Journal of Neuroscience and Neurodevelopmental Disorders (JNDD)

OLITES PUBLISHERS
A Global Approach For Research

Open Access

Research Paper

Unraveling Parkinson's Disease: From Molecular Mechanisms to Modern Therapeutic Strategies

Brett W. Lester*, Paul A. Schick, Dora W. Crum, David B. Clements
***Corresponding Author:** Brett W. Lester, Cognitive Neuroscience, Pain, and Rehabilitation Research Group,Spain

Citation: Brett W. Lester, Unraveling Parkinson's Disease: From Molecular Mechanisms to Modern Therapeutic Strategies V1(2),2025

Received date: August 18, 2025: **Accepted date:** August 25, 2025: **Published date:** August 30, 2025

Keywords: Parkinson's disease, dopamine, neurodegeneration, α-synuclein, motor symptoms, non-motor symptoms

Abstract

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder that primarily affects motor function but also produces a wide range of non-motor symptoms. Characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta and the presence of Lewy bodies composed largely of misfolded α-synuclein, PD represents a major public health challenge worldwide. The disease predominantly affects older adults, with increasing prevalence due to global population aging. This paper provides a comprehensive overview of Parkinson's disease, including its epidemiology, pathophysiology.

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. First described in 1817 by British physician James Parkinson in his essay *An Essay on the Shaking Palsy*, the disease has since been recognized as a complex neurological condition involving both motor and non-motor dysfunctions. Although PD is traditionally defined by its motor features, it is now well established that non-motor symptoms such as cognitive impairment, mood disorders, sleep disturbances, and autonomic dysfunction significantly affect quality of life.

markedly with age, typically manifesting after the age of 60, although early-onset Parkinson's disease can occur in younger individuals. Men are slightly Parkinson's disease affects millions of individuals worldwide. The prevalence increases more affected

clinical manifestations, diagnostic approaches, and current as well as emerging treatment strategies. Understanding the complex biological mechanisms and clinical spectrum of PD is essential for early diagnosis, improved symptom management, and the development of disease-modifying therapies

Introduction

The global burden of Parkinson's disease has increased substantially over the past few decades. Advances in medical care have improved life expectancy, resulting in a growing elderly population and, consequently, a higher prevalence of age-related neurodegenerative diseases. Despite extensive research, the exact cause of Parkinson's disease remains unknown, and current treatments are largely symptomatic rather than curative. This paper aims to review the current understanding of Parkinson's disease, focusing on its biological basis, clinical features, diagnostic criteria, and management options.

Epidemiology

than women, suggesting a possible protective role of estrogen or differences in environmental exposures Geographical variations in prevalence have been reported, which may reflect differences in genetic susceptibility, environmental risk factors, and diagnostic practices. With increasing longevity and improved awareness, the number of individuals living with Parkinson's disease is expected to rise, posing significant challenges to healthcare systems, caregivers, and society as a whole.

Pathophysiology

The hallmark pathological feature of Parkinson's disease is the progressive loss of dopaminergic neurons in the substantia nigra pars compacta, a region of the midbrain involved in motor control.

Journal of Neuroscience and Neurodevelopmental Disorders (JNDD)

Dopamine is a critical neurotransmitter that facilitates smooth, coordinated muscle movements. Its depletion leads to the characteristic motor symptoms of PDAnother defining feature is the presence of Lewy bodies and Lewy neurites, intracellular inclusions primarily composed of aggregated α-synuclein protein. The misfolding and accumulation of α-synuclein are believed to play a central role in neuronal dysfunction and cell death. Several mechanisms have been implicated in PD pathogenesis, including mitochondrial dysfunction, oxidative stress, impaired protein degradation via the ubiquitin-proteasome system, neuroinflammation, and genetic mutations.

Although most cases of Parkinson's disease are sporadic, genetic factors contribute to a subset of cases. Mutations in genes such as SNCA, LRRK2, PARK2, PINK1, and DJ-1 have been associated with familial forms of the disease. Environmental factors, including exposure to pesticides, heavy metals, and rural living, have also been linked to increased risk, highlighting the multifactorial nature of the disorder

Clinical Manifestations

Motor Symptoms

The classical motor symptoms of Parkinson's disease are often summarized by the acronym TRAP: tremor, rigidity, akinesia/bradykinesia, and postural instability.

- **Resting tremor** typically begins unilaterally and is most noticeable when the affected limb is at rest **Muscle rigidity** results in stiffness and resistance to passive movement.
- **Postural instability** usually occurs in later stages and increases the risk of falls.
- **Muscle rigidity** results in stiffness and resistance to passive movement.
- **Postural instability** usually occurs in later stages and increases the risk of falls.

