

Parkinson's Disease



National Institute of Neurological Disorders
and Stroke
National Institutes of Health

Hope Through Research

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What is Parkinson's disease?

Parkinson's disease (PD) is a movement disorder of the nervous system that worsens over time. As nerve cells (neurons) in parts of the brain weaken or are damaged or die, people may begin to notice problems with movement, tremor, stiffness in the limbs or the trunk of the body, or impaired balance. As these symptoms become more obvious, people may have difficulty walking, talking, or completing other simple tasks. Not everyone with one or more of these symptoms has PD, as the symptoms appear in other diseases as well.

No cure for PD exists today, but research is ongoing and medications or surgery can often provide substantial improvement with motor symptoms.

What are the symptoms of the disease?

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The four primary symptoms of PD are:

- **Tremor.** Tremor (shaking) often begins in a hand, although sometimes a foot or the jaw is affected first. The tremor associated with PD has a characteristic rhythmic back-and-forth motion that may involve the thumb and forefinger and appear as a “pill rolling.” It is most obvious when the hand is at rest or when a person is under stress. This tremor usually disappears during sleep or improves with a purposeful, intended movement.
- **Rigidity.** Rigidity (muscle stiffness), or a resistance to movement, affects most people with PD. The muscles remain constantly tense and contracted so that the person aches or feels stiff. The rigidity becomes obvious when another person tries to move the individual's arm, which will move only in ratchet-like or short, jerky movements known as “cogwheel” rigidity.

- **Bradykinesia.** This slowing down of spontaneous and automatic movement is particularly frustrating because it may make simple tasks difficult. The person cannot rapidly perform routine movements. Activities once performed quickly and easily—such as washing or dressing—may take much longer. There is often a decrease in facial expressions.
- **Postural instability.** Impaired balance and changes in posture can increase the risk of falls.

Do symptoms get worse?

PD does not affect everyone the same way. The rate of progression and the particular symptoms differ among individuals.

PD symptoms typically begin on one side of the body. However, the disease eventually affects both sides, although symptoms are often less severe on one side than on the other.

Early symptoms of PD may be subtle and occur gradually. Affected people may feel mild tremors or have difficulty getting out of a chair. Activities may take longer to complete than in the past. Muscles stiffen and movement may be slower. The person's face may lack expression and animation (known as “masked face”). People may notice that they speak too softly or with hesitation, or that their handwriting is slow and looks cramped or small. This very early period may last a long time before the more classical and obvious motor (movement) symptoms appear.

As the disease progresses, symptoms may begin to interfere with daily activities. Affected individuals may not be able to hold utensils steady or they may find that the shaking makes reading a newspaper difficult.

People with PD often develop a so-called *parkinsonian gait* that includes a tendency to lean forward, taking small quick steps as if hurrying (called festination), and reduced swinging in one or both arms. They may have trouble initiating movement (start hesitation), and they may stop suddenly as they walk (freezing).

What other changes may occur with PD?

Other problems may accompany PD, some of which can be treated with medication or different types of therapy (for example, physical therapy to maintain flexibility and help with balance, occupational therapy to learn new ways of handling everyday tasks that may be affected by the disease or its complications, vocational, and speech-language to help with speaking and swallowing).

- *Depression.* Some people lose their motivation and become dependent on family members.
- *Emotional changes.* Some people with PD become fearful and insecure, while others may become irritable or uncharacteristically pessimistic.
- *Difficulty with swallowing and chewing.* Problems with swallowing and chewing may occur in later stages of the disease. Food and saliva may collect in the mouth and back of the throat, which can result in choking or drooling. Getting adequate nutrition may be difficult.
- *Speech changes.* About half of all individuals with PD have speech difficulties that may be characterized as speaking too softly or in a monotone. Some may hesitate before speaking, slur, or speak too fast.

- *Urinary problems or constipation.* Bladder and bowel problems can occur due to the improper functioning of the autonomic nervous system, which is responsible for regulating smooth muscle activity.
- *Skin problems.* The skin on the face may become oily, particularly on the forehead and at the sides of the nose. The scalp may become oily too, resulting in dandruff. In other cases, the skin can become very dry.
- *Sleep problems.* Common sleep problems in PD include difficulty staying asleep at night, restless sleep, nightmares and emotional dreams, and drowsiness or sudden sleep onset during the day. Another common problem is “REM behavior disorder,” in which people act out their dreams, potentially resulting in injury to themselves or their bed partners. The medications used to treat PD may contribute to some of these sleep issues. Many of these problems respond to specific therapies.

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Difficulty staying asleep at night is a common sleep problem for people with PD.

