Journal of Advanced Scientific Research

Available online through https://sciensage.info

ISSN

0976-9595

Review Article

Genomic Insights in Parkinson's Disease: A Reviews

Mayuri Chavan*, Apoorva Ranade, Rucha Kajbaje, Rucha Pusegaonkar, Snnehaa Bhosale, Meera Deshmukh

TMV's Lokmanya Tilak Institute of Pharmaceutical Sciences, Pune, Maharashtra, India.

Corresponding author: mayurichavan0820@gmail.com

Received: 15-03-2026; Accepted: 22-03-2026; Published: 30-03-2026

https://doi.org/10.55218/JASR.2026170306

ABSTRACT

Parkinson's disease is a neurological condition that affects 8.5 million individuals worldwide and is characterised by tremors, slower movements, loss of balance, and stiffness. Over the last decade, progress in genomic research on complicated diseases has increased rapidly and emerged as a potent means of understanding the pathogenesis of Parkinson's disease. Parkinson's disease has both familial and sporadic genetic forms, with rare mutations and monogenic variants linked to disease risk. Common variations, like SNCA, MAPT, and HLA, increase the probability of developing the disease, highlighting the complex interaction between inherited variables and disease pathogenesis. Novel PD risk loci and genes have been reported through genomic investigations, particularly genome-wide association studies (GWAS), creating a path for precision medicine techniques along with targeted therapeutics. Polygenic risk scores (PRS) are used to assess risk, allowing for early intervention and individualised care for those who are at risk. This review aims to offer a thorough analysis of the functions of genomics in Parkinson's disease, comprising its genetic architecture, genomic studies for determining the genetic components that influence PD risk and pathophysiology, implications for risk assessment, diagnosis using various novel biomarkers, therapeutic advances, research gaps, challenges such as heterogenicity, underdiagnosis, adverse effects of medicines and future directions along with the additional research in these fields may pave the path for cutting-edge treatment and diagnostic approaches that eventually improve the lives of people with Parkinson's disease (PD).

Keywords: Parkinson's disease, Genomics, Marker, Mutation, Gene, Familial, Sporadic, Alpha-synuclein.

INTRODUCTION

In the past 25 years, cases of Parkinson's disease (PD) doubled globally; in 2019, it was estimated that 8.5 million people worldwide had PD. The number of people living with PD has grown by over a 100% since 2000, and disability-adjusted life years have increased by 81% [1]. The disease's hallmarks include Lewy bodies, intracellular inclusions that contain synuclein aggregates that are linked to the condition, as well as dopaminergic neurons of the substantia nigra pars compacta die selectively. In addition to motor symptoms, including resting tremor, bradykinesia, postural instability and rigidity, PD clinically displays non-motor symptoms such as cognitive decline, sleep difficulties, dysautonomia, and mental abnormalities[2]. It is essential to research Parkinson's disease genetics for several reasons. Parkinson's disease develops and progresses primarily because of genetic factors. Numerous studies have connected the alpha-synuclein (SNCA), parkin (PARK2), leucine-rich repeat kinase 2 (LRRK2), and glucocerebrosidase (GBA) genes to Parkinson's disease[3–5]. Important new information about the underlying mechanisms of Parkinson's disease can be obtained from genetic research. Genetic analysis can be used to identify those who are more prone to getting Parkinson's disease. Specific genetic variants raise the chance of acquiring Parkinson's disease. For instance, certain mutations in the LRRK2 gene have been integrated with a greater chance of acquiring Parkinson's disease[4]. By identifying people who have these genetic variants, early interventions or preventive measures can be implemented to lower the risk or delay the onset of the disease. Genetic research can shed light on the causes, progression, and mechanisms of disease. Uncovering the biological pathways and molecular mechanisms underlying Parkinson's disease can help explain its genetic components. For instance, the identification of mutations in the SNCA gene, which encodes for the protein alpha-synuclein, has provided the significance of protein dysfunction and aggregation in the pathophysiology of Parkinson's disease [6,7]. These discoveries have opened the door for investigation into protein aggregation and misfolding as potential therapeutic targets. Personalised treatments can be developed with the help of genetic studies. Researchers can find potential therapeutic targets and create individualised treatment plans by understanding the genetic variations linked to Parkinson's disease. Examples include the investigation of enzyme replacement therapy and small molecule chaperones as potential therapeutic approaches because of the identification of the GBA gene as a risk factor for Parkinson's disease.[8,9]

Importance of Genomics in Understanding Parkinson's Disease Pathogenesis

Understanding the pathogenesis of Parkinson's disease (PD) has benefited greatly from genomic research. Researchers have been able to pinpoint specific genetic variants linked to PD by analysing the genetic make-up of PD patients, shedding light on the disease's underlying mechanisms. The discovery of genetic risk factors is one of the most important contributions of genomics to Parkinson's disease research. Specific genetic mutations that increase PD susceptibility have been found in several studies. For instance, both sporadic and familial forms of PD have been connected to LRRK2 gene mutations. This study highlights the usefulness of genomics in discovering significant genetic variables implicated in the aetiology of the disease[10,11]. Other genes may be involved in Parkinson's disease, according to genomic studies. A possibility of developing Parkinson's disease (PD) has been linked to several typical genetic mutations through genome-wide association studies (GWAS). For example, the SNCA and MAPT genes, which are recognised as having a function in the pathogenesis of the disease, were found to be associated with several loci in the GWAS performed by Nalls *et al*. (2014) that were associated with PD[4]. By studying gene expression patterns in Parkinson's disease patients, researchers uncovered dysregulated genes and pathways that may be involved in the disease's progression. For example, a large-scale gene expression study from 2009 revealed that PD patients had changed expression of mitochondrial function-related genes and the response to oxidative stress[12]. Researchers have discovered genetic variations that alter the risk related to exposure to specific environmental toxins or factors through gene-environment interaction studies. As one possible environmental risk factor for Parkinson's disease (PD), studies have revealed that some genetic polymorphisms, such as those in the GSTT1 and GSTM1 genes, may make people more susceptible to the toxic effects of pesticides. [13,14]

The Genetics of Parkinson's Disease

Familial versus sporadic Parkinson's Disease

Sporadic and familial are the two forms of Parkinson's disease, which are different manifestations of the same neurodegenerative disorder, but they have different primary causes and modes of inheritance. Parkinson's disease with a known genetic component or a family history of the condition is referred to as familial Parkinson's disease. The genes SNCA, PARK2, LRRK2, DJ-1, and PINK1 have all been connected to familial Parkinson's disease. People who have a family history of the condition are more likely to inherit these mutations, increasing the threat of getting Parkinson's disease[15]. Conversely, sporadic Parkinson's disease, which often results from a confluence of genetic and environmental variables, affects people who have no family history of the disease. Age, exposure to certain toxins, and certain genetic variations that increase susceptibility to the disease have all been recognized as risk factors for sporadic Parkinson's disease, though its exact causes are still unknown[16]. Even though familial Parkinson's disease accounts for a relatively small percentage of all cases (roughly 5–10% of cases), it has helped us in better understanding the disease's primary mechanisms and the more widespread sporadic form. Overall, the absence or presence of a family history and the involvement of genetic factors distinguish familial from sporadic Parkinson's disease.

