molecular diagnostics and biomarkers

The investigation of biomarkers for the early detection and diagnosis of AD and PD has seen significant advancements in the clinical settings. Among all biomarkers, cerebrospinal fluid (CSF) analysis is one of the most informative approaches as clinicians can directly measure critical proteins level associated with neurodegeneration. Specifically, biomarkers directly associated with tau pathology and amyloid deposition are crucial for identifying the presence of AD pathology. This involves measuring the decreasing level of amyloid-beta 42 (Aβ42) and evaluating the levels of phosphorylated tau (p-tau) and total-tau (t-tau) in CSF. These tau protein biomarkers are indicative of neurodegeneration, while Aβ proteins point to the amyloid protein pathway, both of which are central to AD. Despite their significant diagnostic value, the invasive nature of CSF collection limits their practicality for routine screenings and monitoring [15–17].

Blood-based biomarkers

Emerging research indicates that high-throughout analysis of microRNAs and DNA methylation patterns can provide promising genetic and epigenetic markers. The patterns of these markers reflect significant changes as disease progress. Moreover, researchers are studying the elevation of protein marker panels including C-reactive protein, interleukins, glial fibrillary acidic protein, apolipoprotein E (ApoE), and oxidized DJ-1. These proteins show potential for reflecting central nervous system pathology using less-invasive blood samples. However, despite their promise, most of these biomarkers still need thorough clinical validation before being applied in clinical practice [18]. Additionally, a comprehensive approach that combines proteomics

(analyzing all proteins) and epigenomics (studying gene regulation patterns) in serum or plasma can uncover early biological disturbances. These disturbances might be linked to oxidative stress, inflammation, and other molecular changes observed in neurodegenerative diseases. While these approaches may pave way for more holistic view of disease progression, they are technically more complex and require further standardization before implementing in clinical practice [19].

