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REVIEW ARTICLE

Harnessing artificial intelligence for enhanced Parkinson's disease management: Pathways, treatment, and prospects

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ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disorder characterized by the accumulation of misfolded proteins and impaired protein degradation mechanisms. Dysregulation of protein degradation processes, including autophagy and the ubiquitin-proteasome system, has been implicated in the pathogenesis of PD. Recently, artificial intelligence (AI) has emerged as a powerful tool to enhance our understanding of protein degradation in PD. This abstract provides an overview of the advancements in studying protein degradation in PD with the aid of AI. The integration of AI techniques, such as machine learning and data mining, has enabled the identification and characterization of protein degradation pathways involved in PD. By analyzing large-scale protein-protein interaction networks, AI algorithms have revealed key interactions and pathways underlying protein degradation dysfunction in PD. Furthermore, AI models can predict the efficiency of protein degradation processes and identify potential targets for enhancing protein degradation in PD, aiding in the development of novel therapeutic interventions.AI-based approaches have also been instrumental in drug discovery and target identification, as they can screen vast databases of compounds to identify potential drugs or small molecules that modulate protein degradation pathways relevant to PD. Additionally, deep learning algorithms have facilitated the analysis of protein structures, predicting protein stability and folding patterns that impact protein degradation. Moreover, AI has played a crucial role in the identification of protein biomarkers associated with protein degradation dysfunction in PD. These biomarkers can aid in early diagnosis and monitoring of the disease, enabling timely intervention and personalized treatment strategies. The advancements presented in this abstract highlight the transformative potential of AI in elucidating the intricate mechanisms of protein degradation in PD. Collaborations between AI researchers, biologists, and clinicians are essential to translate these findings into effective diagnostic tools and therapeutic interventions for PD patients.

Keywords: Parkinson's disease; artificial intelligence; neurodegenerative disorder; pathways; treatment optimization

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1. Introduction

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder, following Alzheimer's disease. It is classified as a synucleinopathy and has a frequency of 160/100,000 in Western Europe, with a higher prevalence of 4% in individuals over 80 years old. This condition affects various systems within the body, including the gastrointestinal, peripheral, and central nervous systems. The pathogenic process of PD involves multiple neural systems and progresses slowly, primarily affecting specific types of sensitive nerve cells with cytoskeleton changes. It took over a century for the identification of neuron loss in the substantia nigra pars compacta (SNpc) as a primary pathological feature of PD. However, the

discovery of dopamine (DA) in the mammalian brain led to accelerated advancements in understanding PD. It was subsequently revealed that the SNpc neurons constitute the nigrostriatal dopaminergic pathway, leading to two significant findings. Firstly, the primary symptoms of PD result from a deficiency of striatal DA caused by the death of these SNpc neurons. Secondly, the administration of the striatal DA precursor levodopa (L-3,4-dihydroxyphenylalanine) through oral medication can alleviate the reduction in these neurotransmitters and replenish striatal DA levels[1]. Pathological features of Parkinson's disease are the development of abnormal protein aggregates called Lewy bodies in the neurons. These Lewy bodies primarily consist of a protein called alpha-synuclein. In some cases, mutations in the genes that code for alpha-synuclein can lead to an inherited form of Parkinson's disease. Additionally, excessive expression or misfolding of alpha-synuclein protein can increase the risk of developing the sporadic form of the disease.

Protein misfolding and aggregation, and disruptions in cellular processes as autophagy (the process by which cells degrade and recycle damaged or unnecessary components), ER stress, improper mitochondrial working, and impaired protein degradation, play important roles in the development and progression of PD. These abnormalities can lead to the accumulation of damaged or abnormally modified proteins, causing cellular dysfunction and eventually death[2]. Neuroinflammation is another important component of PD pathology. It leads the activation of immune cells in the brain, and releases the inflammatory molecules that can contribute to the degeneration of neurons[3,4].

Parkinson's disease manifests with a range of clinical features encompassing both motor and non-motor symptoms. Motor symptoms comprise a resting tremor (tremor during periods of inactivity), bradykinesia (reduced movement speed), rigidity (muscular stiffness), and postural instability. Non-motor symptoms encompass cognitive impairments, mood alterations, disruptions in sleep patterns, autonomic dysfunction, and sensory abnormalities. Treatment strategies for Parkinson's disease aim to reduce symptoms and improve quality of life. The main approach has been to compensate for the reduced dopamine levels in the brain. Levodopa, a precursor of dopamine that can cross the blood-brain barrier, is commonly administered to increase dopamine levels. Other medications that mimic the action of dopamine or enhance dopamine function in the brain, such as dopamine agonists, may also be prescribed. In some cases, deep brain stimulation (DBS) surgery, which involves implanting electrodes in specific brain regions, may be considered to help control symptoms. It's important to note that while current treatments help manage the symptoms of PD, they do not provide a cure or slow down the underlying neurodegenerative process. Ongoing research is focused on disease-modifying therapies that can target the mechanisms of the condition and potentially lowers its progression.

- Diagnosis challenges: PD diagnosis is challenging and often relies on clinical evaluation. Computer-aided diagnosis using AI algorithms has been explored to assist in PD diagnosis. Voice recordings, gait patterns, and electroencephalography (EEG) signals have been proposed as potential biomarkers for early detection of PD.
- EEG signals as biomarkers: EEG signals measure the electrical activity of the brain and can be used to analyze brain function. EEG signals have been employed to predict PD, but they have limitations such as low spatial resolution and noise. Advanced signal processing techniques, like blind source separation and characteristic extraction methods, are used to enhance the analysis of EEG signals.
- Extraction of Hjorth features: Hjorth features, which describe EEG signals in terms of amplitude, time, and spectral information, have been successfully employed in emotion recognition and tremor identification in PD patients. These features were extracted from EEG signals recorded during the 3-Auditory oddball task.
- Machine learning classification: Supervised machine learning algorithms such as SUPPORT VECTOR MACHINE (SVM), k-nearest neighbors (KNN), and random forest classifiers were utilized for PD classification based on the extracted Hjorth features.

- Contribution of the survey: The survey aims to assess the research landscape of AI-based PD diagnosis, focusing on machine learning and deep learning aspects. It also discusses the potential use of mobile-based technologies for PD detection and management, highlighting open challenges and future directions[5].

2. Neuropharmacology of PD

Parkinson's disease (PD) is characterized by the loss or deterioration of dopaminergic neurons responsible for producing dopamine in the substantia nigra, along with the formation of Lewy bodies, an identifiable pathological feature. These pathological changes may occur over a period of twenty years or more before observable symptoms manifest. The selective degeneration of dopamine-producing neurons has a substantial impact on motor control, leading to significant impairments. Lewy bodies, which are abnormal aggregations within cells, contain two proteins called alpha-synuclein and ubiquitin (**Figure 1)**. These proteins disrupt normal neuronal functioning and contribute to the progression of the disease[6]. Emerging research suggests that the process of aging and exposure to environmental stressors can contribute to the development of neuropathology, specifically persistent low-level inflammation within the brain. Factors such as exposure to environmental pollutants like pesticides, illicit substances, and the natural stress of aging can promote this inflammatory response, commonly referred to as "inflammaging." As this inflammatory process persists over time, it leads to cellular aging of neurons in the brain[6–8].