- *Dementia or other cognitive problems.* Some people with PD develop memory problems and slow thinking. Cognitive problems become more severe in late stages of PD, and some people are diagnosed with Parkinson's disease dementia (PDD). Memory, social judgment, language, reasoning, or other mental skills may be affected.
- *Orthostatic hypotension.* Orthostatic hypotension is a sudden drop in blood pressure when a person stands up from a lying down or seated position. This may cause dizziness, lightheadedness, and, in extreme cases, loss of balance or fainting. Studies have suggested that, in PD, this problem results from a loss of nerve endings in the sympathetic nervous system that controls heart rate, blood pressure, and other automatic functions in the body. The medications used to treat PD may also contribute to this symptom.
- *Muscle cramps and dystonia.* The rigidity and lack of normal movement associated with PD often causes muscle cramps, especially in the legs and toes. PD can also be associated with dystonia—sustained muscle contractions that cause forced or twisted positions. Dystonia in PD is often caused by fluctuations in the body's level of dopamine (a chemical in the brain that helps nerve cells communicate and is involved with movement).
- *Pain.* Muscles and joints may ache because of the rigidity and abnormal postures often associated with the disease.
- *Fatigue and loss of energy.* Many people with PD often have fatigue, especially late in the day. Fatigue may be associated with depression or sleep disorders, but it may also result from

muscle stress or from overdoing activity when the person feels well. Fatigue may also result from *akinesia*—trouble initiating or carrying out movement.

- **Sexual dysfunction.** Because of its effects on nerve signals from the brain, PD may cause sexual dysfunction. PD-related depression or use of certain medications may also cause decreased sex drive and other problems.
- Hallucinations, delusions, and other psychotic symptoms can be caused by the drugs prescribed for PD.

Who gets Parkinson's disease?

Risk factors for PD include:

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- **Age.** The average age of onset is about 70 years, and the incidence rises significantly with advancing age. However, a small percent of people with PD have “early-onset” disease that begins before the age of 50.
- **Sex.** PD affects more men than women.
- **Heredity.** People with one or more close relatives who have PD have an increased risk of developing the disease themselves. An estimated 15 to 25 percent of people with PD have a known relative with the disease. Some cases of the disease can be traced to specific genetic mutations.
- **Exposure to pesticides.** Studies show an increased risk of PD in people who live in rural areas with increased pesticide use.

What causes the disease?

The precise cause of PD is unknown, although some cases of PD are hereditary and can be traced to specific genetic mutations. Most cases are sporadic—that is, the disease does not typically run in families. It is thought that PD likely results from a combination of genetics and exposure to one or more unknown environmental factors that trigger the disease.

Parkinson’s disease occurs when nerve cells, or neurons, in the brain die or become impaired. Although many brain areas are affected, the most common symptoms result from the loss of neurons in an area near the base of the brain called the *substantia nigra*. Normally, the neurons in this area produce dopamine. Dopamine is the chemical messenger responsible for transmitting signals between the substantia nigra and the next “relay station” of the brain, the *corpus striatum*, to produce smooth, purposeful movement. Loss of dopamine results in abnormal nerve firing patterns within the brain that cause impaired movement. Studies have shown that most people with Parkinson’s have lost 60 to 80 percent or more of the dopamine-producing cells in the substantia nigra by the time symptoms appear. People with PD also lose the nerve endings that produce the neurotransmitter norepinephrine—the main chemical messenger to the part of the nervous system that controls many automatic functions of the body, such as pulse and blood pressure. The loss of norepinephrine might explain several of the non-motor features seen in PD, including fatigue and abnormalities of blood pressure regulation.

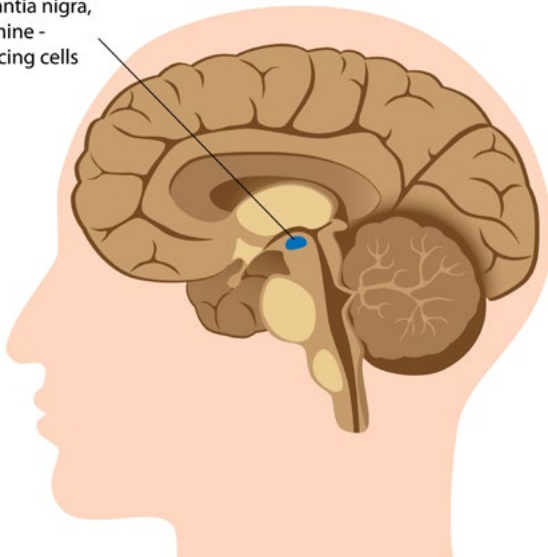
The protein alpha-synuclein. The affected brain cells of people with PD contain Lewy bodies—deposits of the protein alpha-synuclein. Researchers do not yet know why Lewy bodies form or what role they play in the disease. Some research suggests that the cell's protein disposal system may fail in people with PD, causing proteins to build up to harmful levels and trigger cell death. Additional studies have found evidence that clumps of protein that develop inside brain cells of people with PD may contribute to the death of neurons.