These motor symptoms progress gradually and often begin asymmetrically before becoming bilateral

Non-Motor Symptoms

Non-motor symptoms are increasingly recognized as integral components of Parkinson's disease and may precede motor symptoms by years. These include cognitive impairment, depression, anxiety, apathy, sleep disorders, autonomic dysfunction (such as constipation and orthostatic hypotension), sensory disturbances, and fatigue. Cognitive decline can range from mild cognitive impairment to Parkinson's disease dementia

Neuropsychiatric symptoms significantly impact patient well-being and caregiver burden, underscoring the need for comprehensive management strategies

Diagnosis

The diagnosis of Parkinson's disease is primarily clinical, based on medical history and neurological examination. There is no single definitive laboratory test for PD. Diagnostic criteria emphasize the presence of bradykinesia along with at least one additional motor symptom, such as tremor or rigidity.

Neuroimaging techniques, including magnetic resonance imaging (MRI), are mainly used to exclude other neurological conditions. Functional imaging studies, such as dopamine transporter (DAT) scans, can support the diagnosis by demonstrating reduced dopaminergic activity in the basal ganglia. However, these tools are adjunctive and not routinely required.

Early and accurate diagnosis can be challenging, particularly in the initial stages when symptoms are subtle. Ongoing research aims to identify reliable biomarkers for earlier detection and disease monitoring.

Management and Treatment

Pharmacological Treatment

The cornerstone of Parkinson's disease treatment is dopamine replacement therapy. Levodopa, often combined with carbidopa, remains the most effective medication for alleviating motor symptoms. Other pharmacological agents include dopamine agonists, monoamine oxidase-B (MAO-B) inhibitors, and catechol-O-methyltransferase (COMT) inhibitors.

While these medications improve symptoms, long-term use, particularly of levodopa, may lead to motor complications such as fluctuations and dyskinesias. Treatment regimens are therefore individualized, balancing symptom control with side-effect management.

Surgical and Non-Pharmacological Approaches

Deep brain stimulation (DBS) is an established surgical option for selected patients with advanced Parkinson's disease who experience significant motor complications despite optimal medical therapy. DBS involves the implantation of electrodes in specific brain regions to modulate abnormal neural activity.Non-pharmacological interventions, including physiotherapy, occupational therapy, speech therapy, and regular physical exercise, play a crucial role in maintaining mobility, communication, and overall quality of life. Psychological support and patient

education are also essential components of comprehensive care.

Emerging Therapies and Future Directions

Current research efforts are focused on developing disease-modifying therapies that can slow or halt neurodegeneration. Approaches under investigation include immunotherapies targeting α-synuclein, gene therapy, stem cell-based treatments, and neuroprotective agents.

Advances in understanding the molecular mechanisms of Parkinson's disease have opened new avenues for personalized medicine. Improved biomarkers, digital health technologies, and artificial intelligence-based tools may enhance early diagnosis, disease monitoring, and treatment optimization in the future.

Conclusion

Parkinson's disease is a complex, progressive neurodegenerative disorder with significant motor and non-motor manifestations. Despite substantial advances in understanding its pathophysiology and improving symptomatic treatment, a definitive cure remains elusive. Early diagnosis, individualized treatment strategies, and multidisciplinary care are essential for improving patient outcomes

Ongoing research into the underlying mechanisms of Parkinson's disease offers hope for the development of disease-modifying therapies. As the global burden of PD continues to rise, sustained efforts in research, clinical care, and public health are critical to addressing the challenges posed by this debilitating condition

References

1. Dauer, W., & Przedborski, S. (2003). Parkinson's disease: mechanisms and models. *Neuron*, 39(6), 889–909.
2. Kalia, L. V., & Lang, A. E. (2015). Parkinson's disease. *The Lancet*, 386(9996), 896–912.
3. Poewe, W., Seppi, K., Tanner, C. M., et al. (2017). Parkinson disease. *Nature Reviews Disease Primers*, 3, 17013.
4. Obeso, J. A., Stamelou, M., Goetz, C. G., et al. (2017). Past, present, and future of Parkinson's disease: a special essay on the 200th anniversary of the Shaking Palsy. *Movement Disorders*, 32(9), 1264–1310.
5. Yeo, B.T.; Krienen, F.M.; Sepulcre, J.; Sabuncu, M.R.; Lashkari, D.; Hollinshead, M.; Roffman, J.L.; Smoller, J.W.; Zöllei, L.; Polimeni, J.R.; et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J. Neurophysiol.* 2011, *106*, 1125–1165.
6. Boeve, B.F.; Silber, M.H.; Saper, C.B.; Ferman, T.J.; Dickson, D.W.; Parisi, J.E.; Benarroch, E.E.; Ahlskog, J.E.; Smith, G.E.; Caselli, R.C.; et al. Pathophysiology of REM sleep behaviour disorder and relevance to neurodegenerative disease. *Brain* 2007, *130*, 2770–2788

Journal of Neuroscience and Neurodevelopmental Disorders (JNDD)