The pathogenic alterations typical of PD patient, such as depigmentation, neuronal loss, and gliosis, have an impact on the substantia nigra pars compacta and the protein locus coeruleus the brain. In the substantia nigra pars compacta 60%–70% of the neurons have died by the time PD symptoms appear[9]. The CNS protein-coding genetic mutation play a part in neuronal death. Specifically, Alpha-synuclein self-aggregates and behaves abnormally. Lewy bodies, cellular inclusion that are hallmark of Parkinson's disease are primarily made up of this aggregated, insoluble alpha-synuclein. Additionally, mechanism like the ubiquitin-proteasome system, which are intended to break out aberrant oxidative stress brought on by reactive oxygen species leading to neuronal death are further defective mechanisms leading to Parkinson's disease[2,9].

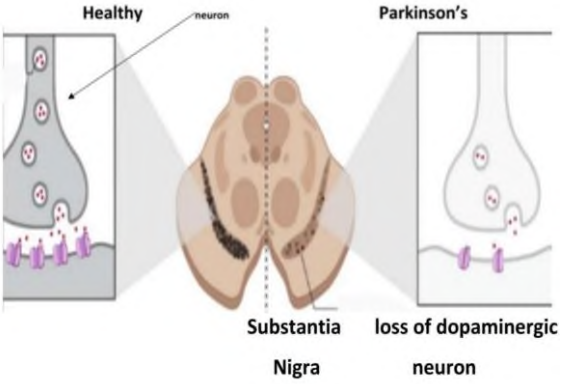

Figure 1. Parkinson's disease.

Parkinson's disease there is the degradation of dopaminergic neuron in the brain. Due to their vast branching and the high quantities of the energy needed to transmit nerve signals throughout this extensive network, these neurons are susceptible to degeneration. The central nervous system's protein-coding genetic mutations play a part in neuronal death. Specifically, alpha-synuclein self-aggregates and behaves abnormally. Lewy bodies, cellular inclusions that are the hallmark of Parkinson's disease (PD), are primarily made up of this aggregated, insoluble alpha-synuclein. Furthermore, there are dysfunctional mechanisms within the brain that play a role in Parkinson's disease (PD). For instance, the ubiquitin-proteasome system, responsible for eliminating abnormal proteins, experiences impairment. In addition, there is mitochondrial dysfunction and an

increase in oxidative stress caused by reactive oxygen species, leading to the death of neurons. These defective mechanisms are thought to contribute to the development and progression of Parkinson's disease (**Table 1**)[10,11].

Table 1. Tabular form summarizing the neurophysiology of Parkinson's disease.

Neurophysiological aspect	Description
Dopamine depletion	Significant reduction in dopamine levels in the brain due to degeneration and loss of dopaminergic neurons in the substantia nigra pars compacta.
Basal ganglia dysfunction	Disruption of the normal functioning of the basal ganglia, a group of structures involved in motor control, due to the reduced dopamine levels.
Direct pathway	Impaired activation of the direct pathway in the basal ganglia, resulting in decreased activation of motor circuits and reduced facilitation of movement.
Indirect pathway	Insufficient inhibition of the indirect pathway in the basal ganglia, leading to increased inhibition of motor circuits and further impairment of movement.
Disrupted cortical-basal ganglia loop	The communication pathway between the basal ganglia and different areas of the cerebral cortex, known as the cortical-basal ganglia loop, can be disrupted. This disruption interferes with the normal flow of information within this loop.
Lewy bodies	The presence of anomalous accumulations of protein known as Lewy bodies. These aggregates are predominantly composed of alpha-synuclein and are distinctive markers of the disease.

The neuropharmacology of PD involves the use of medications to manage symptoms and improve the quality of life for patients

Artificial intelligence (AI) can play a role in enhancing the understanding and treatment of PD by providing advanced data analysis techniques, predictive modeling, and personalized medicine approaches. Here's how AI intersects with the neuropharmacology of PD[12]:

- Medication development: AI can assist in the discovery and development of new medications for PD. Machine learning algorithms can analyze large datasets, including genetic information, clinical data, and drug libraries, to identify potential drug candidates or repurpose existing drugs for PD treatment. AI can accelerate the drug discovery process by predicting drug-target interactions, optimizing molecular structures, and simulating drug effects.
- Personalized treatment: PD is a heterogeneous disease, and individual responses to medications can vary. AI algorithms can analyze patient-specific data, such as genetic profiles, clinical history, and imaging data, to predict optimal treatment strategies. By considering multiple factors, AI can help tailor medication choices, dosage adjustments, and treatment plans for each patient, maximizing therapeutic outcomes and minimizing side effects.
- Adverse event monitoring: AI techniques, such as natural language processing and data mining, can be applied to analyze large volumes of biomedical literature, electronic health records, and social media data to detect and monitor adverse drug reactions associated with PD medications. AI algorithms can identify patterns and signals of drug-related side effects, helping healthcare professionals and regulatory authorities make informed decisions regarding medication safety and usage.
- Real-time monitoring and wearable devices: AI algorithms can process data from wearable devices, such as smartwatches or biosensors, to monitor PD symptoms and medication response in real-time. Machine learning models can analyze sensor data, including gait patterns, tremor severity, and medication adherence, to provide continuous monitoring and personalized feedback to patients. This can help optimize medication dosing, track disease progression, and enable early intervention.
- Treatment response prediction: AI models can learn from large datasets of patient characteristics, clinical assessments, and treatment outcomes to predict individual treatment responses. By leveraging machine learning algorithms, clinicians can have access to predictive models that estimate the likelihood of

medication efficacy, identify non-responders, and guide treatment decisions. This can help optimize therapy selection and minimize trial-and-error in medication management.

- Decision support systems: AI can be utilized to develop decision support systems for healthcare professionals involved in PD treatment. By integrating patient data, medication information, and scientific knowledge, AI-powered systems can provide evidence-based recommendations, treatment guidelines, and assist in medication dosage adjustments. This can enhance clinical decision-making and improve patient care[12].

3. Etiology

The development of Parkinson's disease (PD) involves a complex interplay of genetic and environmental factors, making its etiology multifactorial. Although the precise cause of PD remains elusive, various significant factors have been recognized as contributors to the onset and progression of the disease. Here is a detailed explanation of the etiology of PD.

3.1. Genetic factors

Mutations: Specific genetic mutations have been linked to a higher susceptibility to Parkinson's disease (PD). Variations in genes such as SNCA, LRRK2, PARK2, PINK1, and DJ-1 have been identified as playing a role in familial cases of PD[7].

Genetic variants: Variations in specific genes, like GBA and MAPT, identified as risk factors for PD. These variants may influence the susceptibility to the disease or modulate its progression (**Table 2**).

Table 2. Tabular form summarizing the etiology of Parkinson's disease (PD).

Etiological factors	Description
Aging	Increasing age is the primary risk factor for PD, the incidence and prevalence of the disease rising with advancing age.
Genetic factors	Certain genetic mutations, such as mutations in the α-synuclein (SNCA) gene, parkin (PARK2) gene, PTEN-induced kinase 1 (PINK1) gene, and leucine-rich repeat kinase 2 (LRRK2) gene, are associated with an increased risk of developing PD.
Environmental factors	Exposure to few environmental toxins, pesticides and industrial chemicals, increases risk of PD.
Oxidative stress	The degeneration of dopaminergic neurons in Parkinson's disease (PD) is influenced by oxidative stress, which arises from an imbalance between the generation of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms. This imbalance disrupts the normal functioning of dopaminergic neurons, contributing to their degeneration in PD.
Mitochondrial dysfunction	Impaired mitochondrial function, including defects in mitochondrial respiratory chain complexes, can contribute to PD pathology by affecting energy production and increasing oxidative stress.
Protein misfolding	Abnormal protein aggregation, specifically the misfolding and accumulation of α-synuclein protein, is an attribute of PD. These protein aggregates form Lewy bodies, which are characteristic pathological features observed in PD brains.

