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Next-Generation Insights into Parkinson's Disease: A Comprehensive Review with Diagnosis, Pathogenesis and Therapeutic Frontiers

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ABSTRACT

Parkinson disease (PD) is a progressive neuro degenerative disorder of the dopaminergic neurons mainly in the substantia nigra, which causes the lack of motor dysfunction and various non-motor symptoms. Here, the review not only uncovers an essential review of the pathogenesis of PD, but complex pathogenesis includes an α-synuclein cluster, mitochondrial and lysosomal abnormalities, neuroinflammatory response, and gut-brain axis. It also talks about the issue of making a diagnosis and that clinical manifestations are heterogeneous. The standard treatment is symptomatic, and levodopa treatment methods are the core, although they have long-term side effects. New treatments, such as pilot gene therapy, immunotherapy and mitochondrial-targeted agents, provide hope in changing the disease. Individualized care and diagnosis is rechanging with advances in precision medicine, neuroimaging, and biomarkers. The issue of physical exercise, multidisciplinary applications, and inclusions of digital health tools were mentioned as crucial elements of PD management. Research with more and more innovation is essential to coming up with therapies that changing the course of the disease and enhancing quality of life of PD patients.

Keywords: *Parkinson's disease, neurodegeneration, α-synuclein, precision medicine, disease-modifying therapies*

1. INTRODUCTION

Parkinson disease (PD) refers to a chronic neurodegenerative disease; it was initially reported in 1817 by James Parkinson as shaking palsy. It has since emerged to be the second most common neurodegenerative disease in the world with a prevence rate of about 1 percent of people aged above 60. With the increasing aging of the global population, cases of PD will develop to unimaginable levels and this will overwhelm the healthcare system and indeed the society. It is a condition that is defined as the progressive degeneration of dopaminergic neurons in the substantia nigra resulting in deficiency of dopamine, that results in motor effects, which include, resting tremor, bradykinesia, rigidity, and postural instability. Besides these motor movements, it is further realized that PD is a multi-system disorder with non-motor symptoms composed of cognitive decline, sleep complaints, depression, autonomic disturbances and sensory impairment that may precede motor symptoms and have a significant influence on the quality of life and caregiver burden of patients.

Recent developments in fields of neuroimaging, genetics and molecular biology have given more insights towards the pathogenesis of PD. Mutation of the genes SNCA, LRRK2 and GBA have been seen as an environmental factor as well as exposures to pesticides and heavy metals have been determined to contribute to both inherited and sporadic forms of the disease. There is an improved comprehension of mechanisms involved, especially the protein aggregation, mitochondrial aberration, neuroinflammation, and the gut-brain axis. The increased awareness of the heterogeneity of PD has led to attempts to classify the disease on various subtypes depending on clinical presentation, genetics and biomarker profiles. The structural division plays a very important role in breeding more specific and effective cures. Proper diagnosis, disease-modifying therapies, and proper management of the symptoms is crucial in order to promote patient outcome early. This review will give a detailed description of PD, its diagnosis difficulty,

pathophysiology, existing treatment options and potential study areas which can lead to further treatment [1-5].