Identification of monogenic forms of Parkinson's disease-

Parkinson's disease, which is produced by mutations in a single gene, is indicated as having a monogenic form. Commonly, these genetic mutations are inherited either as autosomal dominant or autosomal recessive. It has been determined that several genes contribute to monogenic forms of Parkinson's disease. While most PD cases are considered sporadic or idiopathic, around 5 to 10% of cases have a monogenic inheritance pattern, meaning they are caused by mutations in a single gene[17].

Genomic Studies in Parkinson's Disease

Genome-wide association studies in Parkinson's Disease

GWAS has been a potent technique for determining the genetic components that influence PD risk and pathophysiology. The genetics of Parkinson's disease over time, from 1997 to 2018, is summarized in Fig 1.

GWAS has shed light on the genetics of PD by examining the whole genomes of significant cohorts of patients and controls. To identify genetic changes associated with the condition, GWAS compares the genomes of individuals with Parkinson's disease (PD) and healthy individuals (controls). To cover the complete genome, single-nucleotide polymorphisms (SNPs) are widely used in this research as markers. Two GWAS initiatives in PD are the International Parkinson's Disease Genomics Consortium (IPDGC) and the Genetic

Epidemiology of Parkinson's Disease Consortium (GEO-PD)[18]. GWAS has discovered several novel, previously unidentified PD risk loci. As an example, it was among the first and most well-identified hazards for PD was the SNCA locus, which codes for alpha-synuclein. Additionally, the discovery of the tau protein-related MAPT locus has shed light on the genetic causes of both sporadic and familial PD[19]. The molecular mechanisms involved in the development of PD have been clarified by GWAS results. Important risk factors for PD have been found to include genes like LRRK2 and GBA1. Among the most common genetic reasons for familial PD is an LRRK2 mutation, while GBA1 mutations raise the likelihood of developing

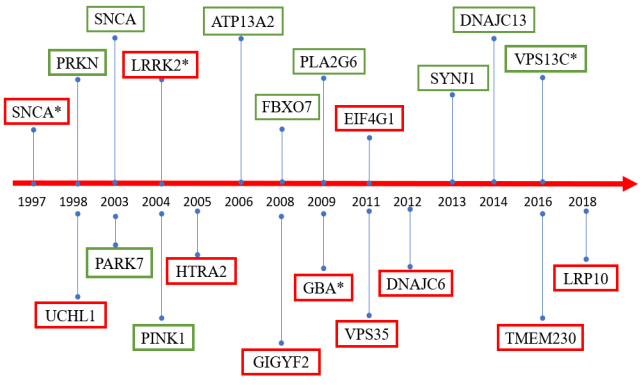

Fig 1: The genetics of Parkinson's disease over time. * Indicate genome-wide association studies. Red squares represent dominant genes. Green squares represent recessive genes.

PD, particularly in some ethnicities[20,21]. The polygenic aspect of PD has been highlighted by GWAS, with several genetic variations influencing disease risk. Furthermore, GWAS has demonstrated that PD susceptibility varies among populations, highlighting the significance of taking genetic variation into account in disease investigations[22,23]. GWAS has also revealed the significance of regulatory elements and non-coding genetic variations in the progression of Parkinson's condition. These variations may have an impact on protein function and gene expression, increasing the risk of developing certain diseases[24,25].

Polygenic Risk Scores in Parkinson's Disease-

Polygenic risk scores, which are built on the cumulative impact of numerous genetic variants across the genome, are a quantitative evaluation of a person's genetic propensity to a specific condition, such as Parkinson's disease. Data from genome-wide association studies (GWAS), had found several genetic loci linked to PD risk, are used to calculate PRS. These genetic variants are given weighted scores, which allow researchers to calculate a person's risk of getting PD. The capacity of PRS to determine disease risk before clinical symptoms appear is what makes them potentially useful in PD research[26].

Polygenic Risk Scores in Parkinson's Disease

- Prediction and early detection: In the early detection and prediction of PD, PRS shows significant promise. PRS has shown promise as a prognostic tool, with scores connected to PD risk [27], age at onset [27,28], and higher motor and cognitive decline [29]. The 90 risk loci discovered in the most recent PD meta-analysis are associated with a higher relative risk of acquiring PD, with individuals in the top 10% of PRS being around six times more likely to develop PD than those in the bottom 10% [30]. It has been shown that a composite risk score can be generated with a significant amount of sensitivity and specificity by including additional variables such as family history, age, sex, and hyposmia[31]
- Locating Populations at Risk: Using PRS in population-based studies enables the detection of those who are more likely to develop PD. For focused screening and preventive actions, such information is essential (Fig 2). In research by Noyce *et al.*, PRS was used to identify people at high risk for PD, which allowed for the development of customised interventions aimed at modifying environmental factors and lowering disease risk[29].

Obstacles and Limitations

Although PRS has a lot of potential, several obstacles and constraints need to be removed before it can be widely used in clinical settings.

A lack of thorough genetic information

It is challenging to achieve high predicted accuracy using PRS since most PD-associated genetic variants discovered by GWAS have rather small individual effects. Furthermore, the generalizability of PRS to other populations is constrained by the overwhelming focus of GWAS on people of European ancestry. For the PRS to perform better across different racial/ethnic groups, efforts to broaden the variety of GWAS cohorts are required[32].

Gene-Environment Interactions

Parkinson's disease is influenced by a variety of environmental exposures in addition to genetic variables. An inadequate risk assessment could result if gene-environment interactions are not sufficiently accounted for by PRS[33].

Ethical Matters

The application of PRS in therapeutic settings presents issues of privacy, informed consent, and potential genetic risk-based discrimination. To protect people's rights, healthcare professionals and researchers must ensure the ethical and open use of PRS[34].

Research Progress for Early Diagnosis and Disease Progression Prediction

Early diagnosis and precise disease progression prediction are crucial for optimal therapeutic approaches. Combining imaging, genetic, CSF, and blood-based biomarkers is necessary to accurately predict Parkinson's disease status and progress.

Imaging markers

Many studies have investigated possible biomarkers for PD early detection. Imaging methods like single-photon emission computed tomography (SPECT) and positron emission tomography (PET) can detect early dopaminergic dysfunction in the brain, which could aid in the early diagnosis of Parkinson's disease[35]. Positron emission

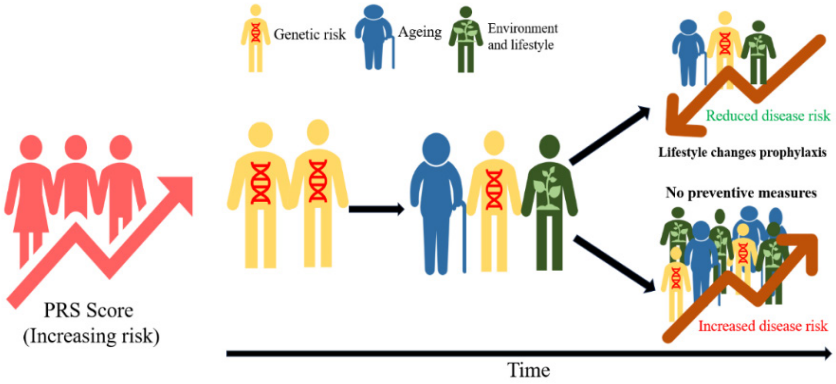

Fig 2: shows how polygenic risk scores, which are calculated using the average number of genetic variants, can be utilized to evaluate an own's propensity for complicated polygenic disorders like Parkinson's disease (PD) and help identify the population members who are most at risk. It may be suggested to those who are at risk to adjust their lifestyles or receive preventative care to lessen the possibility that they may contract a disease (right)

computed tomography (PET) or single photon emission computed tomography (SPECT), two types of molecular imaging technologies, use a specific tracer for localization and quantification to show the existence and course of the disease at a molecular level[36].

