



# A Neurodegenerative Disease: Parkinson's Disease

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## Abstract

Parkinson's disease (PD) is defined as "A progressive multi-system neurodegenerative disease that is characterized by shaking of hands, tremors, difficulty in movement, balance and coordination and stiffness of jaws". It is the disorder of the Central Nervous System (CNS) that affects the motor and non-motor functions. Symptoms of Parkinson's disease gradually increase over time. It is the second most common disorder after Alzheimer's disease. Above 60 ages, 2% population is affected by Parkinson's disease. In this disease, dopaminergic neurons that produce dopamine are lost.

**Keywords:** Parkinson's disease; Motor symptoms; Dopamine drugs; Non-motor symptoms

## Introduction

Parkinson's disease was first described by James Parkinson as the neurological syndrome in 1817 and later it was taken his name. This disease has clear neuropathological changes in brain [1-6]. Lewy bodies are formed which are proteinaceous spherical bodies and a spindle or thread-like structures. Primary neuropathological disorder is the degeneration of the dopamine producing nigrostriatal neurons with the Lewy bodies [6-10].

Parkinson's disease symptoms are generally described as the disturbances of motor functions but this may be due to disturbances in other functions of nervous system [11-14]. The symptoms are categorized into motor and non-motor symptoms. In motor symptoms, bradykinesia (slowness of movement), rigidity of muscles and tremors are included. In non-motor symptoms, olfactory dysfunction, cognitive impairment, psychiatric symptoms and autonomic disorder are included [14-20].

## Symptoms

Generally Parkinson's disease symptoms are divided into two categories (Table 1).

- Motor symptoms
- Non-Motor symptoms

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Received Date: 22 Mar 2021

Accepted Date: 16 May 2021

Published Date: 20 May 2021

### Citation:

Khalid S. A Neurodegenerative  
Disease: Parkinson's Disease. *Ann  
Neurol Surg.* 2021; 5(1): 1024.

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## Motor symptoms

About 80% of dopamine producing cells (dopaminergic neurons) are lost in the nigrostriatal system before appearance of Parkinson's disease [21-28]. By first motor symptoms Parkinson's disease is diagnosed. Motor symptoms include;

- Bradykinesia
- Tremors
- Rigidity
- Postural deformities
- Postural instability
- Freezing

**Bradykinesia:** Bradykinesia is defined as "slowness of movement" and is the major clinical characteristics of Parkinson's disease, although, in depression the symptoms of bradykinesia is also seen but in PD it is most common [29-32]. Bradykinesia is a disorder of basal ganglia, difficulties with planning, initiating and carry out movement and with performing sequential and simultaneous tasks occur [33-38]. In this, routine activities are also affected and there is difficulty in performing daily activities and reaction times. It includes difficulties while performing such task s that require fine motor control (handling, use of utensils) [39,40].

**Table 1:** Motor and Non-Motor Symptoms.

Motor Symptoms	Non-Motor Symptoms
Tremors, bradykinesia, rigidity, postural instability	Cognitive impairment, bradyphrenia, tip-of-the-tongue (word finding) phenomenon
Hypomimia, dysarthria, dysphagia, sialorrhoea	Depression, apathy, anhedonia, fatigue, other behavioral and psychiatric problems
Micrographia, cutting food, feeding, hygiene, slow activities of daily living	Dysautonomia (orthostatic hypotension, constipation, urinary and sexual dysfunction, abnormal sweating, seborrhoea), weight loss
Glabellar reflex, blepharospasm, dystonia, striatal deformity, scoliosis, camptocormia	Sleep disorders (REM behavior disorder, vivid dreams, daytime drowsiness, sleep fragmentation, restless legs syndrome)
Decreased arm swing, shuffling gait, festination difficulty arising from chair, turning in bed	Sensory symptoms: anosmia, ageusia, pain (shoulder, back), paresthesias

Other demonstrations of bradykinesia are loss of movements and gesturing, hypomimia (loss of facial expression) and decreased in blinking, and reduction of arm swing while walking [41-47]. Bradykinesia is one of the most easily known symptoms of Parkinson's disease, before any formal neurological diagnosis that may become apparent.

