***Review Article***

# Neurodegenerative Disease: Parkinson's -AComprehensive Review


## Abstract

The most prevalent neurodegenerative condition is Parkinson's Disease. The pathologic characteristic of Parkinson's Disease (PD), a neurodegenerative condition, is the substantia nigra pars compacta experiencing dopaminergicneuron loss [1]. These are the four main motor signs of Parkinson's disease stiffness, trouble with coordination and balance also when the illness worsens, many people have mental and behavioural changes, sleep problems, depression and fatigue [2]. Many people with PD also develop Dementia in the course of this ailment. Moreover, Parkinson's disease risk related with age and compared to women, men are more impacted. The chance of getting certain diseases may be increased by environmental variables such as pesticides, air pollution, and industrial solvents, according to various research [3]. According to Parkinson's disease symptoms, the Michael J. Fox Foundation for Parkinson's Research often start to manifest in patients around the age of 60, and many people continue to survive for 10 to 20 years after receiving a diagnosis. Patients with PD can be treated with several drugs and medications- Levodopa, dopamine agonists, mono-oxidase B inhibitors, and amantadine are a few medications that are specially designed to address motor symptomatology.The most effective medication is Levodopa, but its usage is restricted by its short-and long-term side effects [4].



Keywords: Neurodegenerative disease; Parkinson's; Dopamine; hypokinesia; neurotransmeter

## Introduction

Parkinson's disease is a neurological illness that worsens with time and is mostly brought on by a deficiency in the brain's chemical dopamine. Dopaminergic cell loss causes lower levels of this neurotransmitter, which is important in motivation, memory, locomotion, and other behaviours, to be present in PD brains [5]. Dopamine depletion in the PD brain is what causes movement dysfunction and possibly the cognitive deficiency found in some PD patients [6]. Although roughly 5% to 10% of Parkinson's patients suffer onset before the age of 50, most Parkinson's patients first experience the disease beyond the age of 60. While not always hereditary, early-onset Parkinson's disease has been linked to specific genetic changes in some cases. Moreover, Parkinson's disease is pathologically marked by a loss of nigrostriatal dopaminergic innervation, but other neurons in the neural network are also affected by neurodegeneration, which is not just a problem for nigral dopaminergic neurons [7]. Because of its widespread underlying disease, PD is a very heterogeneous condition, and there is no accurate diagnostic technique at this time. The presence of two of the clinical signs of rigidity, postural instability, bradykinesia, resting tremor, or both are required for a diagnosis [8]. A conclusive diagnosis of Parkinson's Disease can only be made through histological examination and the detection of Lewy bodies that contains α-Synuclein [9]. The main stay of treatment is using drugs that either work on striatal post-synaptic dopamine receptors or enhance dopamine levels in the striatum, which primarily aims to relieve symptoms numerous also additionally, various medicines are used to treat certain symptoms, such as depression or dementia because dopamine is not the only transmitter implicated in Parkinson's disease. More studies and inventive medications are required to slow the progress of neurodegeneration or even to restore the lost dopaminergic cells, even though some are still in the early phases of human trials. The potential for the development of enzymes that modify disease is encouraging as our knowledge of the etiology of Parkinson's Disease expands, and new therapeutic targets are better understood [10].

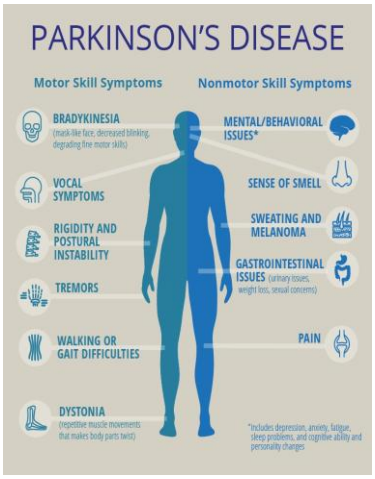


**Fig1. Symptoms and Epidemiology of Parkinson's Disease**

The Parkinson's Disease (PD) is a neurological condition that improves over time. Also, it results in unintentional or involuntary movements, such as tremors and stiffness, as well as balance and coordination problems, are the result. Symptoms begin mild and become worsens over time. Additionally, people may experience depression, weariness, and changes in their behaviour and minds [11]. Parkinson's Disease most prominent signs and symptoms are mostly caused by the loss or death of nerve cells in the basal ganglia, an area of the brain that controls movement. These nerve cells or neurons continuously create dopamine, a crucial neurotransmitter in the brain [12].