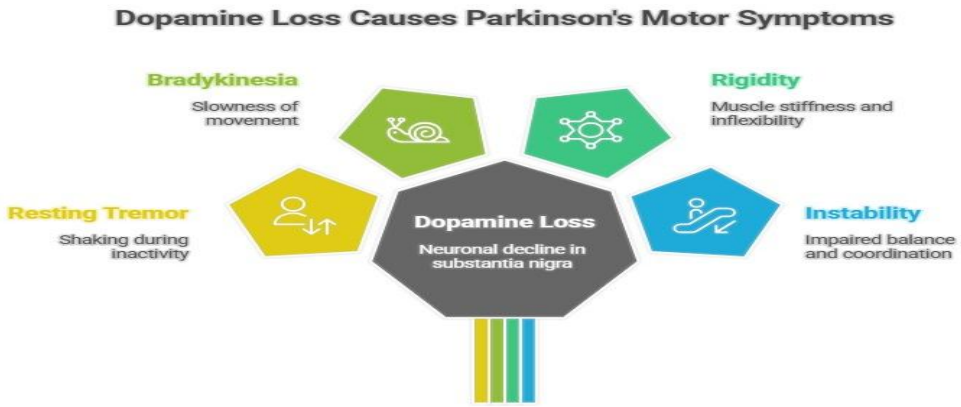

Figure 1: Parkinson's Disease and Symptoms

2. Clinical Diagnosis

P The major clinical feature of Parkinson disease (PD) is based on the diagnosis which is mainly achieved by the evaluation of the broad profile of motor symptoms such as bradykinesia, resting tremor, muscle rigidity, and postural instability. Due to the presence of at least one other symptom in combination with bradykinesia, which is regarded the most reliable diagnostic indicator, this is estimated to be an accurate diagnostic measure. But at the initial stages of PD these symptoms are very mild or often even symmetrical, and may be confused with other neurodegenerative disorders, thus early and clinical detection of these is cumbersome [6-8].

One of the challenges to the diagnosis of PD is the high rate of misdiagnosis especially at an early phase. Research studies have revealed that as much as 20-30 percent of all cases originally diagnosed as PD turned out to be other conditions such as multiple system atrophy (MSA), progressive supranuclear palsy (PSP) or essential tremor. This kind of misdiagnosis may result in unnecessary therapy and ineffective care of the patient, so more accurate diagnosis of diseases, as well as increased training of clinicians, should be promoted [9,10]. Furthermore, misdiagnosis might be observed in cases associated with the variable manifestation of symptoms i.e., the emergence of more tremor and fewer rigidity in some patients, and slowness in movement and postural problems with little tremor in others although the difference is understood to be trivial to even the most experienced clinicians. This points to the need of comprehensive evaluation tools and continued symptom observation. They have come up with standardized clinical definitions, like the UK Parkinson Pathology Spaces Brain Bank Criteria or Movement Disorder Society (MDS) Clinical Diagnostic Criteria to help make the diagnosis yet, diagnosis based on such criteria still has reliance on interpretation skills of the clinician and therefore, is contingent on expertise and experience [11-13].

Table 2: Parkinson's Disease Diagnosis Process

3. Pathogenesis and Underlying Mechanisms

α-Synuclein Aggregation

Neuronal protein alpha-synuclein misfolding as well as formation of intracellular aggregates called Lewy bodies and Lewy neurites are important pathological hallmarks of Parkinsonis disease (PD). They are mainly situated in the substantia nigra cells, among other brain areas and interfere with the homeostasis of the cell and induce neurodegeneration, which frequently ignites apoptosis. The pathological process that occurs during aggregation of alpha-synuclein is thought to be a prion like process, such that the misfolded protein exists between cells in a cell to cell spread that propagates the pathology. This has been confirmed by in vitro models and observations when transplanted fetal neurons fashioned the same pathology (Lewy bodies) several years onwards in PD patients. The accelerators of aggregation can include oxidative stress, failure of protein turnover, malfunctioning of the mitochondria, mutation of the SNCA gene with subsequent formation of toxic conditions, which cause impairment of neurons and loss of neurons.

Not only does alpha-synuclein exist in the brain, but also in the enteric nervous system, skin and salivary glands, which implies a peripheral origin of some PD pathologies. This substantiates the dual-hit theory that holds that PD pathology can commence in the bowel or olfactory bulb and its expansion to the brain through the vagus nerve or olfactory pathway. The treatment approach of alpha-synuclein disease may include agents targeting alpha-synuclein aggregation (monoclonal antibodies, vaccines), which are under investigation to reverse the development of the toxic forms of proteins. These immunotherapy tactics are associated with potentially modifying the disease pathology in PD although they are still in the clinical research stages [15-17].

Mitochondrial and Lysosomal Dysfunction

Parkinson disease (PD) has been associated with mitochondrial abnormality since mitochondria usually produce energy, apoptosis regulation and the management of reactive oxygen species (ROS). Damage of dopamine producing neurons has been found to occur due to mitochondrial dysfunction and elevated oxidative stress which are especially sensitive to metabolic stress in PD. The early evidence on the pathogenesis of the mitochondrial involvement in PD is the fact that the mitochondria complex I inhibitors like the toxin MPTP do cause parkinsonism in humans and higher primates. This has resulted in creation of animal models and additional investigations elucidating mitochondrial defects in PD patients.