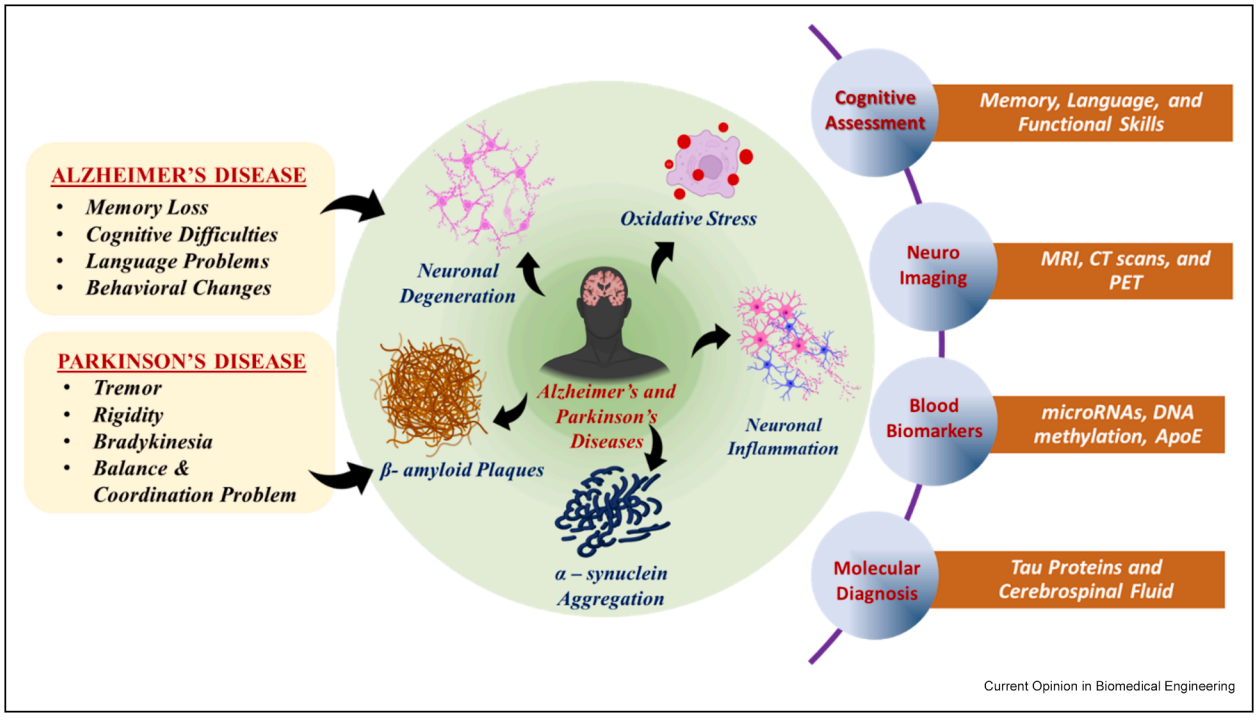
Neuroimaging

Neuroimaging plays a crucial role in diagnosing neurodegenerative diseases. Specifically, MRI is a valuable tool for analyzing brain atrophy, particularly in the medial temporal lobe in AD. MRI can also aid in distinguishing PD from other parkinsonian syndromes by measuring the midbrain to pons ratio and putamen volume. Although MRI provides noninvasive, quantitative data for analyzing and tracking diseases progression, its high cost limits its affordability and clinical utility for large-scale population screening. Additionally, PET scans offer molecular imaging capabilities, enabling the visualization of amyloid plaques and tau tangles—pathological hallmarks of AD. PET can also detect deficits in dopaminergic function, thereby strengthening the diagnoses and providing specific insights into diseases pathology. However, similar to MRI, the cost of PET scans significantly limits their widespread use [20,21] (see Figures 1 and 2).

Improving clinical measurement by integrating AI with diagnostic tools

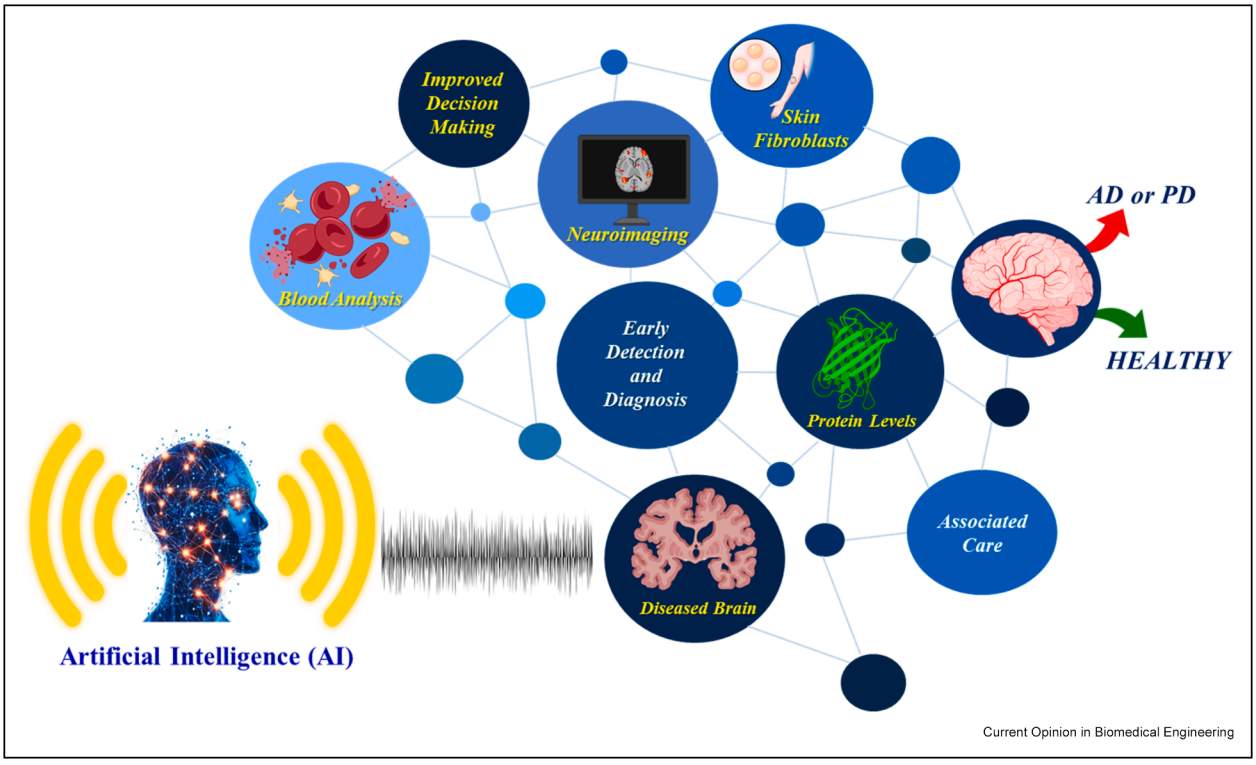
Recent advancements in AI have greatly enhanced the current clinical assessment approaches for the early detection of AD and PD. These AI-driven techniques are increasingly being incorporated into various aspects of patient assessment and care. A noteworthy development is the video-based symptom assessment systems through smartphone apps that utilize machine learning (ML) algorithms to analyze the patent's movements specifically focusing on finger tapping, hand movements, and supination—pronation movements of the hands. These systems provide potential solution for accurate and timely diagnosis by objectively analyzing the moments and associated symptoms [22]. An innovative study from Massachusetts Institute of Technology (MIT) introduces an AI-driven tool for PD diagnosis and progression monitoring utilizing nocturnal breathing pattern. This objective, nonobstructive, and cost-effective system utilizes a breathing belt and a wireless data-transfer device to collect breathing-pattern signals at home, offering early point-of-care (POC) detection even before the motor symptoms appear. The neural network interface allows personalized disease