Bradykinesia depends on the emotional condition of the patient, for example; patient that are unable to move who become excited and may be able to show quick response such as catching a ball or able to run when someone shouts "fire". It suggests that there is a need of external trigger for Parkinson's disease patient having intact motor programs [48-53].

It is concluded that bradykinesia results due to the disruption of normal motor cortex activities that is interceded by decrease of dopaminergic functions. It is suggested that impairment in the new growing cortical and subcortical systems causes bradykinesia [54-61].

**Tremor:** Tremor is the most common motor symptoms that generally recognized in patients having Parkinson's disease. Tremors appear between 4 Hz to 6 Hz frequency and are easily noticeable in the distal part. Hand tremors start and passed from one hand to other hand and these are termed as supination-pronation tremors. Rest tremor vanishes during sleep [62-64].

There are postural tremors other than rest tremors that are most prominent and disabling. Postural tremors appear at the early stage of Parkinson's disease. The tremors in the Parkinson's disease are different from the essential tremors because postural tremors appear at the same frequency [65,66]. In patients having Parkinson's disease, rest tremors vary among patients and during disease course. It is reported by Hughes and his colleagues that 69% Parkinson's disease patients had rest tremors at their early age of disease while 75% had tremors during their course. The 9% patients have lost tremors in the late stage of this disease [67-70]. The 11% patients never had tremors.

**Rigidity:** It is defined as the stiffness or inflexibility in muscles. It is one of the most common symptoms of Parkinson's disease beside tremor and bradykinesia. Rigidity generally occurs at neck, shoulders, hips, wrist and ankles etc. Sometimes, rigidity is associated with pain and pain in shoulders is the appearance of Parkinson's disease but it is commonly diagnosed as arthritis. There was held a study, where 6,038 persons were observed having stiffness, tremors and imbalance but no evidence of dementia or Parkinson's disease were found [71,72].

**Postural deformities:** In the postural deformities symptom of Parkinson's disease flexed neck and trunk postures are resulted and knees and elbows become rigid. Abnormal axial postures results in addition to rigidity of neck and trunk. Generally, flexed postures occur in the late stage of disease [73-76].

Deformities in the striatal limbs also occur in some patient

**Figure 1:** Foot deformity.**Figure 2:** Hand deformity.

having Parkinson's disease. According to a study, 21% patient was diagnosed with Parkinson's disease having symptoms of striatal toe deformity. Striatal deformities usually occur in the early stage of Parkinson's disease and mostly in younger patients. There are also other deformities that include extreme flexion in neck, truncal and sideway curvature of spine (scoliosis) (Figure 1, 2) [77,78].

**Postural instability:** Loss of postural reflexes causes postural instability. Postural instability usually occurs at the late stages of Parkinson's disease. To check retropulsion (pulling from behind) or propulsion (pushing from forward), pull test is done. In this pull test, patient is pulled backward or forward quickly. If a patient takes two steps backward or forward or no posture is seen, then it indicates the abnormal postural response/postural instability. Postural instability is the major cause of hip fractures and falls [79]. The average time of the first fall was 108 months in patients having Parkinson's disease compared with the patients having PSP (Progressive Supranuclear Palsy) and MSA (Multiple System Atrophy) with 16.8 and 42 months

respectively [80]. There are many other factors that cause postural instability in patients having Parkinson's disease. These factors include orthostatic, hypotension, age related sensory changes etc. There was held a study that showed 38% evaluated experienced falls and 13% fell more than one time in a week. Treatment may improve some axial signs but not permanently recovers postural instability [81].

**Freezing:** Freezing, in Parkinson's disease, refers to motor blocks. It is a form of loss of movements (akinesia) and the most disturbing symptoms of Parkinson's disease [81]. This symptom does not occur universally. According to a report, freezing occur more commonly in men than women. In this symptom of Parkinson's disease, legs are most affected during walking.

Freezing occurs as a sudden and transient failure to move. It may also include hesitation during turning or walking through a narrow passage, crossing overcrowded streets etc. Freezing is thought as the common cause of falls [82]. There are five subtypes of freezing:

- Start hesitation
- Turn hesitation
- Hesitation in tight quarters
- Hesitation of destination
- Open space hesitation.