3.2. Environmental factors

Oxidative stress: Arises from an imbalance between the generation of reactive oxygen species (ROS) and the body's capacity to eliminate them. This imbalance can result in cellular damage, affecting essential components such as proteins and DNA, ultimately leading to neuronal dysfunction and degeneration. Mitochondrial dysfunction: Impaired mitochondrial function and energy production have been observed in PD. It leads to higher oxidative stress and neuronal damage. Protein aggregation: The deposition of abnormal protein, such as alpha-synuclein, in Lewy bodies in PD. Misfolding and aggregation of these proteins leads to neuronal toxicity and cell death. Neuroinflammation: Chronic inflammation in the brain, characterized by the activation of microglial cells and increased cytokine production, has been implicated in the pathogenesis of PD. Inflammation can contribute to neuronal damage and accelerate disease progression. Environmental toxins: Exposure to few environmental toxins, i.e., pesticides, herbicides, and heavy metals, has been associated with

high risk of PD. These toxins can induce oxidative stress, disrupt mitochondrial function, and promote protein misfolding and aggregation.

3.3. Aging

Advancing age is the most significant risk factor for PD. The incidence of PD increases with age, suggesting that age-related changes in cellular processes and neuronal vulnerability contribute to disease development.

The interplay between genetic and environmental factors is complex, and the specific mechanisms are still under investigation. Additionally, not all individuals with genetic or environmental risk factors will develop PD, indicating that other factors, such as individual susceptibility and gene-environment interactions, are active in disease onset and progression[8,9].

3.4. Etiology and correlation with AI

While AI is not directly involved in the etiology of PD, it can contribute to understanding the disease's etiology by analyzing large datasets, identifying patterns, and generating hypotheses. Here's how AI can intersect with the etiology of PD:

- Data analysis: AI techniques, such as machine learning and data mining, can analyze diverse datasets including genetic information, clinical records, environmental factors, and lifestyle data. By processing and integrating these large datasets, AI algorithms can identify potential risk factors, genetic markers, or environmental exposures that may contribute to the development or progression of PD. AI can help uncover associations and patterns that may not be readily apparent through traditional analysis methods.
- Genomic studies: AI algorithms can be used to analyze genetic data, such as genome-wide association studies (GWAS), to identify genetic variants associated with PD. By considering numerous genetic markers and their interactions, AI can help identify susceptibility genes and potential genetic pathways involved in PD pathogenesis. AI techniques like deep learning can identify complex patterns in genomic data and predict disease risk or disease progression.
- Environmental risk factors: AI can assist in identifying potential environmental risk factors associated with PD. By analyzing large-scale environmental data, such as air quality measurements, geographical information, or occupational exposures, AI algorithms can help identify environmental factors that may contribute to the development or exacerbation of PD. This can help in understanding the interplay between genetics, environmental factors, and PD etiology.
- Systems biology and network analysis: AI can contribute to understanding the complex interactions and networks involved in PD pathogenesis. By integrating multiple types of biological data, including gene expression data, protein-protein interactions, and metabolic pathways, AI algorithms can identify key biological pathways and mechanisms underlying PD. AI can help build comprehensive models of PD etiology by incorporating data from various biological domains and analyzing their interactions.
- Hypothesis generation: AI techniques, such as natural language processing and literature mining, can analyze scientific publications, medical databases, and research articles to extract relevant information about PD etiology. By automatically processing vast amounts of scientific literature, AI can help generate new hypotheses or identify novel connections between different factors that contribute to PD. AI can assist researchers in discovering new directions for investigation and guide future studies on PD etiology.
- It's important to note that while AI can aid in understanding the etiology of PD, it should be used in conjunction with traditional research methods and expert knowledge. AI-driven findings and hypotheses should be further validated through experimental studies and rigorous scientific investigation. AI is a tool that can assist researchers and clinicians in analyzing and interpreting complex data, but it does not replace the need for domain expertise and critical thinking in understanding disease etiology[5,12].

4. Correlation of age and Parkinson's disease

Age is the most important risk factors for PD because it typically manifests between the ages of 50 and 60[31,32], it has also been proven how significant pesticides exposure and family history (a hereditary factor) are. Although more risk factors have been identified, it is whether their effects on men and women may differ[33]. Numerous cellular processes that are predisposed to the pathogenesis of PD. The development of Parkinson's disease (PD) may accelerate with age as a result of the buildup age- related somatic damage and the failure of compensatory system. Louis body development could be sign of age-related preventive mechanism against nervous system failure and degeneration. Older person may exhibit mild Parkinson symptoms, which are linked to decreased function. Result from vascular pathology, early PD and Alzheimer disease degenerative disease (such as Alzheimer disease and early PD) accidental Lewis body disease, or age-related decline in dopaminergic function.

The clinical manifestation of Parkinson disease may change people age, and this change may include changing pharmacological side effect, and increase risk of dementia, and increase likely would of nursing care admission. Instant of being correlated with age of illness onset, PD progression include the emergence of dementia and hallucinations. In vulnerable brain regions, which are made more sensitive by aging, PD maybe reflection of a breakdown of the usual sale or compulsory processes. PD is among the best illusion of an age-related illness[68].

Other factors

While the epidemiological evidence may not be as robust, numerous other factors have been suggested as potential risk factors for Parkinson's disease (PD). These factors encompass consuming well water, dairy product consumption, overweight status, exposure to hydrocarbon solvents, residing in rural areas, working in agriculture or farming, exposure to copper, manganese, and lead in urban settings, consuming iron-rich foods, having a history of anemia, and possessing higher education levels[34].

5. Diagnosis of Parkinson's with the help of AI

Neurological imaging is not frequently employed and only has a minor function in the diagnosis of PD. Studies including positron emissions tomography (PET) scan, MRIs, and ultrasonography don't provide enough evidence to diagnose Parkinson's disease. They cannot, at best, help identify idiopathic PD from MSA or MSA or essential tremor[35]with the most advanced surgical and medical treatment currently available slowly gets worse in time for both motor and non-motor components. PD patient have higher mortality rates than matched control. Regardless of the age of disease onset and level of disease care, the average age at the death is similar (mid-70s)[36].

Advancements in the diagnosis of Parkinson's disease (PD) with the help of artificial intelligence (AI) have shown great potential in improving accuracy, efficiency, and early detection of the disease. Here are some key advancements in PD diagnosis facilitated by AI:

- Machine learning algorithms: Machine learning techniques, such as support vector machines (SVM), random forests, and neural networks, have been employed to develop predictive models for PD diagnosis. These models are trained on large datasets containing various data types, including clinical assessments, genetic information, imaging data, and biomarkers. By analyzing these diverse data sources, AI algorithms can identify patterns and features that distinguish PD patients from healthy individuals, enabling accurate diagnosis.
- Voice and speech analysis: PD often affects vocal function, leading to changes in speech patterns. AI algorithms can analyze voice recordings and extract acoustic features, such as pitch, intensity, and speech rate, to detect subtle changes associated with PD. Machine learning models trained on voice data have

shown high accuracy in distinguishing PD patients from healthy individuals, providing a non-invasive and cost-effective method for early PD detection.