Genetics. Several genetic mutations are associated with PD, including the alpha-synuclein gene, and many more genes have been tentatively linked to the disorder. The same genes and proteins that are altered in inherited cases may also be altered in sporadic cases by environmental toxins or other factors.

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Parkinson's disease

Substantia nigra,
dopamine -
producing cells



The most common symptoms of PD result from the loss of brain cells in the substantia nigra.

Environment. Exposure to certain toxins has caused parkinsonian symptoms in rare circumstances (such as exposure to MPTP, an illicit drug, or in miners exposed to the metal manganese). Other still-unidentified environmental factors may also cause PD in genetically susceptible individuals.

Mitochondria. Mitochondria are the energy-producing components of the cell and abnormalities in the mitochondria are major sources of free radicals—molecules that damage membranes, proteins, DNA, and other parts of the cell. This damage is often referred to as oxidative stress. Oxidative stress-related changes, including free radical damage to DNA, proteins, and fats, have been detected in the brains of individuals with PD. Some mutations that affect mitochondrial function have been identified as causes of PD.

What genes are linked to Parkinson's disease?

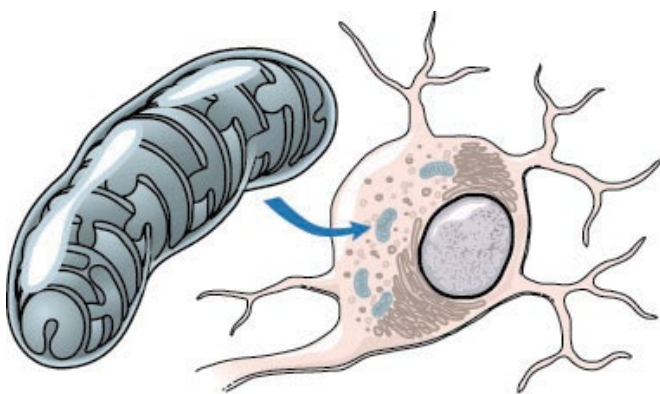
Several genes have been definitively linked to PD:

- **SCNA.** This gene, which makes the protein alpha-synuclein, was the first gene identified to be associated with Parkinson's. Research findings by the National Institutes of Health and other institutions prompted studies of the role of alpha-synuclein in PD, which led to the discovery that Lewy bodies seen in all cases of PD contain clumps of alpha-synuclein. This discovery revealed the link between hereditary and sporadic forms of the disease.
- **LRRK2.** Mutations in LRRK2 were originally identified in several English and Basque families as a cause of a late-onset PD. Subsequent studies

have identified mutations of this gene in other families with PD (such as European Ashkenazi Jewish families) as well as in a small percentage of people with apparently sporadic PD. LRRK2 mutations are a major cause of PD in North Africa and the Middle East.

- **DJ-1.** This gene normally helps regulate gene activity and protect cells from oxidative stress and can cause rare, early forms of PD.
- **PRKN (Parkin).** The parkin gene is translated into a protein that normally helps cells break down and recycle proteins.
- **PINK1.** PINK1 codes for a protein active in mitochondria. Mutations in this gene appear to increase susceptibility to cellular stress. PINK1 has been linked to early forms of PD.
- **GBA (glucocerebrosidase-beta).** Mutations in GBA cause Gaucher disease (in which fatty acids, oils, waxes, and steroids accumulate in the brain), but different changes in this gene are associated with an increased risk for Parkinson's disease as well.

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Abnormalities in the mitochondria—the energy-producing components of a cell—are major sources of free radicals, which are molecules that damage membranes, proteins, DNA, and other parts of the cell.

What diseases and conditions resemble Parkinson's disease?

PD is the most common form of *parkinsonism*, in which disorders of other causes produce features and symptoms that closely resemble Parkinson's disease. Many disorders can cause symptoms similar to those of PD, including:

- **Multiple system atrophy (MSA)** refers to a set of slowly progressive disorders that affect the central and autonomic nervous systems. The protein alpha-synuclein forms harmful filament-like aggregates in the supporting cells in the brain called oligodendroglia. MSA may have symptoms that resemble PD. It may also take a form that primarily produces poor coordination and slurred speech, or it may involve a combination of these symptoms. MSA with parkinsonian symptoms is sometimes referred to as MSA-P (or striatonigral degeneration).
- **Dementia with Lewy bodies** is associated with the same abnormal protein deposits (Lewy bodies) found in Parkinson's disease but in widespread areas throughout the brain. Symptoms may range from primary parkinsonian symptoms such as bradykinesia, rigidity, tremor, and shuffling walk, to symptoms similar to those of Alzheimer's disease (memory loss, poor judgment, and confusion). These symptoms may fluctuate, or wax and wane dramatically. Other symptoms may include visual hallucinations, other psychiatric disturbances such as delusions and depression, and problems with cognition.