Figure 1



Comprehensive overview of AD and PD analysis: Symptoms, biomarkers and diagnostic approaches. AD, Alzheimer's disease; CT, computed tomography; PD, Parkinson's disease; PET, positron emission tomography.

Figure 2



Advancements in AI approaches for early detection and diagnosis for AD and PD. AD, Alzheimer's disease; PD, Parkinson's disease.

management and predicts disease severity and tracks progression with up to 94% accuracy [23], underscoring its potential as a robust digital biomarker for the detection of PD. Researchers have attempted various approaches to improve the diagnostic accuracy of the imaging techniques using AI and ML tools. For example, advanced DL algorithms were used to analyze large data sets and increase the accuracy of PET molecular imaging up to 99% for specific applications [24]. Similarly, ML models were utilized to discriminate PD and normal control images with an improved accuracy of 71%. Additionally, researchers at UC San Francisco made a significant breakthrough by developing ML models to predict the onset of AD up to seven years in advance, even before the symptoms emerge [12,21]. The research utilizes the combination of AI tools, specifically, random forest models and knowledge networks, to predict AD onset years in advance with an aid of electronic health records. They also investigated other health issues that might show up before AD and identified shared genes (such as *APOE*, *ACTB*, *IL6*, and *INS*) between these top predictors and AD through genetic colocalization analysis [25]. Researchers at the University of Cambridge introduced a novel predictive prognostic model (PPM) for early prediction of dementia. To enhance the robustness, the PPM is trained using noninvasive and clinically relevant predictors such as cognitive tests and MRI-derived gray matter atrophy. The AI-guided model generates multimodal markers that reliably predict the future cognitive events with an accuracy of 86% [26]. The ability to interpret complex neuroimaging data has advanced the AI tools in biomarker discovery. Studies using 3D-CNNs to analyze MRI and PET scans have identified nigrostriatal degeneration patterns with 85–90% sensitivity, outperforming traditional radiologic assessments. Performance varies by modality; CNNs on MRI often achieve 90–95% accuracy for AD classification, while recurrent neural networks (RNNs) analyzing speech can reach an accuracy of 93–95% for PD detection, highlighting their respective domain strengths. Additionally, ML algorithms have uncovered novel biomarkers in biofluids, such as serum α-synuclein and CSF neurofilament light chain, which correlate with disease progression [27]. Studies have shown that AI models, such as DL, multimodal data fusion ,and transfer learning, have achieved exceptionally high accuracy (>90%) for the early detection of AD and PD. Using well-curated datasets of MRI, electroencephalogram (EEG), or PET images focusing on early-affected brain regions like the hippocampus, studies have reported the accuracies as high as 98–99% [3,4]. These findings clearly

demonstrate the strong capability of AI models to detect the smallest and earliest pathological changes in the brain. However, the reliable and consistent performance of these models in real-world population is still underexplored [5].