As well, genetic researches have also supported the relationship between mitochondria and PD by the fact that, familial PD has shown an association with mutations to the genes such as PINK1 and PARKIN genes that correspond to mitochondrial quality control and mitophagy. In these mutations, damage to mitochondria cannot be discharged properly making the cells to develop stress and eventually degenerate. Moreover, the impairment of lysosomes, especially in case of GBA gene encoding glucocerebrosidase, enhances the build-up of neurotoxic alpha-synuclein and develops neurotoxicity. Mitochondrial stress treatment intends to elevate mitochondrial functionality and lysosomal clearance, which are in development with coenzyme Q10, NAD + precursors, or small molecules to stimulate mitophagy or GBA. These methods are just experimental but have shown promising method of slowing down the progress of the disease [18-20].

Inflammation and the Gut-Brain Axis

Neuroinflammation has appeared as a major contribution in the pathogenesis of Parkinson disease (PD). Active microglial cells are regularly seen in the brains of PD patients and high levels of inflammatory cytokines. Although these immune responses initially serve as protective mechanisms, they may fail to resolve with the result that they are converted into chronic inflammation that leads to neuronal damage and, therefore, neurodegeneration. There is also involvement of the peripheral immune system in PD where there is raised production of pro-inflammatory cytokine in plasma and cerebrospinal fluid in PD patients. This indicates a two way interaction between central nervous system and the peripheral immunity.

The gut-brain axis is a new frontier of studies that draws attention to the influence of gut microbiome on inflammatory and neurodegenerative processes. The imbalance of intestinal microflora was recorded in PD patients, and it can aggravate the aggregation of alpha-synuclein, raise the intestinal permeability, and provoke general inflammation. It has been hypothesized that PD can start in the gut, since gastrointestinal symptoms are more likely to appear before neurological ones do, and alpha-synuclein has been observed

to be located within the enteric nervous system. In animal studies, alteration of gut microbiota was reported to impact on motor activity and alpha-synuclein pathology. Moreover, and most importantly, experimental vagotomy that interferes with the communication between the gut and the brain has been shown to be protective in certain models of PD and thus holds potential as a treatment, opening a new avenue to explore the modification of the intestinal microbiome as a possible therapy. Some current studies of future treatment can be adrenocorticoid receptors(Targeting microbiome-vagus nerve) anti-inflammatory agents and probiotics, which shows promise as a future treatment to manage neuroinflammation and reduce the pace of progression in the disease [21-23].

4. Cognitive and Psychiatric Features

Cognitive impairment characterises one of the most significant non-motor symptoms of Parkinson disease (PD), whereby it is suffered by a considerable proportion of the patients and in many cases, the condition is chronic and debilitating. It may either take the form of mild cognitive impairment (MCI) or develop into Parkinson dementia (PDD). Executive functions, attention, visuospatial skills, and working memory are the areas of cognitive deficits that usually occur during the initial years of PD. These deficits slowly deteriorate to have a substantial dysfunctional effect on day to day activities and independence which ultimately, contributes to low quality of life and greater burden on the caregiver. Subjective cognitive impairment (SCI) is viewed as a viable, early predictor of progressive cognitive deterioration and is defined as a self-reported low level of cognition that has no objective evidence on neuropsychological assessment among other cognitive tests. Studies indicate that the SCD in PD might be a precursor to the development of MCI or dementia hence early tracking and therapy may be essential. There is active work going in towards the definition of underlying pathology in patients with SCD by using neuroimaging and fluid biomarkers.

PD is severed with dementia that is often observed in more serious phases of a condition, and this process is associated with widespread cortical Lewy bodies pathology. Certain risk factors connected with Parkinson dementia are higher age, longer duration of the disease, hallucinations, and serious motor symptoms. And the pathway of MCI to PDD is unpredictable and not all MCI patients will progress to dementia, which indicates that early interventions and patients who are most likely to respond to interventions to slow down cognitive decline will have to be identified on whom trial could be carried out to see its effect. Some neuropsychiatric symptoms such as depression, anxiety, apathy, hallucination, delusion, and impulse control disorder (ICD), can also be witnessed in PD, and it complicates management as these symptoms may occur before the motor symptoms do. Physical stimulation, cognitive rehabilitation, counseling, cholinesterase inhibitors as a treatment of dementia and SSRIs or SNRIs as therapy of depression and anxiety are all parts of a multidisciplinary approach. Doses of antipsychotic medications should be tapered appropriately because they aggravate the motor symptoms. The new treatment mechanisms that may alleviate such challenging non-motor symptoms in the future include studies on these neuroinflammation, neurotransmitter imbalances, and synaptic dysfunctions [23-30].