Dopaminergic dysfunction

Dopamine transporters (DAT) in the brain have been extensively visualised and quantified using PET and SPECT, providing important insights into the dopaminergic dysfunction characterised by PD[37].

Differential diagnosis

By examining the pattern of dopamine depletion in the basal ganglia, these imaging modalities can distinguish PD from other parkinsonian diseases, such as multiple system atrophy (MSA), essential tremor and progressive supranuclear palsy (PSP)[38].

Early Diagnosis

Presynaptic dopaminergic alterations can be detected by PET and SPECT even before motor symptoms appear, which is crucial to detect Parkinson's disease at an early stage[39].

Development of Biomarkers

Alpha-synuclein deposition, synaptic density, and markers of neuroinflammation have all been investigated as possible indicators of Parkinson's disease (PD) using PET and SPECT[40].

Cerebral Blood Flow and Glucose Metabolism

In addition to dopaminergic indicators, cerebral blood flow and glucose metabolism in PD have also been studied using PET, offering insight into additional pathophysiological features of the disease[41].

Tau pathology

Researchers may now examine the role of tau pathology in PD and its cognitive manifestations because of recent advancements in PET imaging that have made it possible to see clumps of the tau protein[42].

Genetic markers

Genetic markers have helped in the timely diagnosis and individualised therapy of PD patients as well as given vital insights into the underlying genetic basis of the disease. The main genetic indicators for Parkinson's disease are listed below in Table 1. These genetic markers have helped with early diagnosis and individualised therapy strategies while also shedding light on the underlying molecular pathways of Parkinson's disease.

Cerebrospinal fluid (CSF) biomarkers

Cerebrospinal fluid (CSF) biomarkers have shown promising outcomes in the recognition of Parkinson's disease (PD). CSF analysis can distinguish PD from other neurodegenerative diseases and provides insightful information on the pathological processes at play. Alpha-synuclein, beta-amyloid (Aβ42), total tau, phosphorylated tau, neurofilament light chain (NfL), DJ-1 and UCH-L1 are potential CSF biomarkers for Parkinson's disease (PD). Alpha-synuclein is involved in the pathogenesis of PD, forming Lewy bodies. Tau proteins play a role in microtubule stability and are associated with various neurodegenerative diseases. CSF total tau and phosphorylated tau levels have been studied in people with PD, with some studies reporting increased levels while others did not find significant changes[49–51]. Neurofilament light chain (NfL) is an indicator of axonal damage and neurodegeneration, with elevated levels in PD patients suggesting its potential to serve as an indicator for the extent and development of disease[52]. Lysosomal enzymes, such as beta-glucocerebrosidase, have been shown to be altered in PD patients, suggesting their potential role as biomarkers[53]. Synaptic proteins, such as SNAP-25 and neurogranin, have been researched as possible PD CSF biomarkers [54]. CSF biomarkers have shown promise in distinguishing Parkinson's disease (PD) from other neurodegenerative illnesses such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP), assisting in differential diagnosis[55,56].

Blood-based biomarkers

Blood-based biomarkers are listed in Table 2.

Genetic Target Identification

Many genetic risk factors connected to Parkinson's disease have been discovered recently through research. Genetic variants that increase an individual's risk of getting Parkinson's disease (PD) have been discovered using genome-wide association studies (GWAS). For instance, both sporadic and familial types of PD have been linked

Table 1: The main genetic indicators for Parkinson's disease

S.No.	*Genetic marker*	*Description*	*References*
1	SNCA Gene	The alpha-synuclein gene (SNCA) mutation is among the most renowned genetic hazards for Parkinson's disease. Abnormal alpha-synuclein protein aggregation in the brain is a hallmark of PD pathogenesis.	[43]
2	Gene LRRK2	The leucine-rich repeat kinase 2 (LRRK2) gene is mutated most frequently in familial Parkinson's disease. Due to its importance in both familial and idiopathic PD, LRRK2 mutations are also discovered in sporadic instances of Parkinson's disease.	[44]
3	Parkin Gene (PARK2)	Autosomal Recessive Juvenile Parkinsonism (AR-JP), an early-onset type of Parkinson's Disease (PD), is linked to mutations in the parkin gene (PARK2). According to Kitada *et al*. (1998), parkin is essential for ubiquitin-proteasome-mediated protein degradation and cellular homeostasis.	[45]
4	PINK1 Gene (PARK6)	PTEN-induced kinase 1 gene (PINK1) (PARK6) mutations are connected to autosomal recessive early-onset Parkinson's disease. Mitophagy regulation and mitochondrial quality control are both impacted by PINK1	[46]
5	DJ-1 Gene (PARK7)	Parkinson's disease with early onset caused by autosomal recessive mutations in the DJ-1 gene (PARK7). DJ-1 may have neuroprotective effects and is implicated in cellular oxidative stress response	[47]
6	GBA Gene	Mutations in the glucocerebrosidase gene (GBA), particularly in younger patients and a family history of the disorder, significantly increase the risk of developing Parkinson's disease [58].	[48]

to the lysosomal enzyme glucocerebrosidase encoded by the GBA gene. Alpha-synuclein aggregation and lysosomal dysfunction, two characteristics that characterize PD, can result from mutations in this gene[48].

Alpha-Synuclein as a Therapeutic Target

The brain protein alpha-synuclein is prevalent and an important protein in the cause of Parkinson's disease. Alpha-synuclein aggregation forms toxic fibrils, which is a factor in neuronal death. Therefore, it is the right therapeutic approach to lower alpha-synuclein levels or stop protein aggregation. Strategies investigated include small-molecule inhibitors to prevent protein aggregation and gene silencing using RNA interference (RNAi) or antisense oligonucleotides (ASOs)[67].

Targeting Mitochondrial Dysfunction

The pathogenesis of PD is closely connected with mitochondrial dysfunction. Dopaminergic neurons die because of increased oxidative stress and cellular energy deficiencies caused by impaired mitochondrial function. Finding substances that can improve mitochondrial activity and protect neurons against deterioration has been the goal of ongoing research. One such possible therapeutic target is the PGC-1 pathway, a chief regulator of mitochondrial biogenesis[68]. Clinical trials are finding mitochondrial dysfunction in Parkinson's disease patients. The Ketone Ester Elite Endurance Nutrition Drink trial aims to evaluate the tolerance, side effects, and effectiveness of oral ketone esters in Parkinson's patients. Other biochemical routes for mitochondrial dysfunction have shown encouraging outcomes. Functional and metabolomic biomarkers for mitochondrial dysfunction will begin accepting participants in February 2020, according to ClinicalTrials.gov (Table 3).