**Symptoms of Parkinson's Disease:** Symptoms of this disease includes**,** Rigidity; muscular stiffness, which occurs when a muscle is tight for a long time, hypokinesia (motion that is slow), Tremor**,** Postural instability**,** Poor balance and coordination

Additional signs includes: Constipation or urinary issues; trouble swallowing, chewing and speaking; depression and other emotional disturbances

**Diagnosis of Parkinson's Disease**

As PD cannot be diagnosed and no blood and laboratory tests are available in non-genetic cases.

- Parkinson's disease can be detected by a scan for the dopamine transporter (DAT) and a SPECT (single photon emission computerized tomography) scan [13]. To aid and rule out illnesses, imaging tests like MRIs, brain ultrasounds, and PET scans are also employed .

- Levodopa is the primary therapy for Parkinson's disease. To refill the declining ranges of dopamine with inside the brain, levodopa is transformed into dopamine via way of

means of nerve cells. Dopamine Agonists-replace the brain's dopamine and, have a comparable but less potent effect when compared to levodopa.

- Monoamine Oxidase-B inhibitors, including selegiline and rasagiline- Additionally, by preventing the effects of monoamine oxidase-B, an enzyme or brain substance that degrades dopamine, they increase dopamine levels. Apomorphine- is an injectable, short-acting dopamine agonist indicated for prompt relief.

- Catechol O-methyltransferase (COMT) inhibitors- Inhibitors of COMT stands for catechol O-methyltransferase. The two main drugs in this group are entacapone and opicapone. The effects of levodopa therapy are a little bit prolonged by this medication because it prevents an enzyme from degrading dopamine [14].

- Nuplazid (Pimavanserin)-Patients with Parkinson's disease who develop hallucinations and delusions may be treated withthis drug.

- Moreover, cytokines such as IL-2, IL-4, IL-6, IL-10, and TNF-α increase in the serum of PD Patients an association between systemic markers of inflammation and idiopathic PD risks has been reported [15].

**Parkinson's Disease Risk and Protective Factors**

There are several different pathogenicity and morbidity risk factors for PD. Several studies on ageing, cancer prevention, and nutrition have revealed a positive correlation between dairy consumption and the incidence of PD. The lengthening of the plantation period increased the incidence of Parkinson's disease (PD) in the Honolulu-Asian Ageing Research (HAAS) and Cancer Prevention and II Nutritional Research (CPS-IIN) research groups. This finding is consistent with the health of agriculture research that suggests pesticide disclosure raises the danger of acquiring Parkinson's disease (PD) [16].

Pesticides may disrupt mitochondrial function and lead to oxidative stress, trauma to the brain can result in a breach in the blood-brain barrier, decreased mitochondrial activity, and the build-up of brain α-syn protein, all of which may raise the likelihood of developing Parkinson's disease (PD) in years following the injury. According, to a cohort study in Finland, having a high BMI (27.9 to 29.9) or weight will increase your possibility of contracting Parkinson's disease (PD).

Numerous studies have revealed a variety of PD preventive factors. According to longitudinal studies, alcoholics had marginally fewer chances of developing Parkinson's disease (PD) than

non-drinkers, which was consistent with how alcohol affects urate levels in the body. Numerous prospective studies have shown that drinking coffee lowers your risk of Parkinson's disease compared to not drinking it. Black tea's components may assist in lowering the possibility of developing Parkinson's disease (PD), while green tea's outcomemay not have the same effect as black tea.

The risk of PD is lowered by up to 70% with longer smoking periods, and it has risen over time for those who have given up smoking Additionally, the use of antihypertensive medications, exercise, eating a balanced diet can dramatically lessen the damage and ameliorate the disorder of Parkinson's disease patients [17].