- Gait analysis: AI techniques have been applied to analyze gait patterns and detect abnormalities associated with PD. Wearable sensors and motion capture systems capture gait data, which is then processed by machine learning algorithms to identify characteristic gait features specific to PD. These AI-based gait analysis methods can aid in early PD detection and differentiate PD from other movement disorders.
- Imaging techniques: AI has facilitated the analysis of various neuroimaging data, including magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT). Deep learning algorithms can automatically extract features from brain images and identify neuroanatomical changes indicative of PD. AI-based image analysis can assist in early diagnosis, differential diagnosis, and monitoring disease progression in PD.
- Electroencephalography (EEG) analysis: EEG signals have been used as a non-invasive method for PD diagnosis. AI algorithms can analyze EEG data and extract specific features associated with PD, such as abnormal brain wave patterns or event-related potentials. Machine learning models trained on EEG data can differentiate PD patients from healthy individuals and assist in the early detection of PD.
- Integration of multiple data sources: AI can integrate data from various sources, such as clinical records, imaging data, genetic information, and wearable sensor data, to provide a comprehensive diagnostic approach. By combining multiple data modalities, AI algorithms can improve the accuracy and reliability of PD diagnosis by capturing the complex and multi-faceted nature of the disease.
- Computer-aided diagnosis systems: AI-based computer-aided diagnosis (CAD) systems are being developed to assist healthcare professionals in PD diagnosis. These systems utilize machine learning algorithms to analyze patient data and generate diagnostic recommendations. CAD systems can serve as decision support tools, helping clinicians in the interpretation of diagnostic tests, improving diagnostic accuracy, and reducing misdiagnosis rates[16].

The advancements in PD diagnosis with the help of AI offer the potential for earlier and more accurate detection, enabling timely interventions and personalized treatment strategies. However, it is important to note that AI-based diagnostic tools should be validated through rigorous clinical studies and integrated into clinical practice in collaboration with healthcare professionals to ensure their effectiveness, safety, and ethical use (**Table 3**).

Table 3. Tabular form summarizing the diagnosis of Parkinson's disease (PD) with the help of AI, highlighting its uses and drawbacks compared to other methods.

Aspect	Diagnosis of Parkinson's with AI	Drawbacks over other methods
Accuracy	AI algorithms can achieve high accuracy in PD diagnosis by analyzing diverse data sources and patterns.	Traditional diagnostic methods may also have high accuracy rates.
Early detection	AI can aid in the early detection of PD by analyzing subtle changes in various data types, enabling early intervention.	Other diagnostic methods may also enable early detection.
Non-invasive	AI-based diagnostic techniques, such as voice analysis and gait analysis, offer non-invasive approaches to PD diagnosis.	Some traditional diagnostic methods may also be non-invasive.
Integration of multiple data	AI can integrate and analyze data from various sources, providing a comprehensive view of the disease.	Traditional methods may rely on specific data types or assessments.
Efficiency	AI algorithms can process large datasets efficiently, leading to faster diagnosis and reduced workload for clinicians.	Traditional diagnostic methods may require more time and expertise.
Decision support	AI-based computer-aided diagnosis systems can provide decision support to healthcare professionals for more accurate diagnoses.	Traditional methods may rely solely on clinical judgment.
Limitations of AI	AI-based diagnosis may have limitations, such as the need for high-quality data, potential biases, and ethical considerations.	Traditional methods may have their own limitations and challenges.

6. Symptoms

The symptoms of PD can vary from individuals and typically develop gradually over time. The primary symptoms of PD include motor symptoms, which affect movement, and non-motor symptoms, which can affect various body functions. Here are some common symptoms of PD (**Table 4**).

Table 4. Parkinson's disease symptoms.

Motor symptoms	Non-motor symptoms
Tremor, bradykinesia, rigidity instability, hypomania, dysarthria, dysphagia, sialorrhea.	Cognitive impairment, bradyphrenia, tip of the tongue (word finding) phenomenon.
Decrease arm swing, shuffling gait, festination difficulty arising from chair, turning in bed.	Depression, apathy, anhedonia, fatigue other behavioral and psychiatric problems.
Micrography, cutting food, feeding, hygiene, slow activities of daily living.	Sensory symptoms: anosmia ageusia, pain (shoulder, back) parenthesis.
Glabellar reflex, blepharospasm, dystonia, striatal deformity, scoliosis, camptocormia.	Sleep disorder (REM behavior disorder, vivid dreams, daytime drowsiness, sleep fragmentation, restless legs syndrome).

6.1. Motor symptoms

Tremor: Often starting in the hands, fingers, or thumbs, tremors are characteristic shaking or rhythmic movements at rest. Bradykinesia: Slowness of movement, resulting in reduced ability to initiate and perform voluntary movements. Rigidity: Stiffness and resistance in muscles, leading to decreased flexibility and fluidity of movement (**Figure 2**).

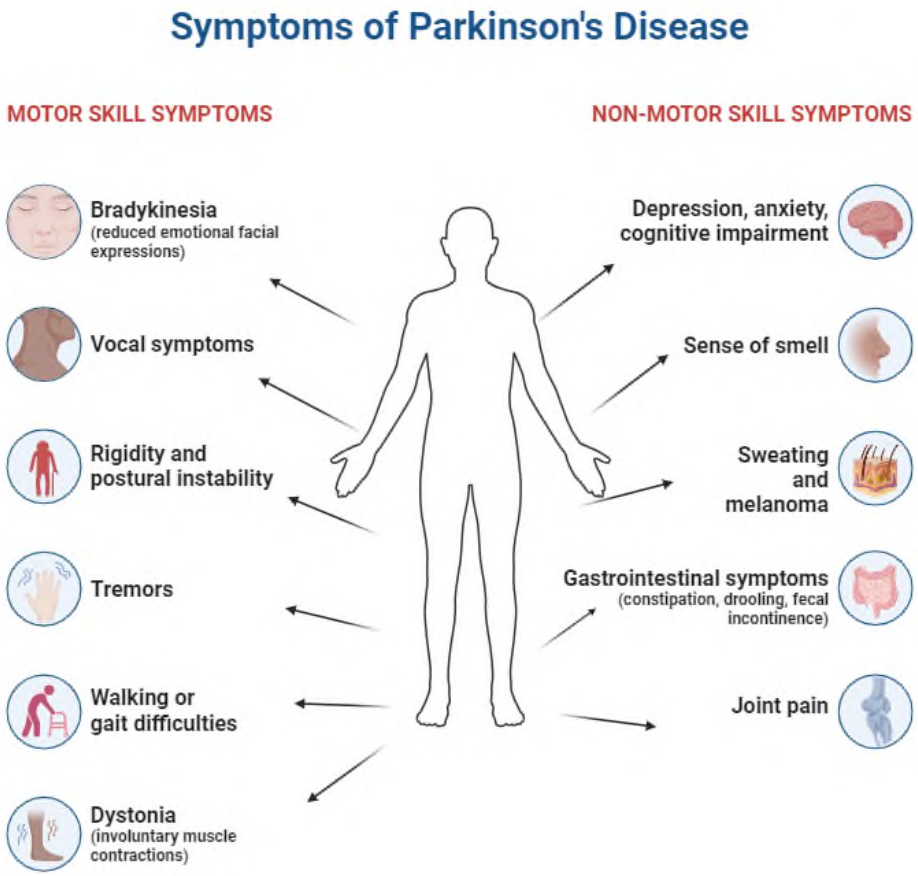

Figure 2. Symptoms of Parkinson's disease.