Neuroinflammation and Immunomodulatory Approaches

Recent studies imply that neuroinflammation is responsible for the development of Parkinson's disease (PD). Microglial activation and the production of pro-inflammatory cytokines worsen neuronal damage. Immunomodulatory treatments are being investigated to reduce neuroinflammation and protect neurons. Targeting the P2X7 receptor, which plays a role in microglial activation and cytokine production, is one such approach [69]. Clinical trials are currently testing various medications for Parkinson's disease (PD), with encouraging results. The UAB Neuroinflammation in PD trial used DPA-714-PET/MRI [NCT03457493] to evaluate brain microglia/macrophages concentration and distribution. Another [18F] NOS [NCT04062526] research investigates the potential of specialized PET/CT scans for PD diagnosis and therapy monitoring. Memantine, an NMDA receptor antagonist [NCT03918616], protects microglial cells' P2X7R, causing neuroinflammation and dopaminergic neurodegeneration. The study ended on February 20, 2017 (clinicaltrials.gov) (Table 3).

LRRK2 Kinase Inhibitors

Leucine-rich repeat kinase 2 (LRRK2) gene mutations are a common hereditary source of familial Parkinson's disease (PD). It has become more common to consider LRRK2 kinase activity as a potential treatment approach. To bring down LRRK2-mediated neurotoxicity and alpha-synuclein disease, a few small-molecule inhibitors have been discovered [70].

Challenges of Parkinson's Disease

Motor Symptoms and the Burden of Underdiagnosis

The patients' quality of life is greatly impacted by the four cardinal motor symptoms of Parkinson's disease (PD), which are stiffness,

Table 2: Blood-based biomarkers for the diagnosis of parkinson's disease

S. No.	*Blood-based biomarkers*	*Description*	*References*
1	Alpha-synuclein in peripheral blood	Lewy bodies, intracellular alpha-synuclein aggregates, are crucial in Parkinson's disease pathophysiology, and measuring alpha-synuclein levels in peripheral blood has been explored for Parkinson's disease diagnosis.	[57]
2	Oligomers of alpha-synuclein	Research indicates oligomeric alpha-synuclein species as potential blood-based biomarkers for Parkinson's disease, potentially indicating early pathogenic alterations before clinical symptoms.	[58]
3	Total tau and phosphorylated tau	Research suggests that abnormal tau protein metabolism in Parkinson's disease patients could serve as a potential blood-based biomarker, indicating a potential neurological condition.	[59]
4	Neurofilament light chain (nfl)	Neurofilament light chain (NfL), a protein released into the bloodstream when neurons are injured or die, has been identified as a marker of neurodegeneration and Parkinson's disease progression.	[60]
5	DJ-1	DJ-1 protein, involved in oxidative stress reaction, has been linked to Parkinson's disease, but its potential as a blood-based biomarker has been mixed.	[61,62]
6	MicroRNAs (miRNAs)	MicroRNAs are non-coding RNA molecules that regulate gene expression. It has been shown that patients with Parkinson's disease have changed miRNA profiles in their blood, and some of these miRNAs could be used as diagnostic biomarkers.	[63,64]
7	LRRK2	LRRK2 gene mutations are typically the cause for familial Parkinson's disease. LRRK2 protein and activity levels have been measured in PD patients' blood, implying that it could be used as a biomarker for LRRK2-related PD.	[65]
8	Urate	Urate is an endogenous antioxidant molecule, and lower levels indicates a growing risk of developing Parkinson's disease. Blood urate levels are explored as a potential biomarker for predicting the risk of developing Parkinson's disease (PD).	[66]

Table 3: Clinical trials data for targets of PD (clinicaltrials.gov)

Target	*Drugs/ Treatments in clinical trials*	*Status*	*Phase*	*Study start date*	*Estimated completion date*	*NCT no.*
Chaperone	Ambroxol hydrochloride	Not yet Recruiting	-	June 1, 2020	June 1, 2023	NCT04388969
	Ambroxol	Completed	Phase 2	December 2016	May 2018	NCT02941822
c-Abl	Nilotinib (c-Abl Inhibitor)	Completed	Phase 1	November 2, 2014	-	NCT02281474
	Nilotinib (c-Abl Inhibitor)	Completed	Phase 2	July 2, 2017	-	NCT03205488
	K0706 (c-Abl Inhibitor)	Recruiting	Phase 2	August 31, 2018	-	NCT03655236
GBA1	GBA (OMIM 606,463) gene	Recruiting	-	February 1, 2018	July 2020	NCT03811496
	GBA gene mutation	Recruiting	-	May 1, 2019	April 30, 2021	NCT04101968
	GZ/SAR402671	Active, Not Recruiting	Phase 2	December 15, 2016	February 2023	NCT02906020
	GBA gene mutation	Recruiting	-	July 1, 2017	June 30, 2022	NCT03234478
	Ambroxol	Completed	Phase 2	December 2016	May 2018	NCT02941822
Neuromelanin	Carvedilol	Enrolling by invitation	Phase 2	December 30, 2019	December 30, 2022	NCT04218968
	Diagnostic Test: 3 T MRI	Not yet Recruiting	-	July 1, 2018	July 1, 2021	NCT03572114
	Hydrogen	Recruiting	Phase 2	May 29, 2019	July 1, 2022	NCT03971617
Calcium	CX-8998 (Ca + + channel blocker)	Not yet Recruiting	Phase 2	December 2019	December 2020	NCT03436953
	Vitamin D3	Completed	Phase 2	May 2011	January 2015	NCT01119131
	Isradipine	Completed	Phase 3	November 2014	November 2018	NCT02168842
	Zonegran	Unknown	Phase 4	April 8, 2016	December 31, 2018	NCT03034538
Mitochondria dysfunction (MD)	Ketone Ester Elite Endurance Nutrition Drink	Recruiting	Not Applicable	September 5, 2019	January 5, 2021	NCT04477161
	Biochemical Pathway for MD	Enrolling by invitation	-	August 18, 2017	August 2020	NCT03421899
	Functional and Metabolomic Biomarkers of MD	Recruiting	-	February 24, 2020	November 2020	NCT04300608
UPS	HMS 90® vs. soy protein	Completed	Phase 4	April 2011	December 2012	NCT01662414
Neuroinflammation	DPA-714-PET/MRI	Recruiting	Phase 1/2	March 22, 2018	March 2022	NCT03457493
	[18F] NOS	Recruiting	Early Phase 1	August 14, 2019	August 2022	NCT04062526
	Memantine, Dopamine receptor-agonists	Completed	-	February 20, 2017	March 30, 2019	NCT03918616

tremor, bradykinesia, and postural instability. Tremors can make it difficult to carry out daily activities, including eating, dressing, and writing, which can increase a person's dependence on caregivers. Bradykinesia, characterised by sluggish movement, can exacerbate motor demands, restricting mobility and leading to falls [71].