Table 2: Non-Motor Symptoms in Parkinson's Disease and Their Management

Symptom Category	Common Manifestations	Recommended Management
Cognitive Impairment	MCI, dementia, slowed thinking	Cholinesterase inhibitors, cognitive therapy
Psychiatric Symptoms	Depression, anxiety, hallucinations	SSRIs/SNRIs, atypical antipsychotics (e.g., quetiapine)
Autonomic Dysfunction	Orthostatic hypotension, constipation	Midodrine, fludrocortisone, dietary adjustments
Sleep Disorders	REM sleep behavior disorder, insomnia	Melatonin, clonazepam, sleep hygiene counseling
Fatigue and Apathy	Daytime sleepiness, reduced motivation	Stimulants (modafinil), exercise, structured routines

5. Treatment Approaches

Current Treatments

Drug intervention is very essential in the restoration of the dopamine system in the brain which is pivotal to the management of Parkinson disease (PD). The most commonly used and effective drug in

management of the motor symptoms is levodopa and a peripheral decarboxylase inhibitor i.e. carbidopa. The combination is useful in maximizing the effect of levodopa and reducing peripheral side effects. During the initial phases of the disease, levodopa also causes major symptomatic improvements of bradykinesia, rigidity and tremor. When the disease advances, dopamine agonists like pramipexole, ropinirole, and rotigotine can be prescribed and they are commonly utilized together with levodopa. Such drugs directly activate dopamine receptors with the capacity of delaying motor fluctuations of long-term levodopa use and show some side effects such as hallucinations, somnolence, and impulse control disorders, especially in elderly patients.

Other pharmacotherapeutic agents are monoamine oxidase B (MAO-B) inhibitors (selegiline, rasagiline, etc.), that delay dopamine breakdown, and catechol-O-methyltransferase (COMT) inhibitors (entacapone, opicapone, etc.), which enhance levodopa effectiveness. In certain symptoms such as tremor or dyskinesia, anticholinergic drugs and amantadine can be administered, but are usually not commonly used as they have side effects on the cognition of geriatric patients. Physiotherapy, occupational therapy and speech therapy are all important non-drug interventions with regard to multiple PD management. The treatment of PD now is a multidisciplinary care team that has become the gold standard to make patients satisfied and improve their treatment results. Patient education and counseling as well as caregiver education and counseling are also important, especially in the later stages of PD. Personalized treatment and follow ups are required in order to deal with the range of symptoms and complications that occur during the advanced stages of the disease [30-32].

Disease-Modifying Therapies

Presently, there is no treatment available to slow down or stop the advancement of Parkinson disease but major steps have been made to treat the symptoms. Research continues on disease-modifying therapies (DMTs), to ideally manage the pathophysiology of PD, strategies to block alpha-synuclein aggregation, improve mitochondrial function, and immune response. Among them is immunotherapy, composed, on the one hand, of passive immunization using monoclonal antibodies (e.g., prasinezumab) and active vaccination against alpha-synuclein, on the other hand. These treatments are still under different levels of clinical trials to suppress the presence of toxic aggregates of alpha-synuclein in the brain.

The other area that they are exploring is gene therapy, whereby approaches concentrate on either transferring genes that make dopamine or change how disease happens. Such as, AAV2-GAD gene therapy is aimed in the subthalamic nucleus in order to enhance motor symptoms, and treatment in the genetic variants underlying PD (GBA and LRRK2) are still being developed. Coenzyme Q10 and creatine are mitochondrial stimulants that have varied effects, and NAD+ precursors such as nicotinamide riboside are becoming of greater interest since they may be able to increase energy metabolism and cellular health. Moreover, small molecules which stimulate autophagy and lysosomal turnover, e.g., ambroxol, EGT, are also investigated, especially in patients with GBA mutations. These experimental regimens have a great promise; translating that benefit to the clinical treatment setting is difficult. It is probably best to use DMTs later in future when the condition can be treated even at the prodromal stage of the disease. The use of biomarkers and precision medicine strategies would be essential in designing customised clinical trials as well as in individualising care among patients of PD [33-35].