Postural instability: Impaired balance and coordination, making it difficult to maintain an upright posture and increasing the risk of falls. Gait and balance problems: Walking becomes challenging, with short shuffling steps, difficulty initiating movement, and a stooped or unsteady posture.

6.2. Non-motor symptoms

Sleep disorders: PD can cause sleep disturbances, including insomnia, restless legs syndrome, and REM sleep behavior disorder. Cognitive changes: Some individuals with PD may experience difficulties with memory, attention, and executive functions. Mood and emotional changes: Depression, anxiety, apathy, and irritability are common in PD. Autonomic dysfunction: This can manifest as changes in blood pressure, digestion, bladder control, and sweating. Sensory symptoms: Reduced sense of smell (hyposmia), vision problems, and pain or discomfort may occur in PD. Speech and swallowing difficulties: Speech may become softer, slower, or more monotonous, and swallowing can be impaired[37].

7. Pathway of Parkinson's disease

The pathway of PD Parkinson's disease is incorporated pathway related to synaptic and mitochondrial dysfunction, defective protein degradation, Alpha-synuclein pathobiology and neuroinflammation.

7.1. Synaptic dysfunction

A synapse's primary purpose is to connect neurons and enable communication between them using electrical or chemical signals. A neural structure known as the synapse has emerged as particularly vulnerable to various chronic insult[38,39] in the section below, we go over the mounting research demonstrating that synapses impacted in Parkinson's disease (PD) and that this dysfunction and death contribute to the condition.

Presynaptic protein include α-syn familial PD is linked to point mutations, duplication, or triplication of its gene[40,41]. Prior to neurotransmitter release, it briefly bind to synaptic vesicles in cultured neurons before being quickly redistributed to cytoplasm[42]. It has been demonstrated in mice that α-syn favorably increases functional SNARE level and that it may associate with the synaptic vesicle by binding to protein in the SNARE complex[43,44]. Similar to this overexpression of α-syn in cultured neuron's synapses and cell somas guards against oxidative stress[45]. Since large concentration of a α-syn produce familial PD the preventative effect of α-syn is, however, restricted to a small concentration range[46]. According to report, even slight overexpression of α-syn significantly inhibit neurotransmitter release[47]. Additionally, at the synapse, syn create potentially harmful micro aggregate[48]. The protein LRRK2, which play important roles in both familial and sporadic PD, is also found in synapses. The kinetic of synaptic vesicles release and recycling are impaired but its experimentally induced overexpression or knockdown[49,50]. However, more research has to be done to determine how these mechanisms in PD are affected by mutant or malfunctioning LRRK2. Synapses may be impacted by a variety of additional clinical events connected to PD Due to their High concentration denaturation of α-syn and dopamine, nigrostriatal pathway synapses are most likely to be main site of the formation of hazardous adducted of α-syn and oxidized DA[51–53] furthermore, faulty mitochondria respiration, turnover, or axonal transport may affect the energy requirements of synapses[54] locally abnormal protein turnover and degradation may have direct impact on synaptic development and functions[56].

AI and synaptic dysfunction in PD

AI techniques, particularly machine learning and deep learning, can analyze large-scale molecular, genetic, and imaging data to gain insights into the mechanisms underlying synaptic dysfunction in PD. AI models can integrate multi-omics data, such as gene expression profiles, protein-protein interaction networks, and neuroimaging data, to identify key molecular pathways and genetic factors associated with synaptic dysfunction in PD.

AI algorithms can analyze high-dimensional data and identify patterns and biomarkers that correlate with synaptic dysfunction, aiding in early detection and diagnosis of PD.

Deep learning models can analyze neuroimaging data, such as functional MRI (fMRI) or positron emission tomography (PET), to identify alterations in brain connectivity and synaptic activity in PD patients.

AI algorithms can also simulate and model synaptic dysfunction in PD, allowing researchers to investigate the effects of specific genetic mutations or molecular changes on synaptic function and explore potential therapeutic targets.

Advantages of AI in studying synaptic dysfunction:

- AI can process large and complex datasets, enabling the analysis of diverse factors contributing to synaptic dysfunction in PD.
- AI algorithms can discover novel biomarkers and molecular targets that are difficult to identify using traditional statistical methods.
- AI models can uncover intricate interactions and patterns within molecular networks, providing a systems-level understanding of synaptic dysfunction in PD.
- AI-based simulations and models allow for the exploration of hypotheses and predictions about the mechanisms underlying synaptic dysfunction.

Limitations and challenges:

- AI approaches heavily rely on the quality and availability of data. Obtaining comprehensive and well-curated datasets for studying synaptic dysfunction in PD can be challenging.
- Interpretability of AI models remains a challenge, as they often act as black boxes, making it difficult to understand the exact reasoning behind their predictions.
- Ethical considerations, data privacy, and bias in data collection and analysis are important factors that need to be addressed when using AI in synaptic dysfunction research (**Table 5**).

In summary, AI techniques provide valuable tools for studying synaptic dysfunction in Parkinson's disease. They enable the integration and analysis of complex datasets, identification of biomarkers, and simulation of synaptic dysfunction, contributing to a deeper understanding of the disease and potential therapeutic interventions[5,11,71].

Table 5. Tabular form summarizing the relationship between synaptic dysfunction and AI in the context of Parkinson's disease.

Aspect	Synaptic dysfunction and AI
Understanding mechanisms	AI techniques, such as machine learning and deep learning, can analyze large-scale molecular and genetic data to uncover the mechanisms underlying synaptic dysfunction in Parkinson's disease.
Integration of multi-omics data	AI algorithms can integrate diverse data types, including gene expression profiles, protein-protein interaction networks, and neuroimaging data, to gain insights into synaptic dysfunction in Parkinson's disease.
Biomarker identification	AI models can identify patterns and biomarkers associated with synaptic dysfunction in Parkinson's disease, aiding in early detection and diagnosis.
Neuroimaging analysis	AI algorithms can analyze neuroimaging data, such as fMRI or PET scans, to detect alterations in brain connectivity and synaptic activity related to Parkinson's disease.
Simulation and modeling	AI-based simulations and models allow for the investigation of the effects of specific genetic mutations or molecular changes on synaptic function in Parkinson's disease.
Systems-level understanding	AI approaches provide a systems-level understanding of synaptic dysfunction by analyzing intricate interactions and patterns within molecular networks.
Data processing and analysis	AI can handle large and complex datasets, enabling the processing and analysis of diverse factors contributing to synaptic dysfunction in Parkinson's disease.
Novel discoveries	AI techniques can uncover novel biomarkers and molecular targets that are challenging to identify using traditional statistical methods.
Interpretability	Interpretability of AI models remains a challenge, as they often act as black boxes, making it difficult to understand the exact reasoning behind their predictions in the context of synaptic dysfunction.
Ethical considerations	The use of AI in synaptic dysfunction research requires addressing ethical considerations, data privacy, and potential bias in data collection and analysis.