Non-Motor Symptoms and the Burden of Underdiagnosis

Although frequently ignored, non-motor symptoms of PD can be hampering. These signs include autonomic dysfunction, cognitive decline, anxiety, and sleep difficulties. For example, up to 40% of PD patients experience anxiety or depression, which lowers their overall wellbeing [72]. Orthostatic hypotension, urinary issues, and constipation are just a few symptoms of autonomic dysfunction that can make the condition more challenging[73].

Medication problems and variable motor function

Levodopa is the drug of choice for treating Parkinson's disease (PD). Long-term use, on the other hand, is typically accompanied by motor abnormalities such as dyskinesias and wearing-off stages. Because these shifts might unpredictably alter symptom severity, it can be challenging for patients to keep up with daily tasks and participate in social interactions [74].

Adverse effects of Medicines

Anti-Parkinsonian drugs can ease symptoms, but may also cause hallucinations, psychosis, and impulse control issues. To preserve treatment efficacy without worsening mental symptoms, these consequences must be carefully managed because they can be upsetting for both patients and caregivers [75].

Dementia and a decline in cognition

Up to 80% of PD patients have some degree of cognitive impairment, which is a typical symptom of the disease. About 30% of PD patients experience dementia over time, which increases care requirements and decreases functional independence[76].

Lack of Early Diagnosis Biomarkers

Because there are currently no solid biomarkers for PD, early diagnosis is still tough. A significant fraction of dopaminergic neurons may have already worsened by the time motor symptoms appear. Although their development and validation are still being studied, biomarkers would allow for early intervention and may decrease the progression of disease [77].

PD heterogeneity

Parkinson's disease exhibits a wide range of clinical signs and symptoms as well as varying rates of disease development. Accurately predicting the course of the disease and customizing therapy to each patient are made difficult by this variability[78].

Limited Disease-Modifying Treatments

No disease-modifying treatments for Parkinson's disease (PD) have been established to date, despite multiple clinical studies. While symptomatic treatments offer relief, they have no effect on the neurodegenerative process at its core. Drugs that target the pathogenic pathways causing PD are still being developed and are the subject of current research[79].

High Financial Burden

There is a significant financial burden that includes direct medical expenses, lost productivity, and caregivers' stress. According to studies, the cost of PD to society exceeds $52 billion in just the United States alone each year [80].

Resources and Access to Specialised Care

Geographically and socioeconomically, different people have access to different resources and specialised care for managing PD. Access to specialised therapies, support services, and specialist neurologists may be challenging for low-income and rural communities, further extending health inequities [81].

Stigma and Social Isolation

As tremors and dyskinesias may be mistaken for indicators of weakness or mental disability, Parkinson's disease can be stigmatising. Social exclusion, fewer social interactions, and detrimental effects on mental health might result from this stigma[82].

Effects on Caretakers

Caregiving can be physically and emotionally taxing, but it is an essential part of helping PD sufferers. Increased stress, anxiety, and depression are common among carers, demanding assistance and respite care to preserve their wellbeing[83].

Future Directions

Precision Medicine and Biomarkers

Precision medicine's potential to provide individualised treatment plans for Parkinson's disease patients is very promising. The main goals of research are to identify biomarkers that could forecast disease development, evaluate therapy responses, and help in early diagnosis. PD has been linked to several genetic and molecular markers, including GBA and LRRK2 gene alterations. It may be possible to create precise diagnostic tools by combining these indicators with cutting-edge imaging methods like functional MRI (fMRI) and positron emission tomography (PET)[84].

Therapeutics that alter disease

Most Parkinson's disease medications currently on the market are symptomatic, with the goal of reducing motor symptoms and enhancing quality of life. However, a crucial goal is the creation of disease-modifying treatments that can impede or stop the development of PD. Potential neuroprotective substances such as growth factors, antioxidants, and anti-inflammatory medications are now being researched [85]. Additionally, cutting-edge strategies are being researched to replace damaged neurons and restore function in the afflicted brain regions, such as gene therapies and stem cell-based therapies[86].

Microbiome and the Gut-Brain Axis

The gut-brain axis, a complex relationship between the gut and the brain, has come to light in recent studies. The pathophysiology of Parkinson's disease has been connected to alterations in the gut microbiota, so gut bacteria may contribute to neuroinflammation and alpha-synuclein aggregation [87]. Prebiotics, probiotics, or faecal microbiota transplantation could target the gut microbiome with therapeutic potential and bring up novel PD therapy options [88].

Symptoms Other Than Motor and Quality of Life

Parkinson's disease is not just a movement condition; it also exhibits several non-motor symptoms that have a significant negative impact on patients' quality of life. Depression, anxiety, sleep problems, and cognitive deficits are some of these symptoms. Future studies should concentrate on figuring out the underlying causes of these non-motor symptoms and creating therapies that particularly target them. As prospective treatments for non-motor symptoms in PD patients, cognitive training, physical activity, and neuromodulation approaches are being investigated[89].

Artificial intelligence and large-scale data

The use of analysis of large amounts of data and artificial intelligence (AI) has the potential to completely change Parkinson's disease research. AI algorithms can analyse vast amounts of data from numerous sources, such as health records, imaging studies, and genetic profiles, to uncover patterns and links that human analysis could overlook. Machine learning models have demonstrated potential in early detection, disease development, and treatment outcomes[90]. To fully utilise AI in PD research, collaboration and data sharing between researchers and institutions will be essential.

Remote Monitoring and Wearable Technology

The use of wearable technology to track various health metrics has increased, such as smartwatches and fitness trackers. These technologies provide the possibility of continuous, real-time monitoring of motor symptoms and other physiological changes in the context of Parkinson's disease. Wearable device data can be used

to gain an important understanding of illness development, treatment response, and changes in symptom severity [91].

Neuroprotection and Environmental Factors

The onset and course of Parkinson's disease may be significantly influenced by environmental factors in addition to hereditary ones, according to studies. The risk of PD has been linked to pesticides, heavy metals, and other hazardous substances [92].

CONCLUSION

The review highlights the genetic architecture, genomic studies for determining the genetic components that influence PD risk and pathophysiology, implications for risk assessment, diagnosis using various novel biomarkers, therapeutic advances, research gaps, challenges such as heterogenicity, underdiagnosis, adverse effects of medicines and future directions. Several studies have identified specific genetic mutations that increase susceptibility to PD. For example, both familial and sporadic forms of PD are accompanied by mutations in the LRRK2 gene. The importance of genomics to identify key genes associated with disease progression has been emphasized. The importance of recognizing the pathophysiology of Parkinson's disease is also included in this review. By searching the genomes of PD patients, researchers were able to identify genetic variants associated with the condition, shedding light on the root cause of the disease. The study highlights how genetics has the potential to discover and develop new therapeutic targets and appropriate treatment plans for improving the lives of people with Parkinson's disease (PD). In general, the review provides insightful information on the use of genetics in Parkinson's disease research and how it can improve patient outcomes.