- **Progressive supranuclear palsy (PSP)** is a rare, progressive brain disorder caused by a gradual deterioration of cells in the brain stem. Symptoms may include problems with control of gait and balance (people often tend to fall early in the course of PSP), an inability to move the eyes properly, and alterations of mood and behavior, including depression and apathy as well as mild dementia. PSP is characterized by clumps of a protein called tau.
- **Corticobasal degeneration (CBD)** results from atrophy of multiple areas of the brain, including the cerebral cortex and the basal ganglia. Initial symptoms may first appear on one side of the body, but eventually affect both sides. Symptoms include rigidity, impaired balance, and problems with coordination. Other symptoms may include dystonia that affects one side of the body, cognitive and visual-spatial impairments, apraxia (loss of the ability to make familiar, purposeful movements), hesitant and halting speech, myoclonus (muscular jerks), and dysphagia (difficulty swallowing). CBD also is characterized by deposits of the tau protein.

Several diseases, including MSA, CBD, and PSP, are sometimes referred to as “*Parkinson’s-plus*” diseases because they have the symptoms of PD plus additional features.

In very rare cases, parkinsonian symptoms may appear in people before the age of 20. This condition is called juvenile parkinsonism. It often begins with dystonia and bradykinesia, and the symptoms often improve with levodopa medication.

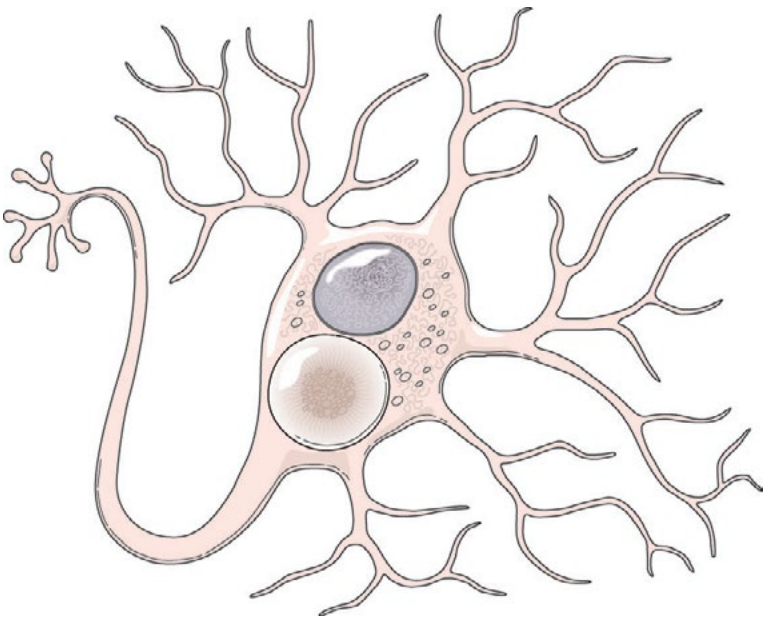
How is Parkinson's disease diagnosed?

There are currently no specific tests that diagnose PD. The diagnosis is based on:

- medical history and a neurological examination
- blood and laboratory tests, to rule out other disorders that may be causing the symptoms
- brain scans to rule out other disorders. However, computed tomography (CT) and magnetic resonance imaging (MRI) brain scans of people with PD usually appear normal.

In rare cases, where people have a clearly inherited form of PD, researchers can test for known gene mutations as a way of determining an individual's risk of developing the disease. However, this genetic testing can have far-reaching implications and people should carefully consider whether they want to know the results of such tests.

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Dementia with Lewy bodies is a neurodegenerative disorder associated with the same abnormal protein deposits, called Lewy bodies, found in PD.

What is the prognosis?

The average life expectancy of a person with PD is generally the same as for people who do not have the disease. Fortunately, there are many treatment options available for people with PD. However, in the late stages, PD may no longer respond to medications and can become associated with serious complications such as choking, pneumonia, and falls.

PD is a slowly progressive disorder. It is not possible to predict what course the disease will take for an individual person.

How is the disease treated?

At present, there is no cure for PD, but medications or surgery can often provide improvement in the motor symptoms.

Drug Therapy

Medications for PD fall into three categories:

- drugs that increase the level of dopamine in the brain. The most common drugs for PD are dopamine precursors—substances such as levodopa that cross the blood-brain barrier and are then changed into dopamine. Other drugs mimic dopamine or prevent or slow its breakdown.
- drugs that affect other neurotransmitters in the body in order to ease some of the symptoms of the disease. For example, *anticholinergic drugs* interfere with production or uptake of the neurotransmitter acetylcholine. These can be effective in reducing tremors.