7.2. Mitochondrial dysfunction in PD

It is now known that mitochondrial dysfunction and inhibition of electron transfer chain are contributing factor in PD. This inhibition causes the cellular energy levels to drop and the production of reactive oxygen species, which can ultimately result in cellular damage and death mediated by excitotoxicity and oxidative stress. The major role of mitochondria in PD is supported by the fact that several genes associated with hereditary form of PD encode protein involved in mitochondrial dysfunction or are somehow related to mitochondrial. Environmental chemical that block the mitochondrial respiratory chain have reportedly been linked to PD, which support their role. The current work reflects the extensive body of research that contain mitochondrial malfunction to neuronal cell to rise attention to the vital need for additional study in this area and two demonstrate mortality in the substantia nigra pars compacta (SNpc) to PD patients[57].

MPP+, a metabolite of MPTP, has been found to induce parkinsonism in humans, as evidenced by research[58]. Furthermore, recent studies have revealed that the pesticide rotenone can lead to neurodegenerative changes similar to Parkinson's disease (PD) in rats[59]. Both of these compounds act as inhibitors of complex 1, a component of the mitochondrial respiratory chain. To further investigate the role of mitochondria in the development of PD, a cybrid approach was employed. This method involved fusing cell lines lacking functional mitochondria with mitochondria obtained from platelets or other tissues of PD patients. By analyzing PD cybrids, Langston JW and colleagues observed a reduction in complex 1 activity, consistent with findings in PD brains and platelets[60]. These findings provide additional evidence of mitochondrial involvement in the etiology of PD (**Table 6**).

The impairment of complex 1 function leads to an elevated release of superoxide ions from the respiratory chain. This increase in free radicals is associated with a decrease in the activity of respiratory chain proteins and contributes to complex 1 deficiency. Studies have shown that in rodents, the cellular damage induced by rotenone is primarily attributed to the generation of free radicals rather than ATP depletion[59].

Table 6. Tabular form summarizing the main pathways and mechanisms involved in Parkinson's disease (PD).

Pathway/mechanism	Description
Dopamine depletion	The decrease in dopamine levels is a result of the degeneration and loss of dopaminergic neurons in the compact portion of the substantia nigra.
Basal ganglia dysfunction	Impaired functioning of the basal ganglia, a group of structures involved in motor control, due to dopamine depletion.
Direct pathway	Reduced activation of the direct pathway in the basal ganglia, leading to decreased facilitation of movement.
Indirect pathway	Increased inhibition of the indirect pathway in the basal ganglia, resulting in further impairment of movement.
Cortical-basal ganglia loop	Disruption of the flow of information within the cortical-basal ganglia loop, affecting the regulation of voluntary movement.
Lewy bodies	Accumulation of abnormal protein aggregates, mainly alpha-synuclein, in the form of Lewy bodies, which contribute to neuronal toxicity and cell death.
Oxidative stress	Imbalance between the production of reactive oxygen species (ROS) and the body's ability to detoxify them, leading to cellular damage and neuronal dysfunction.
Mitochondrial dysfunction	Impaired mitochondrial function, resulting in reduced energy production, increased oxidative stress, and neuronal damage.
Neuroinflammation	Chronic inflammation in the brain, involving activation of microglial cells and increased production of cytokines, contributing to neuronal damage.
Genetic factors	Mutations and genetic variants in specific genes, such as SNCA, LRRK2, PARK2, PINK1, DJ-1, GBA, and MAPT, can increase the risk of developing PD.
Environmental factors	Exposure to toxins, including pesticides, herbicides, heavy metals, and other environmental factors, which can contribute to oxidative stress and neurodegeneration.
Aging	Advancing age is the most significant risk factor for PD, with the incidence of the disease increasing with age.

Advancement of mitochondrial dysfunction in PD and AI

Mitochondrial dysfunction is a prominent feature of Parkinson's disease (PD), and artificial intelligence (AI) has made significant advancements in understanding and studying its role in the disease. Here's a summary of the advancements in the study of mitochondrial dysfunction in PD with the help of AI (**Table 7**)[5,11].

Table 7. Advancements in the study of mitochondrial dysfunction in PD with the help of AI.

Aspect	Advancements in mitochondrial dysfunction and AI
Identification of genetic factors	AI techniques can analyze large-scale genetic data to identify specific genetic mutations and variations associated with mitochondrial dysfunction in PD.
Integration of multi-omics data	AI algorithms can integrate diverse data types, including genomics, transcriptomics, proteomics, and metabolomics data, to gain a comprehensive understanding of mitochondrial dysfunction in PD.
Prediction of mitochondrial dysfunction	AI models can predict the likelihood of mitochondrial dysfunction based on genetic and molecular data, aiding in early detection and personalized treatment strategies for PD patients.
Biomarker discovery	AI can identify novel biomarkers and molecular signatures related to mitochondrial dysfunction in PD, providing insights into disease progression and potential therapeutic targets.
Neuroimaging analysis	AI algorithms can analyze neuroimaging data, such as functional MRI (fMRI) or PET scans, to assess mitochondrial activity and connectivity patterns in the brain of PD patients.
Drug discovery and repurposing	AI-based approaches can screen large compound libraries and identify potential drugs or repurposed medications that target mitochondrial dysfunction and have therapeutic potential for PD.
Mechanistic insights	AI models and simulations allow for the exploration of complex interactions and pathways involved in mitochondrial dysfunction, providing mechanistic insights into PD pathogenesis.
Personalized medicine	AI can help in developing personalized treatment approaches by considering an individual's specific mitochondrial profile and predicting response to different therapeutic interventions.
Precision diagnosis	AI algorithms can aid in precise diagnosis by integrating clinical and molecular data, including mitochondrial biomarkers, improving accuracy and efficiency in diagnosing PD.
Data processing and analysis	AI can efficiently process and analyze large-scale omics datasets, enabling the identification of complex patterns and correlations related to mitochondrial dysfunction in PD.

AI has shown promising advancements in studying mitochondrial dysfunction in PD, further research and validation are necessary to fully understand its implications and translate them into clinical applications. Collaboration between AI experts, neuroscientists, and clinicians is crucial for the development of robust and reliable AI-driven approaches in the field of mitochondrial dysfunction in PD.

7.3. Protein degradation in PD

The exact mechanism by which PINK1 and DJ-1 are associated with protein degradation in living organisms remains unclear, posing challenges in studying the role of parkin in mediating protein degradation through the ubiquitin-proteasome system (UPS). Although the author's discovery suggests that syphilin-1 is degraded by the PINK1-Parkin-DJ-1 (PPD) complex, it was found that the regulation of syphilin-1 levels is not affected under the tested conditions in parkin-knockout models. Some study provides further evidence that PINK1, parkin, and DJ-1 in the cytoplasm are involved in regulating protein degradation. Identifying in-vivo settings where this occurs is now top priority.

Protein degradation dysregulation is an important aspect of Parkinson's disease (PD) pathophysiology. Impaired protein degradation processes can lead to the accumulation of abnormal proteins, such as alpha-synuclein, and contribute to the formation of Lewy bodies, a hallmark of PD. While there isn't a direct correlation between protein degradation and specific receptors in PD, certain receptor systems play a role in modulating protein degradation pathways (**Figure 3)**. Here's an overview:

- Ubiquitin-proteasome system (UPS): The UPS is responsible for the degradation of short-lived proteins in the cell. It involves the tagging of proteins with ubiquitin molecules, which target them for degradation

by the proteasome. While no specific receptor is directly associated with the UPS dysfunction in PD, altered proteasome activity has been observed in the disease, potentially contributing to protein aggregation and neuronal damage.