REFERENCES

1. Parkinson's Disease 2023. https://www.who.int/news-room/fact-sheets/detail/parkinson-disease (accessed December 5, 2023).
2. Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, Volkmann J, *et al*. Parkinson's disease. Nat Rev Dis Primers 2017;3:1–21. https://doi.org/10.1038/nrdp.2017.13.
3. Pankratz ND, Dumitriu A, Hetrick KN, Sun M, Latourelle J, Wilk JB, *et al*. Copy Number Variation in Familial Parkinson Disease. PLoS One 2011;6.
4. Nalls MA, Pankratz N, Lill CM, Do CB, Hernandez DG, Saad M, *et al*. Large-scale meta-analysis of genome-wide association data identifies six new risk loci for Parkinson's disease. Nat Genet 2014;46:989–93.
5. Tan M, Malek N, Lawton M, Hubbard L, Pittman A, Joseph T, *et al*. Genetic analysis of Mendelian mutations in a large UK population-based Parkinson's disease study. Brain 2019;142. https://doi.org/10.1093/brain/awz191.
6. Polymeropoulos MH, Lavedan C, Leroy E, Ide SE, Dehejia A, Dutra A, *et al*. Mutation in the α-synuclein gene identified in families with Parkinson's disease. Science (1979) 1997;276:2045–7.
7. Spillantini MG, Crowther RA, Jakes R, Hasegawa M, Goedert M. α-Synuclein in filamentous inclusions of Lewy bodies from Parkinson's disease and dementia with Lewy bodies. Proceedings of the National Academy of Sciences 1998;95:6469–73.
8. Mazzulli JR, Xu Y-H, Sun Y, Knight AL, McLean PJ, Caldwell GA, *et al*. Gaucher disease glucocerebrosidase and α-synuclein form a bidirectional pathogenic loop in synucleinopathies. Cell 2011;146:37–52.
9. Fernandes HJR, Hartfield EM, Christian HC, Emmanoulidou E, Zheng Y, Booth H, *et al*. ER Stress and Autophagic Perturbations Lead to Elevated Extracellular. Stem Cell Reports 2016;6:342–56. https://doi.org/10.1016/j.stemcr.2016.01.013.
10. Paisán-Ruíz C, Jain S, Evans EW, Gilks WP, Simón J, van der Brug M, *et al*. Cloning of the Gene Containing Mutations that Cause PARK8-Linked Parkinson's Disease. Neuron 2004;44:595–600. https://doi.org/https://doi.org/10.1016/j.neuron.2004.10.023.
11. Zimprich A, Biskup S, Leitner P, Lichtner P, Farrer MJ, Lincoln SJ, *et al*. Mutations in LRRK2 Cause Autosomal-Dominant Parkinsonism with Pleomorphic Pathology. Neuron 2004;44:601–7.
12. Simon-Sanchez J, Schulte C, Bras JM, Sharma M, Gibbs JR, Berg D, *et al*. Genome-wide association study reveals genetic risk underlying Parkinson's disease. Nat Genet 2009;41:1308–12.
13. Tanner CM, Kamel F, Ross GW, Hoppin JA, Goldman SM, Korell M, *et al*. Rotenone, paraquat, and Parkinson's disease. Environ Health Perspect 2011;119:866–72.
14. Wang A, Costello S, Cockburn M, Zhang X, Bronstein J, Ritz B. Parkinson's disease risk from ambient exposure to pesticides. Eur J Epidemiol 2011;26:547–55.
15. Lesage S, Brice A. Parkinson's disease: from monogenic forms to genetic susceptibility factors. Hum Mol Genet 2009;18:R48–59.
16. Wirdefeldt K, Adami H-O, Cole P, Trichopoulos D, Mandel J. Epidemiology and etiology of Parkinson's disease: a review of the evidence. Eur J Epidemiol 2011;26:1–58.
17. Jia F, Fellner A, Kumar KR. Monogenic Parkinson's disease: genotype, phenotype, pathophysiology, and genetic testing. Genes (Basel) 2022;13:471.
18. Nalls MA, Pankratz N, Lill CM, Do CB, Hernandez DG, Saad M, *et al*. Large-scale meta-analysis of genome-wide association data identifies six new risk loci for Parkinson's disease. Nat Genet 2014;46:989–93.
19. Simon-Sanchez J, Schulte C, Bras JM, Sharma M, Gibbs JR, Berg D, *et al*. Genome-wide association study reveals genetic risk underlying Parkinson's disease. Nat Genet 2009;41:1308–12.
20. Nalls MA, Blauwendraat C, Vallerga CL, Heilbron K, Bandres-Ciga S, Chang D, *et al*. Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. Lancet Neurol 2019;18:1091–102.
21. Sidransky E, Lopez G. The link between the GBA gene and parkinsonism. Lancet Neurol 2012;11:986–98.
22. Chang D, Nalls MA, Hallgrímsdóttir IB, Hunkapiller J, Van Der Brug M, Cai F, *et al*. A meta-analysis of genome-wide association studies identifies 17 new Parkinson's disease risk loci. Nat Genet 2017;49:1511–6.
23. Foo JN, Chew EGY, Chung SJ, Peng R, Blauwendraat C, Nalls MA, *et al*. Identification of risk loci for Parkinson disease in Asians and comparison of risk between Asians and Europeans: a genome-wide association study. JAMA Neurol 2020;77:746–54.
24. Soldner F, Stelzer Y, Shivalila CS, Abraham BJ, Latourelle JC, Barrasa MI, *et al*. Parkinson-associated risk variant in distal enhancer of α-synuclein modulates target gene expression. Nature 2016;533:95–9.
25. Nalls MA, Blauwendraat C, Vallerga CL, Heilbron K, Bandres-Ciga S, Chang D, *et al*. Expanding Parkinson's disease genetics: novel risk loci, genomic context, causal insights and heritable risk. BioRxiv 2019:388165.
26. Lewis CM, Vassos E. Polygenic risk scores: from research tools to clinical instruments. Genome Med 2020;12:44. https://doi.org/10.1186/s13073-020-00742-5.
27. Ibanez L, Dube U, Saef B, Budde J, Black K, Medvedeva A, *et al*. Parkinson disease polygenic risk score is associated with Parkinson disease status and age at onset but not with alpha-synuclein cerebrospinal fluid levels. BMC Neurol 2017;17:1–9.