- medications that help control the non-motor symptoms of the disease, that is, the symptoms that don't affect movement. For example, people with PD-related depression may be prescribed antidepressants.

Symptoms may significantly improve at first with medication but symptoms reappear over time as the Parkinson's worsens and drugs become less effective.

Medications for Parkinson's include:

- **Levodopa/Carbidopa.** The cornerstone of therapy for PD is the drug levodopa (also called L-dopa). Nerve cells can use levodopa to make dopamine and replenish the brain's reduced supply. People cannot simply take dopamine pills because dopamine does not easily pass through the blood-brain barrier. (The blood-brain barrier is a protective lining of cells inside blood vessels that regulate the transport of oxygen, glucose, and other substances in the brain.)

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Usually, people are given levodopa combined with another substance called carbidopa. When added to levodopa, carbidopa prevents the conversion of levodopa into dopamine except for in the brain; this stops or diminishes the side effects due to dopamine in the bloodstream. Levodopa/carbidopa is often very successful at reducing or eliminating the tremors and other motor symptoms of PD during the early stages of the disease. Levodopa usually helps most with the slowing of movement and rigidity. It allows most people with PD to extend the period of time in which they can lead active, productive lives.

People may need to increase their dose of levodopa gradually for maximum benefit. Levodopa can reduce the symptoms of PD but it does not replace lost nerve cells or stop its progression.

Initial side effects of levodopa/carbidopa may include:

- nausea
- low blood pressure
- restlessness
- drowsiness or sudden sleep onset.

Side effects of long-term or extended use of levodopa may include:

- hallucinations and psychosis
- dyskinesia, or involuntary movements such as twisting and writhing that may be either mild or severe.

Later in the course of the disease, people with PD may begin to notice more pronounced symptoms before their first dose of medication in the morning

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Presently, there is no cure for PD, however, medications or surgery may improve motor symptoms. When recommending treatment, a doctor will assess a person's symptoms and then tailor therapy to the person's particular condition.

and between doses as the period of effectiveness after each dose begins to shorten, called the *wearing-off effect*. People experience sudden, unpredictable “off periods,” where the medications do not seem to be working. One approach to alleviating these side effects is to take levodopa more often and in smaller amounts. People with PD should never stop taking levodopa without their physician’s input, because rapidly withdrawing the drug can have potentially serious side effects.

- **Dopamine agonists.** These mimic the role of dopamine in the brain and can be given alone or with levodopa. They are somewhat less effective than levodopa in treating PD symptoms but work for longer periods of time. Many of the potential side effects are similar to those associated with the use of levodopa, including drowsiness, sudden sleep onset, hallucinations, confusion, dyskinesias, edema (swelling due to excess fluid in body tissues), nightmares, and vomiting. In rare cases, they can cause an uncontrollable desire to gamble, hypersexuality, or compulsive shopping. Dopamine agonist drugs include apomorphine, pramipexole, ropinirole, and rotigotine.
- **MAO-B inhibitors.** These drugs block or reduce the activity of the enzyme monoamine oxidase B, or MAO-B, which breaks down dopamine in the brain. MAO-B inhibitors cause dopamine to accumulate in surviving nerve cells and reduce the symptoms of PD. These medications include selegiline and rasagiline. Studies supported by the NINDS have shown that selegiline (also called deprenyl) can delay the need for levodopa therapy by up to a year or more. When selegiline is given with levodopa, it appears to enhance and prolong the response to levodopa and thus may reduce wearing-off.

Selegiline is usually well-tolerated, although side effects may include nausea, orthostatic hypotension, or insomnia. The drug rasagiline is used in treating the motor symptoms of PD with or without levodopa.

- **COMT inhibitors.** COMT stands for catechol-O-methyltransferase, another enzyme that breaks down dopamine. The drugs entacapone and tolcapone prolong the effects of levodopa by preventing the breakdown of dopamine. COMT inhibitors can decrease the duration of “off periods” of one’s dose of levodopa. Side effects may include diarrhea, nausea, sleep disturbances, dizziness, urine discoloration, abdominal pain, low blood pressure, or hallucinations. In a few rare cases, tolcapone has caused severe liver disease, and people taking tolcapone need regular monitoring of their liver function.
- **Amantadine.** This antiviral drug can help reduce symptoms of PD and levodopa-induced dyskinesia. It can be prescribed alone in the early stages of the disease and also can be used with an anticholinergic drug or levodopa. After several months, amantadine’s effectiveness wears off in up to half of the people taking it. Amantadine’s side effects may include insomnia, mottled skin, edema, agitation, or hallucinations. Researchers are not certain how amantadine works in PD, but it may increase the effects of dopamine.
- **Anticholinergics.** These drugs, which include trihexyphenidyl, bztropine, and ethopropazine, decrease the activity of the neurotransmitter acetylcholine and can be particularly effective for tremor associated with PD. Side effects may include dry mouth, constipation, urinary

retention, hallucinations, memory loss, blurred vision, and confusion.