- Autophagy-lysosomal pathway: Autophagy is a cellular process lead to degradation and recycling of damaged or misfolded proteins and organelles. It relies on the fusion of autophagosomes with lysosomes, forming autolysosomes, where cargo is degraded. Several receptors and signaling pathways are implicated in the regulation of autophagy, including:
- Lysosomal-associated membrane protein 2A (LAMP2A): LAMP2A is an important receptor involved in the fusion of autophagosomes with lysosomes, promoting degradation. Mutations in the LAMP2A gene associated to a rare form of PD called Chediak-Higashi syndrome.
- MTOR (mechanistic target of rapamycin): MTOR is a signaling protein that regulates cell growth and autophagy. Dysregulation of MTOR signaling has been implicated in PD, with evidence suggesting that reduced MTOR activity may impair autophagy and protein clearance.
- PINK1 (PTEN-induced kinase 1) and Parkin: PINK1 and Parkin are proteins associated with familial forms of PD. They play crucial roles in mitochondrial quality control and are involved in the recognition and clearance of damaged mitochondria through a process called mitophagy.
- Chaperone-mediated autophagy (CMA): CMA is particular autophagy pathway responsible for the degradation of specific proteins. It involves the recognition of target proteins by chaperone proteins, such as heat shock cognate 70 (HSC70), and their translocation to lysosomes for degradation. While not directly related to receptors, CMA dysregulation has been implicated in PD, as alpha-synuclein, a key protein in PD pathology, can be degraded via CMA.

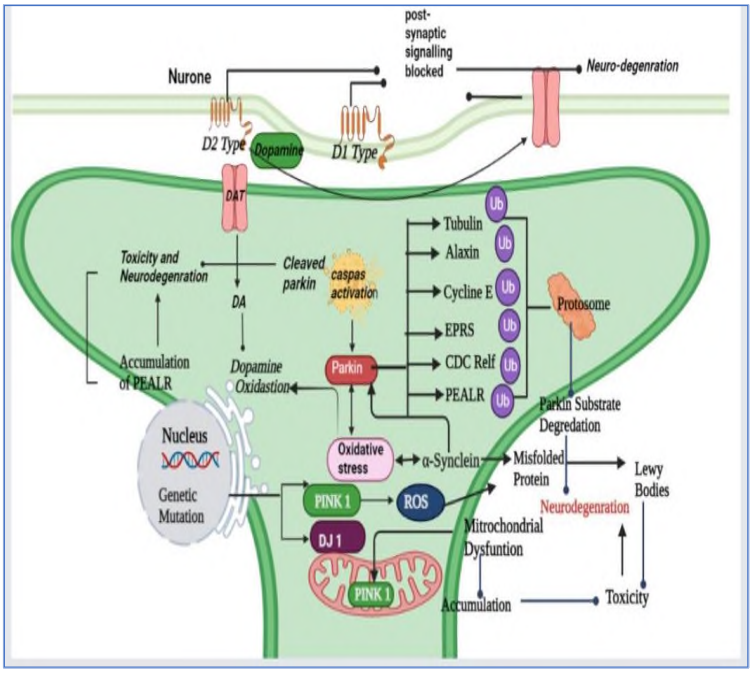

Figure 3. Protein degradation in PD: ROS—reactive oxygen species, PINK1-(phosphate and tension homologous)-induces kinase 1, DJ—protect against degeneration of nigral dopaminergic neuron Ub-ubiquitin, EPRS—Extrapyramidal reactions).

Advancement of protein degradation in PD with AI

Protein degradation is a crucial process in maintaining cellular homeostasis, and dysregulation of protein degradation mechanisms has been implicated in PD. Artificial intelligence (AI) has contributed to advancements in understanding and studying protein degradation in PD. Here are some key advancements in this area (**Table 8**)[70,71].

Table 8. Advancement of Protein degradation in PD with AI.

Aspect	Advancements in protein degradation and AI in PD
Identification of protein degradation pathways	AI techniques, such as machine learning and data mining, have been used to identify and characterize protein degradation pathways involved in PD.
Protein-protein interaction analysis	AI algorithms can analyze protein-protein interaction networks to uncover key interactions and pathways involved in protein degradation in PD.
Prediction of protein degradation efficiency	AI models can predict the efficiency of protein degradation processes and identify potential targets for enhancing protein degradation in PD.
Drug discovery and target identification	AI-based approaches can screen large databases of compounds to identify potential drugs or small molecules that modulate protein degradation pathways relevant to PD.
Systems biology approaches	AI can integrate multi-omics data, including transcriptomics, proteomics, and metabolomics, to provide a comprehensive understanding of protein degradation networks in PD.
Deep learning for protein structure analysis	Deep learning algorithms can analyze protein structures and predict protein stability, folding patterns, and interactions relevant to protein degradation in PD.
Biomarker identification	AI models can identify novel protein biomarkers associated with protein degradation dysfunction in PD, aiding in early diagnosis and monitoring of the disease.
Data processing and analysis	AI can efficiently process and analyze large-scale protein datasets, enabling the identification of complex patterns and correlations in protein degradation processes in PD.

These advancements demonstrate how AI has contributed to the understanding of protein degradation mechanisms in Parkinson's disease. AI-driven approaches have the potential to accelerate drug discovery, identify therapeutic targets, and provide valuable insights into the underlying molecular mechanisms of protein degradation dysfunction in PD. Further collaboration between AI researchers, biologists, and clinicians is needed to translate these advancements into effective treatments and diagnostic tools for PD[60].

8. Neuro inflammation

The characteristic feature of brain inflammation, referred to as neuroinflammation, is marked by the activation of glial cells, particularly microglia[61]. Microglia, the immune cells of the brain, undergo activation in response to harmful or pathological conditions[62,63]. Astrocytes can also be activated by inflammatory or neurotoxic factors released by reactive microglia and damaged neurons. The binding of pro-inflammatory cytokines to their receptors on dopamine (DA) neurons initiates signaling pathways that induce apoptosis (**Table 9**).

Table 9. Tabular form summarizing the role of neuroinflammation in Parkinson's disease (PD).

Aspect	Description
Inflammatory response	Activation of inflammatory stages in brain, involving the activation of microglial cells, the resident immune cells of the CNS.
Microglial activation	In the presence of abnormal proteins, such as alpha-synuclein aggregates, microglial cells are triggered to become activated. As a response, they release pro-inflammatory molecules like cytokines, chemokines, and reactive oxygen species.
Cytokine production	Elevated production of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), is associated with neuroinflammation and can lead to neuronal damage.
Oxidative stress	Neuroinflammation can lead to the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS), resulting in oxidative stress, which can damage cellular components and contribute to neurodegeneration.
Damage to neurons	Prolonged neuroinflammation releases toxic substances and the activation of immune responses that can damage and kill neurons, particularly dopaminergic neurons in the substantia nigra.
Amplification of inflammation	Neuroinflammation can initiate a positive feedback loop, wherein the release of pro-inflammatory molecules further activates microglia and perpetuates the inflammatory response, contributing to disease progression.

Table 9. (*Continued*).

Aspect	Description
Role of genetic factors	Genetic factors associated with PD, such as mutations in the LRRK2 and GBA genes, can influence the immune response and increase the susceptibility to neuroinflammation in PD.
Therapeutic target	Neuroinflammation has emerged as a specific target in PD, with research focusing on developing interventions to modulate or reduce the inflammatory response to mitigate neuronal damage.