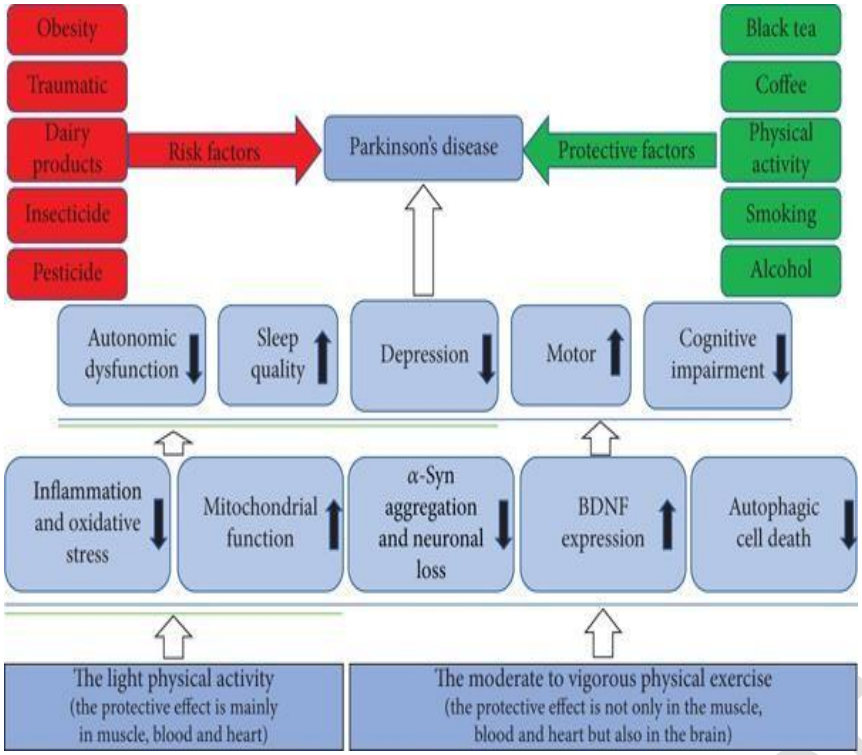


**Figure 2: Representation of Parkinson's disease physical activity [Reference 18]**

Research on embryonic stem cells is a promising area that has stirred both ethical and political debate. Parkinson's patients will receive dopamine neurons from human stem cells in a transplant in the laboratory. In the future, Parkinson's patients may have hope if a limitless supply of dopamine neurons can be successfully generated. Embryonic stem cells (undifferentiated cells collected for several scientific purposes, day-old embryos are currently being employed. A large percentage of these embryos were created by in vitro fertilization procedures. Theoretically able to be modified into a component of any body tissue, researchers think they may be able to stimulate these cells to grow in place of those lost as the disease progresses.

Hope exists that adult stem cells, which are taken out of bone- marrow, could be applied similarly to produce outcomes. Although this form of research raises fewer ethical considerations, some professionals think that using adult stemcells may be more challenging than using those from embryos.

In either case, there is a strong consensus among scientists that preventing them from using both types of stem cells will hamper their ability to conduct research and hinder any possible discoveries. Studies on neurotrophic factors in humans are also under consideration. This protein family has been found in animal tests to significantly reduce symptoms by awakening

dormant brain cells and promoting dopamine synthesis [19].

## Conclusion and Future Direction for Research

The prevalence of morbidity and mortality rates are elevated in Parkinson's disease, one of the most prevalent neurodegenerative diseases affecting the elderly. Knowledge of symptoms of the disease, potential therapy, and long-term progression is necessary for appropriate case management. Knowing the neuropathology of Parkinson's disease and how it affects the neurological system as a whole also evolved tremendously. Neither of these remedies, however, are curative [20]. The most important unmet needs that need to be addressed by ongoing and future research initiatives are that PD is a condition that worsens with time, and eventually ends in severe impairment because of how severe the treatment-resistant motor and non-motorsymptoms are.

The creation of a medication that slows the neurodegenerative processes unrelenting progression is the biggest Parkinson's disease has a significant unmet therapeutic need. The term "disease modification" refers to a variety of interventions, from those that aim to halt the underlying degeneration to those that replace or regenerate damaged neurons [21]. All current efforts to create efficient disease-modifying therapies have been ineffective. Numerous explanations for these failures have been put forth, including our incomplete understanding of illness etiology and the belief that most individuals with the same clinical diagnosis will be affected by each targeted disease mechanism.

To progress Parkinson's illness disease modification, we emphasize therapies under ongoing clinical development that reveal a wide range of serious unresolved difficulties and concerns. It is still unknown if the defective molecular pathways/organelles subject to alteration emerge differently in distinct molecular subtypes of Parkinson's disease (PD) or arise sequentially across the majority of clinically affected patients. There may not be a "type of disruption" that applies to subgroups depending on unknown factors such as genetic variability and other sources of PD heterogeneity, rather than an "order of disruption" that applies to the majority of patients [22].

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