When recommending a course of treatment, a doctor will assess how much the symptoms disrupt the person's life and then tailor therapy to the person's particular condition. Since no two people will react the same way to a given drug, it may take time and patience to get the dose just right. Even then, symptoms may not be completely alleviated.

Surgery

Before the discovery of levodopa, surgery was an option for treating PD. Studies in the past few decades have led to great improvements in surgical techniques, and surgery is again considered for people with PD for whom drug therapy is no longer sufficient.

Medications to Treat the Motor Symptoms of Parkinson's Disease

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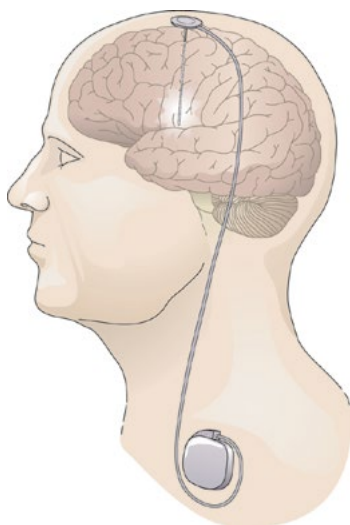
Category	Generic	Brand name
Drugs that increase brain levels of dopamine	Levodopa/carbidopa	Parcopa, Sinemet
Drugs that mimic dopamine (dopamine agonists)	Apomorphine Pramipexole Ropinirole Rotigotine	Apokyn Mirapex Requip Neupro
Drugs that inhibit dopamine breakdown (MAO-B inhibitors)	Rasagiline Selegiline (deprenyl)	Azilect Eldepryl, Zelapar
Drugs that inhibit dopamine breakdown (COMT inhibitors)	Entacapone Tolcapone	Comtan Tasmar
Drugs that decrease the action of acetylcholine (anticholinergics)	Benzotropine Ethopropazine Trihexyphenidyl	Cogentin Parsidol Artane
Drugs with an unknown mechanism of action for PD	Amantadine	Symmetrek

Pallidotomy and Thalamotomy. The earliest types of surgery for PD involved selectively destroying specific parts of the brain that contribute to PD symptoms. Surgical techniques have been refined and can be very effective for the motor symptoms of PD. The most common lesion surgery is called *pallidotomy*. In this procedure, a surgeon selectively destroys a portion of the brain called the globus pallidus. Pallidotomy can improve symptoms of tremor, rigidity, and bradykinesia, possibly by interrupting the connections between the globus pallidus and the striatum or thalamus. Some studies have also found that pallidotomy can improve gait and balance and reduce the amount of levodopa people require, thus reducing drug-induced dyskinesias. Another procedure, called *thalamotomy*, involves surgically destroying part of the thalamus; this approach is useful primarily to reduce tremor.

Because these procedures cause permanent destruction of small amounts of brain tissue, they have largely been replaced by *deep brain stimulation* for treatment of PD. However, a method using focused ultrasound from outside the head is being tested because it creates lesions without the need for surgery.

Deep Brain Stimulation. Deep brain stimulation, or DBS, uses an electrode surgically implanted into part of the brain, typically the subthalamic nucleus or the globus pallidus. Similar to a cardiac pacemaker, a pulse generator (battery pack) that is implanted in the chest area under the collarbone sends finely controlled electrical signals to the electrode(s) via a wire placed under the skin. When turned on using an external wand, the pulse generator and electrodes painlessly stimulate the brain in a

way that helps to block signals that cause many of the motor symptoms of PD. (The signal also can be turned off using the wand.) Individuals must return to the medical center frequently for several months after DBS surgery in order to have the stimulation adjusted very carefully to give the best results. DBS is approved by the U.S. Food and Drug Administration and is widely used as a treatment for PD.



Deep brain stimulation, which involves surgical stimulation of the brain, helps to block signals that cause many of the motor symptoms of PD.

DBS is primarily used to stimulate one of three brain regions: the subthalamic nucleus, the globus pallidus interna, or the thalamus. Stimulation of either the globus pallidus or the subthalamic nucleus can reduce tremor, bradykinesia, and rigidity. Stimulation of the thalamus is useful primarily for reducing tremor.

