



UNDERSTANDING THE GENETICS OF PARKINSON'S DISEASE

Over the last 30 years, it has become clear that genetics drives a substantial proportion of the risk for Parkinson's disease. Research funded by the National Institutes of Health (NIH) continues to shape our mechanistic understanding of Parkinson's, improve early diagnosis, and contribute to emerging therapeutics that might slow or stop the progression of this disease.

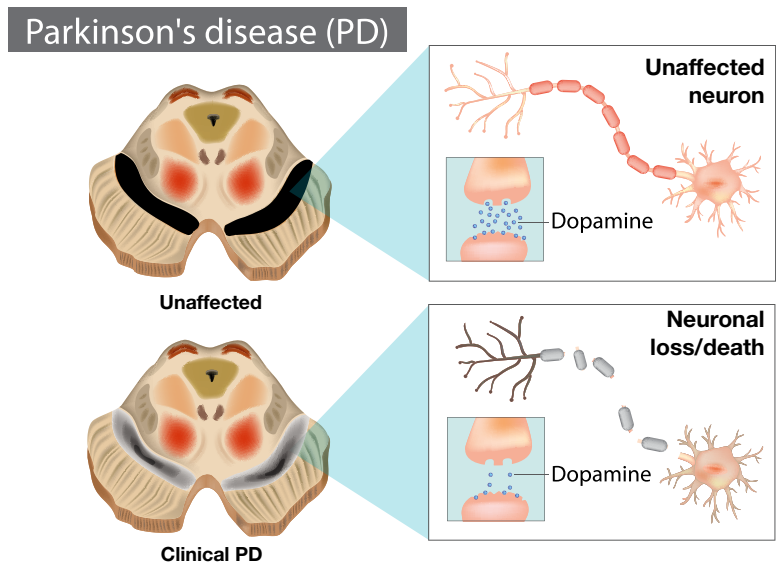
What is Parkinson's Disease?

Parkinson's disease is a chronic and relentlessly progressive movement disorder affecting more than 1% of people over age 60 - over 6 million people worldwide.¹ It occurs when specific nerve cells in the brain that produce the chemical messenger dopamine die or become impaired. This leads to difficulties with movement, including tremors, muscle rigidity, and impaired balance. These symptoms worsen over time.²

Genetic Contributions

The exact cause of Parkinson's disease is unknown, but it appears to be influenced by both genetic and environmental factors.

Some forms of Parkinson's have a strong genetic component and can be traced to specific genetic variants. These forms run in families and are known as *familial* Parkinson's. However, the majority of cases are sporadic. These are not caused by a single genetic mutation, but rather researchers are discovering they result from the individually small effects of weaker variants in many genes acting to increase susceptibility to environmental factors (such as head trauma or exposure to toxins).³



Scientists have discovered approximately 20 rare, disease-causing genetic mutations associated with familial Parkinson's.⁴ These were discovered through genetic studies of large families affected by the disease and include the genes *SNCA*, *PRKN*, *LRRK2*, and *GBA*.^{5,6}

Some of the same genes—and many more—have been implicated in sporadic Parkinson's. Scientists use genome-wide association studies involving large numbers of people with and without the disease to find these mutations. To date, scientists have identified 90 common genetic variants that individually contribute a small amount to the risk of developing Parkinson's.⁷

Research Informs Emerging Treatments

Currently, there are no treatments that can halt or slow the progression of Parkinson's disease. Available treatment options focus on replacing dopamine to help manage symptoms. However, over time, these treatments lose effectiveness and may cause significant side effects.⁸

NIH-supported research has identified specific genes and biological pathways that, in turn, have led to the development of new gene therapies for Parkinson's. There are currently gene therapies in clinical trials aimed at reducing the activity of genes responsible for some cases of familial Parkinson's, including *SNCA*, *LRRK2*, and *GBA*.⁹ However, because there are so many different genetic contributors to Parkinson's, these therapies may only be effective in the group of patients who harbor that specific mutation.¹⁰

Genetics research is informing another therapeutic avenue: targeting inflammation. Genome-wide association studies of Parkinson's have implicated genes involved in immune processes and inflammation in the brain. This adds to the evidence that brain inflammation drives nerve cell loss in Parkinson's and other neurodegenerative diseases. There are several emerging therapeutic strategies that target inflammation in Parkinson's. One is a new class of drugs known as GLP1R agonists, which are currently in clinical trials.^{11,12}

Why Aren't Gene Therapies Available Now?

We have made great progress in understanding the genetic basis of Parkinson's disease, and promising avenues for gene therapies are under investigation. However, it has remained challenging to translate the promising results seen in animal models to effective treatments for human patients, demonstrating gaps in our knowledge of the disease.

One issue is that by the time motor symptoms allow a diagnosis of Parkinson's, 40-60% of dopamine-producing nerve cells may already be lost.^{13,14} Further research is needed to understand when neurodegeneration begins in Parkinson's and when intervention is optimal.



How Can Congress Support Research?

Parkinson's disease affects over 6 million people worldwide. With the rapidly aging population, that number is expected to double by 2040.¹⁵ In addition to tragically disrupting the lives of Parkinson's patients and their families, the economic impact of the disease is immense, costing Americans nearly \$52 billion in 2018 alone.¹⁶

Sustained, robust federal funding for genetics and genomics research will lead to further discoveries that may inform prevention and treatment of Parkinson's disease. Such support will help not only millions of patients and their families, but also alleviate the public health burden on the country's healthcare system and economy.

Additional Resources

NIH: Parkinson's Disease:
<https://www.ninds.nih.gov/health-information/disorders/parkinsons-disease>

NIH National Institute on Aging
<https://www.nia.nih.gov/health/parkinsons-disease#:~:text=Parkinson's%20disease%20is%20a%20brain,have%20difficulty%20walking%20and%20talking.>

Parkinson's Foundation:
<https://www.parkinson.org/>

References:
[ashg.org/advocacy/fact-sheets/](https://www.parkinson.org/advocacy/fact-sheets/)