9. Treatment of PD

Since there is no treatment to stop the advancement of PD, there is no known cure. However, a variety of medication can be used to treat the symptoms. The medication used to treat PD either increase the brain levels of dopamine or mimic it' s effect[65].

9.1. Medication used in PD

Levodopa: levodopa can lessen many of the Motor symptoms of Parkinson's disease (PD) but it has a little effect on non-motor symptoms or the degradation of dopaminergic nigral neurons. Patients who have a history of heart illness should be concerned about cardiac arrhythmias[66] (**Table 10**).

Table 10. Medicine used for PD[67,68].

Drug class	Generic name	Brand name
Levodopa	Carbidopa-levodopa	Sinemet, Parcopa, Rytary, Duopa
Dopamine agonist	Pramipexole, Ropinirole, Rotigotine, Apomorphine	Apokyn, Requip, Neupro (Patch), Mirapex
MAO-B inhibitor	Rasagiline, Selegiline	Deprenyl, Zelapar
COMT inhibitor	Entacapone, Tolcapone	Comtan, Tasmar
Anticholinergic	Benztropine, Trihexphenidyl	Cogentine, Artane
Amantadin	Amantadin	Symmeterel

9.2. Surgical method

Before levodopa became commercially available, the primary approach to treating Parkinson's disease (PD) involved surgical interventions. These interventions mainly targeted the reduction of tremors but did not effectively address the more disabling symptom of bradykinesia. However, surgical interventions have been demonstrated to provide benefits for patients with refractory symptoms of PD[68].

10. Advancement of artificial intelligence (AI) in Parkinson's disease

The advancement of artificial intelligence (AI) has the potential to contribute to the treatment of Parkinson's disease (PD) in various ways. While AI is not a standalone treatment for PD, it can be integrated into existing therapeutic approaches to enhance disease management. Here are some potential applications of AI in the treatment of PD[70]:

- Early detection and diagnosis: AI algorithms can analyze data from various sources, such as medical records, imaging scans, and sensor data from wearable devices, to aid in the early detection and diagnosis of PD. Machine learning models can learn patterns and identify biomarkers that may indicate the presence of PD, allowing for early intervention and treatment.
- Objective assessment of symptoms: AI-based technologies, such as smartphone apps or wearable devices, can objectively assess motor symptoms associated with PD, such as tremors, bradykinesia, and dyskinesia. These technologies use machine learning algorithms to analyze movement patterns and provide real-time feedback to patients and healthcare providers, enabling better symptom monitoring and treatment adjustments.

- Personalized treatment optimization: AI algorithms can analyze large datasets and patient-specific information to optimize treatment strategies for individuals with PD. By considering factors such as genetic profile, disease stage, medication response, and comorbidities, AI can help personalize treatment plans, including medication dosages and scheduling, to improve symptom management and minimize side effects.
- Prediction of disease progression: AI models trained on longitudinal data can predict the progression of PD, helping clinicians and patients anticipate future symptoms and plan appropriate interventions. These predictive models can assist in treatment decision-making, including when to adjust medication, consider surgical interventions like deep brain stimulation (DBS), or explore other therapeutic options.
- Medication adherence and monitoring: AI-powered systems can remind patients to take their medication on time and monitor their adherence to prescribed regimens. These systems can also collect data on medication usage and provide insights to healthcare providers, facilitating better medication management and optimizing treatment outcomes.
- Supportive therapies and rehabilitation: AI-based technologies, such as virtual reality (VR) and robotics, can provide supportive therapies and rehabilitation for individuals with PD. VR-based programs can assist in motor rehabilitation, gait training, and balance exercises, while robotics can aid in physical therapy and assist with activities of daily living.

It's important to note that while AI holds great promise, its implementation in PD treatment should be done in collaboration with healthcare professionals and should complement existing clinical practices. AI technologies require rigorous validation, continuous improvement, and integration into clinical workflows to ensure their safety and efficacy in improving patient outcomes[70,71].

11. Conclusion and perspective

In conclusion, Parkinson's disease is a complex neurodegenerative disorder with a multifactorial etiology and a range of clinical manifestations. While the primary treatment approach involves dopamine replacement therapy, the understanding of the disease's pathways, such as protein misfolding, autophagy disruption, and neuroinflammation, has opened up new avenues for therapeutic exploration. The integration of artificial intelligence (AI) in Parkinson's disease management shows promising prospects for enhancing various aspects of diagnosis, treatment, and patient care. AI technologies offer the potential to improve early detection and accurate diagnosis of PD, enabling timely interventions. The objective assessment of motor symptoms through AI-powered tools can enhance monitoring and facilitate personalized treatment optimization. AI algorithms trained on large datasets can predict disease progression, aiding in treatment planning and improving patient outcomes.

Furthermore, AI can play a crucial role in medication adherence monitoring, reminding patients to take their medications on time and providing insights to healthcare providers. Additionally, AI-based supportive therapies, such as virtual reality and robotics, have the potential to improve rehabilitation outcomes for individuals with PD. While AI holds significant promise, further research and development are necessary to refine and validate these technologies for widespread clinical use. Ethical considerations, data privacy, and regulatory frameworks must be carefully addressed. Collaborative efforts between healthcare professionals, researchers, and AI experts are crucial to harness the full potential of AI in Parkinson's disease management. In the future, the integration of AI with emerging technologies, such as wearable devices, genetic profiling, and advanced imaging techniques, could further enhance the accuracy of diagnosis, personalization of treatment, and monitoring of disease progression. Continued advancements in AI algorithms and increased availability of high-quality data will contribute to improving our understanding of Parkinson's disease and optimizing treatment strategies. Overall, the integration of AI in Parkinson's disease management offers exciting possibilities for improving patient outcomes, enhancing treatment efficacy, and advancing our

understanding of the disease. Continued research and collaboration will pave the way for the realization of these prospects, ultimately benefiting individuals living with Parkinson's disease.

In conclusion, the advancements in understanding protein degradation in Parkinson's disease (PD) with the help of artificial intelligence (AI) have provided valuable insights into the underlying molecular mechanisms of the disease. AI techniques, including machine learning, data mining, and deep learning, have played a significant role in identifying protein degradation pathways, predicting protein stability, and discovering potential therapeutic targets. The integration of multi-omics data and the analysis of protein-protein interaction networks have enhanced our understanding of the complex networks involved in protein degradation dysfunction in PD. AI-driven approaches have also contributed to the identification of novel protein biomarkers, enabling early diagnosis and monitoring of the disease. Moreover, AI has facilitated drug discovery and target identification by screening large databases of compounds, potentially leading to the development of new therapeutic interventions that modulate protein degradation pathways in PD. The ability of AI models to predict protein degradation efficiency holds promise for the enhancement of protein clearance mechanisms in the disease. By unraveling the intricate processes underlying protein degradation in PD, AI has provided a foundation for personalized medicine approaches. The integration of AI into PD research has the potential to accelerate the development of effective diagnostic tools and targeted therapies, ultimately improving patient outcomes. However, it is important to acknowledge that further research, validation, and collaboration between AI experts, biologists, and clinicians are necessary to fully exploit the potential of AI in the field of protein degradation in PD. Continued efforts in this area will deepen our understanding of PD pathogenesis, facilitate early detection, and contribute to the development of innovative treatments for this debilitating neurodegenerative disorder.

Conflict of interest

The authors declare no conflict of interest.

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