DBS does not stop PD from progressing, and some problems may gradually return. While the motor function benefits of DBS can be substantial, it usually does not help with speech problems, “freezing,” posture, balance, anxiety, depression, or dementia.

DBS is generally appropriate for people with levodopa-responsive PD who have developed dyskinesias or other disabling “off” symptoms despite drug therapy. DBS has not been demonstrated to be of benefit for “atypical” parkinsonian syndromes such as multiple system atrophy, progressive supranuclear palsy, or post-traumatic parkinsonism, which also do not improve with Parkinson’s medications.

Complementary and Supportive Therapies

A wide variety of complementary and supportive therapies may be used for PD, including:

A healthy diet. At this time there are no specific vitamins, minerals, or other nutrients that have any proven therapeutic value in PD. The National Institute of Neurological Disorders and Stroke (NINDS) and other components of the National Institutes of Health are funding research to determine if caffeine, antioxidants, and other dietary factors may be beneficial for preventing or treating PD. A normal, healthy diet can promote overall well-being for people with PD just as it would for anyone else. Eating a fiber-rich diet and drinking plenty of fluids also can help alleviate constipation. A high protein diet, however, may limit levodopa's absorption.

Exercise. Exercise can help people with PD improve their mobility, flexibility, and body strength. It also can improve well-being, balance, minimize gait problems, and strengthen certain muscles so that people can speak and swallow better. General physical activity, such as walking, gardening, swimming, calisthenics, and using exercise machines, can have other benefit. People with PD should always check with their doctors before beginning a new exercise program.

Alternative approaches that are used by some individuals with PD include:

- tai chi. A NINDS-funded clinical trial demonstrated the benefit of tai chi exercise compared to resistance or stretching exercises in people with PD.
- massage therapy, to reduce muscle tension
- yoga, to increase stretching and flexibility
- hypnosis
- acupuncture



Some complementary and supportive therapies used by people with PD include yoga, massage therapy, acupuncture, Alexander technique, and hypnosis.

- the Alexander technique, which optimizes posture and muscle activity.

How can people cope with Parkinson's disease?

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While PD usually progresses slowly, eventually daily routines may be affected—from socializing with friends to earning a living and taking care of a home. These changes can be difficult to accept. Support groups can help people cope with the disease's emotional impact. These groups also can provide valuable information, advice, and experience to help people with PD, their families, and their caregivers deal with a wide range of issues, including locating doctors familiar with the disease and coping with physical limitations. A list of national organizations that can help people locate support groups in their communities appears at the end of this information. Individual or family counseling may also help people find ways to cope with PD.

People with PD may also benefit from being proactive and finding out as much as possible about the disease in order to alleviate fear of the unknown and to take a

positive role in maintaining their health. Many people with PD continue to work either full- or part-time, although they may need to adjust their schedule and working environment to accommodate their symptoms.

What research is being done?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use the knowledge to reduce the burden of neurological disease. NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world. NINDS conducts and supports three types of research: *basic*—scientific discoveries in the lab, *clinical*—developing and studying therapeutic approaches to Parkinson’s disease, and *translational*—focused on tools and resources that speed the development of therapeutics into practice. The goals of NINDS-supported research on Parkinson’s disease are to better understand and diagnose PD, develop new treatments, and ultimately, prevent PD. NINDS also supports training for the next generation of PD researchers and clinicians and serves as an important source of information for people with PD and their families.

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Establishing PD research priorities

The NINDS-organized *Parkinson’s Disease 2014: Advancing Research, Improving Lives* conference brought together researchers, clinicians, patients, caregivers, and nonprofit organizations to develop 31 prioritized recommendations for research on PD. These recommendations are being implemented through investigator-initiated grants and several NINDS programs.

NINDS and the NIH's National Institute of Environmental Health Sciences held the *Parkinson's Disease: Understanding the Environment and Gene Connection* workshop to identify priorities for advancing research on environmental contributors to PD.

Research recommendations for Lewy Body Dementia, including Parkinson's disease dementia, were updated during the *NIH Alzheimer's Disease-Related Dementias Summit 2019*.

Key programs and resources

The Parkinson's Disease Biomarkers Programs (PDBP), a major NINDS initiative, is aimed at discovering ways to identify individuals at risk for developing PD and Lewy Body Dementia and to track the progression of the disease. It funds research and collects human biological samples and clinical data to identify biomarkers (signs that may indicate risk of a disease and improve diagnosis) that will speed the development of novel therapeutics for PD. Goals are improving clinical trials and earlier diagnosis and treatment. Projects are actively recruiting volunteers at sites across the U.S. NINDS also collaborates with the Michael J. Fox Foundation for Parkinson's Research (MJFF) on **BioFIND**, a project collecting biological samples and clinical data from healthy volunteers and those with PD. For more information about the PDBP and how you can get involved, please visit the PDBP website at <http://pdbp.ninds.nih.gov/>.