28. Escott-Price V, Consortium IPDG, Nalls MA, Morris HR, Lubbe S, Brice A, *et al*. Polygenic risk of P arkinson disease is correlated with disease age at onset. Ann Neurol 2015;77:582–91.
29. Paul KC, Schulz J, Bronstein JM, Lill CM, Ritz BR. Association of polygenic risk score with cognitive decline and motor progression in Parkinson disease. JAMA Neurol 2018;75:360–6.
30. Nalls MA, Blauwendraat C, Vallerga CL, Heilbron K, Bandres-Ciga S, Chang D, *et al*. Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. Lancet Neurol 2019;18:1091–102.
31. Nalls MA, McLean CY, Rick J, Eberly S, Hutten SJ, Gwinn K, *et al*. Diagnosis of Parkinson's disease on the basis of clinical and genetic classification: a population-based modelling study. Lancet Neurol 2015;14:1002–9.
32. Pasaniuc B, Price AL. Dissecting the genetics of complex traits using summary association statistics. Nat Rev Genet 2017;18:117–27.
33. Ball N, Teo W-P, Chandra S, Chapman J. Parkinson's disease and the environment. Front Neurol 2019:218.
34. Lewis ACF, Green RC. Polygenic risk scores in the clinic: new perspectives needed on familiar ethical issues. Genome Med 2021;13:14. https://doi.org/10.1186/s13073-021-00829-7.
35. Tang CC, Poston KL, Eckert T, Feigin A, Frucht S, Gudesblatt M, *et al*. Differential diagnosis of parkinsonism: a metabolic imaging study using pattern analysis. Lancet Neurol 2010;9:149–58.
36. Yao N-T, Zheng Q, Xu Z-Q, Yin J-H, Lu L-G, Zuo Q, *et al*. Positron emission computed tomography/single photon emission computed tomography in Parkinson disease. Chin Med J (Engl) 2020;133:1448–55.
37. Catafau AM. Brain SPECT in clinical practice. Part I: perfusion. Journal of Nuclear Medicine 2001;42:259–71.
38. Djang DSW, Janssen MJR, Bohnen N, Booij J, Henderson TA, Herholz K, *et al*. SNM practice guideline for dopamine transporter imaging with 123I-ioflupane SPECT 1.0. Journal of Nuclear Medicine 2012;53:154–63.
39. Guttman M, Burkholder J, Kish SJ, Hussey D, Wilson A, DaSilva J, *et al*. [11C] RTI-32 PET studies of the dopamine transporter in early dopa-naive Parkinson's disease: implications for the symptomatic threshold. Neurology 1997;48:1578–83.
40. Matuskey D, Tinaz S, Wilcox KC, Naganawa M, Toyonaga T, Dias M, *et al*. Synaptic changes in Parkinson disease assessed with in vivo imaging. Ann Neurol 2020;87:329–38.
41. Eidelberg D. Metabolic brain networks in neurodegenerative disorders: a functional imaging approach. Trends Neurosci 2009;32:548–57.
42. Smith R, Schain M, Nilsson C, Strandberg O, Olsson T, Hägerström D, *et al*. I ncreased basal ganglia binding of 18 F-AV-1451 in patients with progressive supranuclear palsy. Movement Disorders 2017;32:108–14.
43. Spillantini MG, Schmidt ML, Lee VM-Y, Trojanowski JQ, Jakes R, Goedert M. α-Synuclein in Lewy bodies. Nature 1997;388:839–40.
44. Paisán-Ruíz C, Jain S, Evans EW, Gilks WP, Simón J, Van Der Brug M, *et al*. Cloning of the gene containing mutations that cause PARK8-linked Parkinson's disease. Neuron 2004;44:595–600.
45. Kitada T, Asakawa S, Hattori N, Matsumine H, Yamamura Y, Minoshima S, *et al*. Mutations in the parkin gene cause autosomal recessive juvenile parkinsonism. Nature 1998;392:605–8.
46. Valente EM, Abou-Sleiman PM, Caputo V, Muqit MMK, Harvey K, Gispert S, *et al*. Hereditary early-onset Parkinson's disease caused by mutations in PINK1. Science (1979) 2004;304:1158–60.
47. Bonifati V, Rizzu P, Van Baren MJ, Schaap O, Breedveld GJ, Krieger E, *et al*. Mutations in the DJ-1 gene associated with autosomal recessive early-onset parkinsonism. Science (1979) 2003;299:256–9.
48. Sidransky E, Nalls MA, Aasly JO, Aharon-Peretz J, Annesi G, Barbosa ER, *et al*. Multicenter analysis of glucocerebrosidase mutations in Parkinson's disease. New England Journal of Medicine 2009;361:1651–61.
49. Mollenhauer B, Trautmann E, Taylor P, Manninger P, Sixel-Döring F, Ebentheuer J, *et al*. Total CSF α-synuclein is lower in de novo Parkinson patients than in healthy subjects. Neurosci Lett 2013;532:44–8.
50. Parnetti L, Castrioto A, Chiasserini D, Persichetti E, Tambasco N, El-Agnaf O, *et al*. Cerebrospinal fluid biomarkers in Parkinson disease. Nat Rev Neurol 2013;9:131–40.
51. Alves G, Pedersen KF, Bloem BR, Blennow K, Zetterberg H, Borm GF, *et al*. Cerebrospinal fluid amyloid-β and phenotypic heterogeneity in de novo Parkinson's disease. J Neurol Neurosurg Psychiatry 2013;84:537–43.
52. Hall S, Surova Y, Öhrfelt A, Study SB, Blennow K, Zetterberg H, *et al*. L ongitudinal M easurements of C erebrospinal F luid B iomarkers in P arkinson's D isease. Movement Disorders 2016;31:898–905.
53. Alcalay RN, Levy OA, Waters CH, Fahn S, Ford B, Kuo S-H, *et al*. Glucocerebrosidase activity in Parkinson's disease with and without GBA mutations. Brain 2015;138:2648–58.
54. Kester MI, Teunissen CE, Crimmins DL, Herries EM, Ladenson JH, Scheltens P, *et al*. Neurogranin as a cerebrospinal fluid biomarker for synaptic loss in symptomatic Alzheimer disease. JAMA Neurol 2015;72:1275–80.
55. Bäckström DC, Domellöf ME, Linder J, Olsson B, Öhrfelt A, Trupp M, *et al*. Cerebrospinal fluid patterns and the risk of future dementia in early, incident Parkinson disease. JAMA Neurol 2015;72:1175–82.
56. Skillbäck T, Farahmand BY, Rosen C, Mattsson N, Nägga K, Kilander L, *et al*. Cerebrospinal fluid tau and amyloid-β1-42 in patients with dementia. Brain 2015;138:2716–31.
57. Donadio V, Incensi A, Rizzo G, Capellari S, Pantieri R, Maserati MS, *et al*. A new potential biomarker for dementia with Lewy bodies: skin nerve α-synuclein deposits. Neurology 2017;89:318–26.
58. Kang J-H, Mollenhauer B, Coffey CS, Toledo JB, Weintraub D, Galasko DR, *et al*. CSF biomarkers associated with disease heterogeneity in early Parkinson's disease: the Parkinson's Progression Markers Initiative study. Acta Neuropathol 2016;131:935–49.
59. Shi M, Zabetian CP, Hancock AM, Ginghina C, Hong Z, Yearout D, *et al*. Significance and confounders of peripheral DJ-1 and alpha-synuclein in Parkinson's disease. Neurosci Lett 2010;480:78–82.
60. Gao L, Tang H, Nie K, Wang L, Zhao J, Gan R, *et al*. Cerebrospinal fluid alpha-synuclein as a biomarker for Parkinson's disease diagnosis: a systematic review and meta-analysis. International Journal of Neuroscience 2015;125:645–54.
61. Waragai M, Wei J, Fujita M, Nakai M, Ho GJ, Masliah E, *et al*. Increased level of DJ-1 in the cerebrospinal fluids of sporadic Parkinson's disease. Biochem Biophys Res Commun 2006;345:967–72.
62. Reesink FE, Lemstra AW, van Dijk KD, Berendse HW, van de Berg WDJ, Klein M, *et al*. CSF α-synuclein does not discriminate dementia with Lewy bodies from Alzheimer's disease. Journal of Alzheimer's Disease 2010;22:87–95.
63. Cardo LF, Coto E, Ribacoba R, Menéndez M, Moris G, Suárez E, *et al*. MiRNA profile in the substantia nigra of Parkinson's disease and healthy subjects. Journal of Molecular Neuroscience 2014;54:830–6.
64. Khoo SK, Petillo D, Kang UJ, Resau JH, Berryhill B, Linder J, *et al*. Plasma-based circulating MicroRNA biomarkers for Parkinson's disease. J Parkinsons Dis 2012;2:321–31.
65. Nash Y, Schmukler E, Trudler D, Pinkas-Kramarski R, Frenkel D. DJ-1 deficiency impairs autophagy and reduces alpha-synuclein phagocytosis by microglia. J Neurochem 2017;143:584–94.