6. Role of Drugs in Parkinson's Disease and Insights from Case Studies

Pharmacological therapy is as well the mainstay in the management of Parkinson disease (PD) and the most reliable tool to control the disease debilitating effects. PD develops due to degeneration of dopaminergic cells in the substantia nigra pars compacta causing the tremendous decrease of dopamine in the striatum. This lack of dopamine can be said to cause the typical motor deficit symptoms related with PD such as bradykinesia, rigidity, resting tremor and postural instability. Proper drug treatment should correct the dopaminergic tone in the brain; it would relieve these symptoms and restore the functionality and quality of life of the patient.

The most widely used PD symptomatic treatment is a combination of Levodopa with a peripheral decarboxylase drug such as carbidopa; this is regarded as a gold standard. When it enters the brain, levodopa is turned into dopamine and thus the imbalance in neurotransmitter is corrected. Carbidopa when combined with carbidopa aids diminishing peripheral side effects such as nausea and orthostatic hypotension and improves central delivery of drugs, reducing the dose necessary. Despite the improvement in motor performance that is caused by levodopa, there is usually the development of motor complications lasting several years that may be wearing-off and dyskinesias. Symptom management is also

performed using the other dopaminergic treatments: dopamine agonists (pramipexole, ropinirole), inhibitors of MAO-B (selegiline, rasagiline), inhibitors of COMT (entacapone, opicapone), amantadine and anticholinergics. These medications operate in a manner of supplement of dopamine activity and are chosen depending on the symptoms of the suffering person, age of the person, development of the disease and other conditions. In early-stage PD, one may delay the initiation of levodopa with the help of dopamine agonists and MAO-B inhibitors, whereas in later stages, motor fluctuations may involve using levodopa coupled with other medicines. The disease progression needs a multidisciplinary team comprised of neurologists and therapists that are important in optimizing treatment. Despite being palliative, pharmacological therapies prove to be very effective in ensuring the functionality of PD patients as well as their quality of life [36-40].

Drugs Mechanism of Action and Classes

- **Levodopa/Carbidopa:** The most effective option of treating the motor symptoms is through the conversion of levodopa into the dopamine in the brain. By blocking peripheral metabolite, carbidopa ensures low side effect such as nausea. Long-term treatment however, would see motor fluctuations and dyskinesia as a result of pulsatile stimulation of dopamine receptors.
- **Dopamine Agonists (e.g. pramipexole, ropinirole):** They are drugs that bind directly to dopamine receptors particularly D2-like receptors. In younger people, they can be applied to postpone the complications caused by levodopa; they can also be leveraged with levodopa to lessen motor fluctuations. The side effects are day time sleepiness, hallucination, and impulse control disorder.
- **MAO-B Inhibitors (e.g., selegiline, rasagiline):** These are of the type that prevent the decomposition of dopamine present in the brain by an enzyme known as monoamine oxidase B, and in such a way extending the effect of dopamine. Their effect is of mild alleviation of symptoms and can be applied as monotherapy at an early stage of PD or combination therapy at an advanced stage. There are indications that rasagiline has a neuroprotective effect, but this effect is not proved.
- **COMT Inhibitors (e.g. entacapone, opicapone):** these medications block the degradation of levodopa peripherally, slowing its clearance time and activity. They are especially useful in patients with motor fluctuations, where a once-daily COMT inhibitor (opicapone) is especially efficacious and tolerable compared to older medications.
- **Amantadine and Anticholinergics:** Amantadine is a weak NMDA receptor antagonist that aids the process of releasing dopamine and can be of use in managing levodopa-induced dyskinesias. The anticholinergics, trihexyphenidyl is effective in tremors prominent PD especially in young patients; however, in older patients it can result in cognitive side effects [41-45].