Advanced AI approaches for diagnosing neurodegenerative diseases

Voice and speech analysis

Approximately, 90% of individuals with PD experience vocal impairments, such as changes in pitch variability and breathiness. ML models are proved to be effective in identifying these subtle vocal changes. These models are trained specifically using designated acoustic features such as shimmer, jitter, and harmonic-to-noise ratio and discriminate PD patients from healthy individuals with good accuracy. For example, the model developed using RNNs enhanced the accuracy up to 95% in classification by analyzing sustained vowel recordings. Interestingly, this technology can even detect subclinical vocal changes that are too subtle to differentiate at the clinics using conventional practices [28,29].

Wearable sensors and gait analysis

Wearable sensors (based on accelerometer and gyroscope) are increasingly used to detect freezing of gait (FoG) in PD, particularly in the controlled lab settings, where agreement with clinical ratings is moderate for both short and long FoG episodes, with sensitivity and specificity often between 73% and 100% [9]. Advanced ML and DL models, including those using a shin sensor or a single waist sensor, have demonstrated high accuracy (over 85%—90%) and specificity (up to 100%) in healthy controls during both simulated daily activities and real-time detection. However, their performance tends to decrease for very short FoG episodes and in unsupervised, real-life situations, where factors such as variability in patient movements, sensor noise, and environmental variations induce inconsistent results [10]. Consistency across patient groups can be affected by individual in disease stage, gait patterns variability, and medication state, which may restrict the generalizability of models trained on one group to others [11,30].

Handwriting and drawing kinematics

Micrographia (abnormally small handwriting) and irregular patterns in spiral drawings are recognized as strong early indicators of PD. AI tools based on restricted Boltzmann machines and CNNs have demonstrated superior capabilities in detecting subtle tremors and velocity fluctuations in digitized handwriting samples compared to human evaluation. For instance, a method based on transfer learning achieved an impressive 87% accuracy in classifying PD using spiral sketches [31] (see Table 1).

Integrating different data types like voice, gait, handwriting, and imaging into a single AI model for AD and PD presents several technical challenges. Data heterogeneity is a major issue; each modality (e.g. audio, motion, or images) has different formats, sampling rates, and feature spaces, making it difficult to align and integrate them effectively. Data scarcity and lack of standardization are also significant challenges as collecting large, well-annotated, and synchronized multimodal datasets requires substantial resources. Feature extraction and fusion require sophisticated methods to ensure the relevant information from each modality is captured and combined without losing important details, often requiring complex architectures and carful tuning. As multimodal AI models grow more complex, interpretability declines, making clinical trust harder. Privacy and data security concerns also rise with sensitive, multisource patient data. Overcoming these challenges requires advances in multimodal learning and explainable AI (XAI), as well as the development of large, standardized datasets for secure, reliable model training and validation.

Challenges and ethical considerations

Despite the transformative potential of AI-driven solutions in early diagnosis, personalized treatment, and prognostic modeling for neurodegenerative diseases like

Table 1

Application of AI diagnosis in AD and PD [32–37].

Biomarkers/analysis	Disease	Reported impact/advancement	Application area
Digital biomarkers (facial/eye)	AD and PD	High diagnostic approach (AUC up to 0.89)	CNN, ML [32]
Neuroimaging	AD and PD	Accurate detection	ML, DL, Transfer learning [33]
Fluid biomarkers	PD	Promising, needs further research	AI, DL[34]
Cognitive impairment detection	PD	Notable diagnostic accuracy	ML (various) [35]
Gait freezing prediction	PD	Advancing method	ML, wearable sensors [36]
Speech/Hand writing	AD and PD	Early detection of motor/cognitive decline	ML/DL on audio movement data [37]
Multimodal data fusion	AD and PD	Improved risk prediction	Imaging, genomics, and wearables [37]

AD, Alzheimer's disease; AI, artificial intelligence; AUC, area under the curve; CNN, convolutional neural network; DL, deep learning; ML, machine learning; PD, Parkinson's disease.