66. Ascherio A, LeWitt PA, Xu K, Eberly S, Watts A, Matson WR, *et al*. Urate as a predictor of the rate of clinical decline in Parkinson disease. Arch Neurol 2009;66:1460–8.
67. Khurana V, Lindquist S. Modelling neurodegeneration in Saccharomyces cerevisiae: why cook with baker's yeast? Nat Rev Neurosci 2010;11:436–49.
68. Zheng B, Liao Z, Locascio JJ, Lesniak KA, Roderick SS, Watt ML, *et al*. PGC-1 α, a potential therapeutic target for early intervention in Parkinson's disease. Sci Transl Med 2010;2:52ra73-52ra73.
69. Amoroso F, Capece M, Rotondo A, Cangelosi D, Ferracin M, Franceschini A, *et al*. The P2X7 receptor is a key modulator of the PI3K/GSK3β/VEGF signaling network: evidence in experimental neuroblastoma. Oncogene 2015;34:5240–51.
70. Liu Z, Bryant N, Kumaran R, Beilina A, Abeliovich A, Cookson MR, *et al*. LRRK2 phosphorylates membrane-bound Rabs and is activated by GTP-bound Rab7L1 to promote recruitment to the trans-Golgi network. Hum Mol Genet 2018;27:385–95.
71. Hirsch L, Jette N, Frolkis A, Steeves T, Pringsheim T. The incidence of Parkinson's disease: a systematic review and meta-analysis. Neuroepidemiology 2016;46:292–300.
72. Barone P, Antonini A, Colosimo C, Marconi R, Morgante L, Avarello TP, *et al*. The PRIAMO study: a multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. Mov Disord 2009;24:1641–9.
73. Schrag A, Barone P, Brown RG, Leentjens AFG, McDonald WM, Starkstein S, *et al*. Depression rating scales in Parkinson's disease: critique and recommendations. Movement Disorders 2007;22:1077–92.
74. Stocchi F, Rascol O, Kieburtz K, Poewe W, Jankovic J, Tolosa E, *et al*. Initiating levodopa/carbidopa therapy with and without entacapone in early Parkinson disease: the STRIDE-PD study. Ann Neurol 2010;68:18–27.
75. Weintraub D, David AS, Evans AH, Grant JE, Stacy M. Clinical spectrum of impulse control disorders in Parkinson's disease. Movement Disorders 2015;30:121–7.
76. Aarsland D, Andersen K, Larsen JP, Lolk A. Prevalence and characteristics of dementia in Parkinson disease: an 8-year prospective study. Arch Neurol 2003;60:387–92.
77. Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, *et al*. MDS clinical diagnostic criteria for Parkinson's disease. Movement Disorders 2015;30:1591–601.
78. Lang AE, Espay AJ. Disease modification in Parkinson's disease: current approaches, challenges, and future considerations. Movement Disorders 2018;33:660–77.
79. Group PDMC. Long-term effectiveness of dopamine agonists and monoamine oxidase B inhibitors compared with levodopa as initial treatment for Parkinson's disease (PD MED): a large, open-label, pragmatic randomised trial. The Lancet 2014;384:1196–205.
80. Kowal SL, Dall TM, Chakrabarti R, Storm M V, Jain A. The current and projected economic burden of Parkinson's disease in the United States. Movement Disorders 2013;28:311–8.
81. Willis AW, Schootman M, Kung N, Wang X-Y, Perlmutter JS, Racette BA. Disparities in deep brain stimulation surgery among insured elders with Parkinson disease. Neurology 2014;82:163–71.
82. Schrag A, Jahanshahi M, Quinn N. How does Parkinson's disease affect quality of life? A comparison with quality of life in the general population. Mov Disord 2000;15:1112–8.
83. Gallagher D, Rose J, Rivera P, Lovett S, Thompson LW. Prevalence of depression in family caregivers. Gerontologist 1989;29:449–56.
84. Gan-Or Z, Amshalom I, Kilarski LL, Bar-Shira A, Gana-Weisz M, Mirelman A, *et al*. Differential effects of severe vs mild GBA mutations on Parkinson disease. Neurology 2015;84:880–7.
85. Cheon S-M, Chan L, Chan DKY, Kim JW. Genetics of Parkinson's disease-a clinical perspective. J Mov Disord 2012;5:33.
86. Grealish S, Diguet E, Kirkeby A, Mattsson B, Heuer A, Bramoulle Y, *et al*. Human ESC-derived dopamine neurons show similar preclinical efficacy and potency to fetal neurons when grafted in a rat model of Parkinson's disease. Cell Stem Cell 2014;15:653–65.
87. Sampson TR, Debelius JW, Thron T, Janssen S, Shastri GG, Ilhan ZE, *et al*. Gut microbiota regulate motor deficits and neuroinflammation in a model of Parkinson's disease. Cell 2016;167:1469–80.
88. Keshavarzian A, Green SJ, Engen PA, Voigt RM, Naqib A, Forsyth CB, *et al*. Colonic bacterial composition in Parkinson's disease. Movement Disorders 2015;30:1351–60.
89. Thobois S, Lhommée E, Klinger H, Ardouin C, Schmitt E, Bichon A, *et al*. Parkinsonian apathy responds to dopaminergic stimulation of D2/D3 receptors with piribedil. Brain 2013;136:1568–77.
90. Govindu A, Palwe S. Early detection of Parkinson's disease using machine learning. Procedia Comput Sci 2023;218:249–61. https://doi.org/https://doi.org/10.1016/j.procs.2023.01.007.
91. Espay AJ, Bonato P, Nahab FB, Maetzler W, Dean JM, Klucken J, *et al*. Technology in Parkinson's disease: challenges and opportunities. Movement Disorders 2016;31:1272–82.
92. Cannon JR, Greenamyre JT. The role of environmental exposures in neurodegeneration and neurodegenerative diseases. Toxicological Sciences 2011;124:225–50.

HOW TO CITE THIS ARTICLE: Chavan M, Ranade A, Kajbaje R, Pusegaonkar R, Bhosale S, Deshmukh M. Genomic Insights in Parkinson's Disease: A Reviews. *J Adv Sci Res*. 2026;17(3): 36-45 **DOI:** 10.55218/JASR.2026170306