Table 1: Classes of Drugs Used in Parkinson's Disease and Their Mechanisms

Drug Class	Example Drugs	Mechanism of Action	Common Indications	Notable Side Effects
Levodopa + Carbidopa	Sinemet	Dopamine precursor + DDC inhibitor	Core motor symptoms	Dyskinesia, wearing-off, nausea
Dopamine Agonists	Pramipexole, Ropinirole	Direct dopamine receptor stimulation	Early PD, motor fluctuation adjunct	Hallucinations, impulse control disorders
MAO-B Inhibitors	Selegiline, Rasagiline	Inhibit dopamine breakdown via MAO-B enzyme	Early PD, adjunct to levodopa	Insomnia, serotonin syndrome (with SSRIs)
COMT Inhibitors	Entacapone, Opicapone	Extend levodopa action by blocking peripheral degradation	Wearing-off in advanced PD	Diarrhea, hepatotoxicity (tolcapone)

Amantadine	Amantadine	NMDA antagonist; increases dopamine release	Levodopa-induced dyskinesia	Livedo reticularis, hallucinations
Anticholinergics	Trihexyphenidyl	Inhibit acetylcholine receptors	Tremor in young PD patients	Dry mouth, cognitive decline in elderly

7. Real-World Case Studies

Case Study 1: Levodopa-Induced Dyskinesia

An 8-year-old former history of Parkinson disease in a 62-year-old male characterized with peak-dose dyskinesias that severely affected the patient daily activity. He was first treated using levodopa/carbidopa that helped tremendously in terms of motor benefit. The efficiency of the drug decreased in the course of time, and he started to develop too many involuntary movements. The efforts of controlling the fluctuations by using entacapone produced little benefits. In conclusion, a percutaneous gastrojejunostomy was prepared and the patient was put on a levodopa-carbidopa intestinal gel (LCIG) that induced constant dopaminergic stimulation. This intervention significantly stabilized his plasma levodopa concentration, decreased dyskinesias and enhanced his functional status.

Case Study 2: Impulse Control Disorder with Dopamine Agonist

Pramipexole was ordered as the first treatment of a 55-year-old female diagnosed with early stages of PD. It took her several months before she acquired behavioral changes such as binge eating and compulsive shopping. Such behaviors were described as impulse control disorders and they are a documented side effect of dopamine agonists. She became liberal with pramipexole and when she changed to rasagiline her psychiatric symptoms were corrected and her motor function was sufficiently well controlled. The case highlights the need of periodic psychiatre evaluation of patients taking dopamine agonists.

Case Study 3: Personalized Gene-Targeted Therapy

A 48-year-old man with a significant family history of PD was genetically tested and was found to have harbored a GBA mutation. Within a clinical trial, he had initiation of ambroxol, a repurposed drug considered to promote lysosomal activity. A 12-month follow-up indicated that motor symptoms of the patient had stabilized and he was more cognitively clear. Also, there was a negative trend in his cerebrospinal fluid alpha-synuclein, which indicates the impact of treatment at the biological level. This Case emphasizes the possibility of precision medicine in achieving therapy by means of genetic profiling [46-57].

8. The Role of Physical Exercise

Exercise continues to be shown as a viable non-pharmacologic therapy of Parkinson disease (PD) that drives the reduction of motor symptoms, including bradykinesia, rigidity, and postural instability. It induces neuroplasticity, involves the dopaminergic transmission, and has neuroprotective activities. The main elements of the exercise, e.g. aerobic exercises, resistance training, balance training, flexibility training, may be adjusted to the level of the disease and the functional capacity of the patient. Particularly, exercise can enhance gait and balance that slows down falls which is a significant cause of morbidity in PD. Tango, treadmill training, and tai chi are dance-based therapies that have been proven to be especially effective with gait mechanics and gait stability with these forms of therapy also providing motivation to the patients and getting them to socialize.

Exercise can also be used to treat non-motor symptoms such as depression and anxiety, fatigue, and cognitive decline. Normal physical exercise raises the level of brain-derived neurotrophic factor (BDNF), a neurotrophic protein that promotes neuronal survival and plasticity and improves cognitive capabilities, e.g., executive functions, attention, and working memory. Irrespective of these advantages, exercise may become difficult with the advancement of the disease as the obstacles include the physical limitations of activity, fear of fall, and fatigue. Interventions like custom exercise programs, training managed and monitored by physiotherapists, wearable devices, and online exercise programs provide a good opportunity to address these obstacles and increase patient independence [57-60].