AD and PD, several critical challenges and ethical considerations must be addressed to fully realize their benefits. One significant hurdle is dataset bias, particularly the under-representation of non-Western populations in large language models. Model accuracy may be impacted by differences in language, nutrition, lifestyle, healthcare-seeking behavior, genetic predisposition, and comorbidities, which can change how diseases manifest and biomarker patterns are influenced. To overcome this, region-specific datasets must be developed. For instance, most voice-analysis studies focus on English speakers and neglect tonal languages such as Mandarin, which limits the generalizability of these AI models. Additionally, the 'black-box' nature of DL models raises concerns among clinicians who require interpretable explanations to trust AI-driven solutions. XAI such as Grad-CAM, ResNet, DenseNet, and Layer-wise Relevance Propagation (LRP) aims to overcome the limitation of 'black-box' nature of DL by providing interpretable insights into model predictions. This has prompted the use of techniques like LRP for visualizing key features in predictions. Ethical challenges are another important issue for AI-based diagnostic tools. These issues include the difficulty of implementing federated learning frameworks, managing algorithm bias, overseeing risk assessment, ensuring data privacy, and guaranteeing equitable access to cutting-edge diagnostic tools. Such tools are designed to enable decentralized model development without compromising sensitive patient data. Especially in low-resource settings, these issues necessitate close collaboration between technologists and policymakers. Furthermore, integrating multimodal data, imaging, genetics, gait, and speech holds great promise for creating advanced models for neurodegenerative diseases. Innovative approaches such as generative adversarial networks are being leveraged to synthesize synthetic datasets that preserve privacy and address data security concerns. This ultimately opens the door to earlier intervention and more effective, inclusive health care solutions.

Data heterogeneity is an inherent challenge in AI-based AD/PD diagnosis stemming from semistructured and unstructured clinical notes and the diversity in data from wearable devices, medical records, and cognitive questionnaires. This inconsistent data format restricts the data interoperability for effective AI comprehension. To address this, a combination of data harmonization tools and multimodal federated learning is crucial. While data harmonization tools enable standardization of varied data models, the multimodal AI component (e.g. large language model (LLM)s) plays crucial role in integrating diverse data types to generate streamlined reports. We recognize that the majority of publicly accessible wearable, speech, and neuroimaging datasets for PD/AD originating from Western populations, which may significantly restrict the applicability and generalizability of AI models to patients in underrepresented areas like India. Model accuracy may be impacted by differences in target population, including genetic predisposition, clinical presentation, comorbidities, and lifestyle factors. Moreover, the digital biomarker analysis is susceptible to regional bias as the models can be influenced by differences in language (for voice/gait analysis), culture (for cognitive assessment), and climatic conditions or gait patterns (for wearable devices).

Conclusions

The synergy between neuroscience and AI is restructuring the diagnosis and therapeutic management of neurodegenerative diseases, particularly AD and PD. While the traditional diagnostics and treatment remain essential, the AI-driven innovative technologies offer scalability, precision, and personalization. For instance, in PD, wearable sensors can predict FoG episodes in real time and advanced algorithms are being developed to optimize the outcome of deep brain stimulations. Similarly, in AD, AI leverages digital biomarkers from neuroimaging, gait analysis, and vocal analysis to detect early cognitive decline and provides therapeutic interventions. These innovations effectively bridge the gap between complex pathophysiology and POC solutions by transforming raw data into actionable clinical insights. However, the full realization of AI technology necessitates a careful address of several ethical, clinical, and technical challenges. As AI technologies continue to evolve and be integrated into clinical practice and advanced devices, it promises to unlock transformative advancements in neurodegenerative disease diagnosis and therapeutics, ultimately enhancing the quality of life for millions affected by these conditions.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

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