Factors which cause the development of freezing are rigidity, bradykinesia (slowness of movements), postural instability and long disease span. Contrary to it, tremors at the onset of disease is associated with the decreased risk factor of freezing [83]. Freezing is not predominant symptom and usually occurs in the later stage of Parkinson's disease.

### Non-motor symptoms

There are some non-motor symptoms of Parkinson's disease that include

- Disturbance of autonomic functions
- Neuropsychiatric abnormalities
- Sleep disorders

**Disturbance of autonomic functions:** Disturbance of autonomic function is also characteristics feature of Parkinson's disease, but it is more commonly related with MSA [84]. Before diagnosis, autonomic function's disturbance may present or it may occur with development of disease. Autonomic dysfunction has affected daily life routine of 50% patients [85]. It is due to the involvement of both peripheral and central post-ganglionic autonomic nervous system [86]. Autonomic dysfunction's features are orthostatic hypotension, sweating disturbance, sphincter disturbance and erectile dysfunction. The 30% to 40% patients have been affected by orthostatic hypotension [87].

Parkinson's disease duration is not related to the manifestation of orthostatic hypotension. In autonomic dysfunction, gastrointestinal symptoms are general. Gastrointestinal tract movements slow down. Patients having non-motor symptoms also face difficulties in rectal evacuation, due to the disturbance in rectal sphincter [89]. Erectile dysfunction is more common in male [90]. There are also dermatological symptoms like hyperhidrosis (excessive sweating), increase fat in the central face related to scaling of skin.

**Neuropsychiatric abnormalities:** Neuropsychiatric disturbances can be classified as non-motor symptoms. According to a study hold in Sydney multicenter showed that 84% patients have neuropsychiatric abnormalities and 48% faced dementia after 15 years of follow-up [91]. There is six times increased risk of dementia in patients having Parkinson's disease [92-95]. Many other symptoms include depression, apathy, anxiety, hallucination, obsessive-compulsive and impulsive behaviors are there alongside neuropsychiatric abnormalities [96-97].

According to a study, 27.6% patients out of 114 patients, with Parkinson's disease was reported positive for depression. Other than many symptoms, visual hallucination is the most common of that entire manifest before the drug treatment [98]. These visuals hallucination lasts for few seconds to minutes and re-occur during the whole day. Hallucination may be caused by the higher load of dopamine treatment [99]. As disease progress, paranoid illusions may develop [100]. Because of dopamine treatment, many behavioral abnormalities such as, euphoria, poor organizational skills, risk taking behavior (gambling, excessive spending etc) and hypersexuality may occur [101].

**Sleep disorders:** Sleep disturbances are also associated with Parkinson's disease non-motor symptoms. Sleep disturbance is considered as pre-Parkinson's disease state. Insomnia is also frequent and its manifestation varies in patients. The 50% loss of hypocretin neurons is caused by sleep disturbances in patients having Parkinson's disease [102].

Anatomical structures and neurotransmitters are involved in the sleep cycle, which is being affected by neuropathology of Parkinson's disease, disturb the sleep cycle and cause sleep disorder. Two-third patients are affected by sleep disturbances in Parkinson's disease [103]. There are other Parkinson's disease symptoms that cause fractionated sleep and these include difficulties with turnaround in bed, nocturia (wake up during night for urination) and depression etc [104]. More than 50% patients are observed excessive daytime sleep that is due to dopamine drugs. However, in obstructive sleep apnea breathing stops during sleep in the Parkinson's disease patients [105-108]. It is observed that all dopamine producing drugs cause sleep attacks [109,110].

### Conclusion

Parkinson's disease is a progressive disease that results some motor and non-motor symptoms. Although, there is no such treatment for Parkinson's disease but it is treated with levodopa treatment. Parkinson's disease is much more complex disease than motor manifestations. It results the loss of dopaminergic neurons that produce dopamine. Parkinson's disease varies with patient but it usually occurs more rapid in patients having Postural Instability and Gait Disorder (PIGD).

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