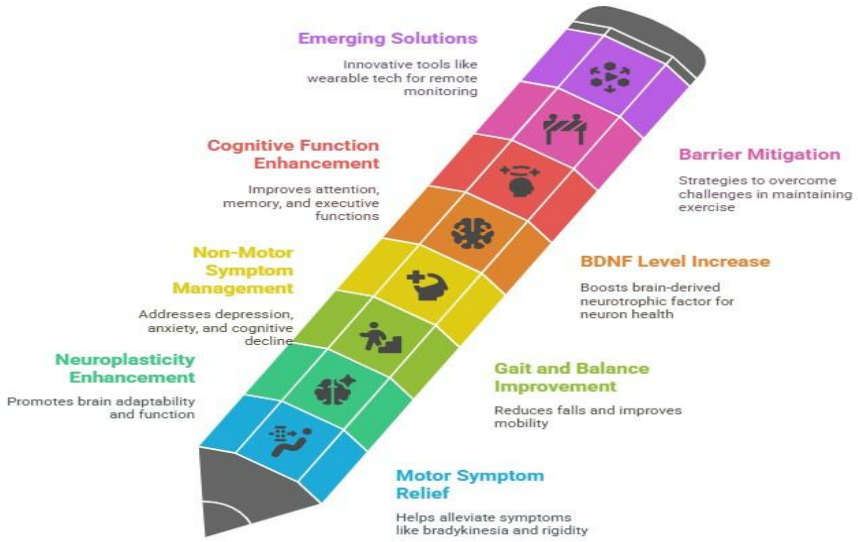

Figure 3: Role of Physical Exercise in Disease control

9. Future Perspectives

Precision medicine is emerging at the center of the treatment of Parkinson disease (PD), and there is an increasing interest in incorporating genetic, molecular and clinical information to customize treatment. Genotype-based interventions have attracted interest following the discovery of genetic mutations, including SNCA, LRRK2 and GBA. Patients are currently being stratified according to genetic subtype in clinical trial in an effort to maximize treatment response. Early diagnosis and real-time monitoring of the disease enable the development of therapeutic interventions via biomarkers which became possible due to the development of imaging systems, cerebrospinal fluid testing, and blood markers that make it possible to see and treat the disease at an early stage. Biomarkers can be integrated with artificial intelligence (AI) that would entail disease modeling and prediction. Technological advancements are changing PD care by using wearable devices and remote monitoring to offer real-time information, assist with care planning, and make care accessible, particularly to patients located in underdeveloped communities. As effective as it proved to be during the COVID-19 times, telemedicine will soon become a new standard of PD management.

The neuroprotective strategies in PD care are also the area of future attention and there are continuous trials discussing the problem of alpha-synuclein aggregation, mitochondrial dysfunction and neuroinflammation. Developing disease-modifying therapies (DMTs), especially those that may be used during the prodromal stage, is an aspect that provides hope of slowing or preventing the onset of the disease. PD will move to the patient-centered, holistic approach where the drug is used in association with devices, psychological support, and physical rehabilitation. Social services and multidisciplinary teams of care providers will be necessary as patients advance and health policy systems need to guarantee equal access to new therapeutics, especially in poor countries. Innovations will be propelled by international research and advocacy by patients, underlining that every individual, who is touched by Parkinson disease, will gain the benefit [50-60].

Table 3: Emerging Therapies and Their Targets in Parkinson's Disease

Investigational Therapy	Target/Mechanism	Current Phase	Example/Comment
Alpha-synuclein antibodies	Prevent aggregation/spread	Phase 2–3	Prasinezumab, cinpanemab
Gene Therapy	Restore enzyme or dopamine synthesis	Early–Mid	GBA, LRRK2 vectors, AAV2-GAD
Ambroxol	Enhances lysosomal glucocerebrosidase	Pilot trials	Especially in GBA mutation carriers
NAD+ precursors	Boost mitochondrial function	Phase 1–2	Nicotinamide riboside
Digital Tools & AI	Remote symptom tracking and modeling	Applied	Wearables, machine learning integration

10. CONCLUSION

Parkinson disease is a multifaceted degenerative disorder of the nervous system that undertakings critical motor and non-motor complications. There have been significant developments in the symptomatic treatments, but the disease-modifying therapeutics are needed and so are the personalized care approaches. New research has been seen on genetics, biomarkers, and neuroprotective agents and provides hope of earlier diagnosis and better outcome and even a possible cure. To achieve this goal of improving the quality of life and respond to the changing terrain of PD care, it will be necessary to adhere to a multidisciplinary, patient-centric approach that will incorporated pharmacological, non-pharmacological, and technological interventions.

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