The NINDS Morris K. Udall Centers of Excellence for Parkinson's Disease Research program supports research centers across the country that work collaboratively to study PD disease mechanisms, the genetic contributions to PD, and potential therapeutic targets and treatment strategies.

The **Accelerating Medicines Partnership for Parkinson's Disease (AMP-PD)** program is a partnership between the National Institutes of Health, multiple biopharmaceutical and life sciences communities, and nonprofit advocacy organizations to identify and validate biomarkers that can track the progression of PD. It allows scientists to perform large-scale genetic analyses and share data to more quickly bring new medicines to people either with or at risk of PD.

The **NINDS Intramural Research Program** conducts clinical studies to better understand PD mechanisms and develop novel and improve treatments.

The **NINDS Biospecimens Repositories** store and distribute DNA, cells, blood samples, cerebrospinal fluid, and autopsy tissue to PD researchers around the world.

Disease research

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NINDS research looks at all aspects of the mechanisms of PD, identifying clues to PD development and its processes, and improving current therapies and testing new ones. Research efforts include:

Cellular Processes. Mutations in alpha-synuclein and dozens of genes (some of which were discovered at NIH) are known to either cause PD or modify a person's risk of developing it. Researchers are investigating how the cellular processes controlled by these genes contribute to neurodegeneration, including the toxic accumulation of alpha-synuclein and how the loss of dopamine impairs communication between nerve cells.

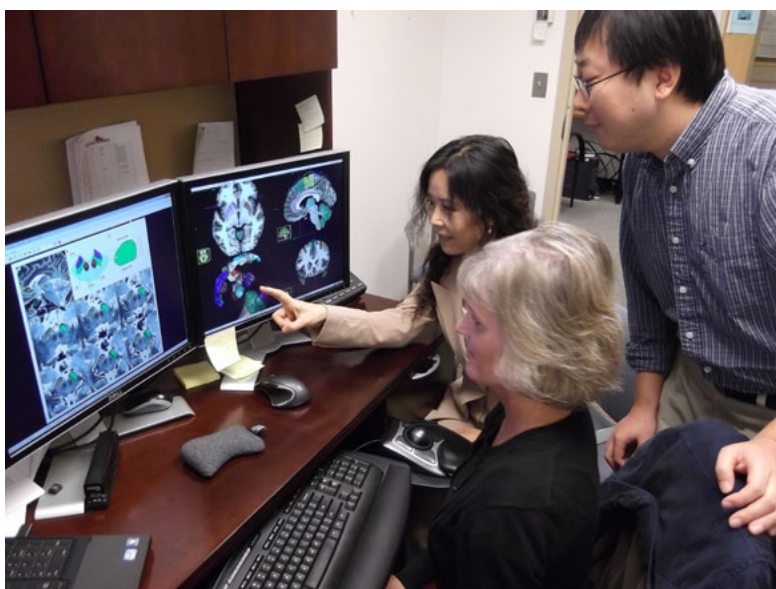
Several cellular process that damage or kill nerve cells in PD are involved in other neurodegenerative diseases such as Lewy Body Dementia, Alzheimer's disease, and amyotrophic lateral sclerosis (ALS). NINDS research is gaining a better understanding of the similarities and differences between these diseases that may lead to treatments for all of them.

Deep brain stimulation. NINDS has been a pioneer in the study and development of DBS, which is now considered a standard treatment for PD. Current NINDS-funded projects include research to fine-tune the optimal site within the brain to implant the DBS electrode, studies to better understand the therapeutic effect of DBS on neural circuitry and brain regions affected by PD, and different forms of brain stimulation on different parts of the brain.

Environmental studies. Risk factors such as repeated occupational exposure to certain pesticides and chemical solvents may influence who develops PD. A NINDS-funded research consortium is hunting for environmental risk factors that increase susceptibility to developing PD.

Genetic studies. A better understanding of genetic risk factors is playing a critical role in revealing PD disease mechanisms. A NINDS workshop contributed to the

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Scientists involved in the Parkinson's Disease Biomarkers Program aim to identify biomarkers that will speed the development of novel therapeutics for PD.

development of NeuroX, the first DNA chip that can identify genetic changes in persons at risk for a number of late-onset neurodegenerative diseases, including PD. Another NINDS collaborative, the Consortium On Risk for Early-onset Parkinson's Disease (CORE PD), hopes to identify the genetic factors that contribute to the development of early-onset PD. Current clinical studies include the genetic connection to memory and motor behavior, the search for genes that may increase the risk of PD and related neurodegenerative disorders, and identifying biomarkers for PD.

Motor complications. Involuntary movement, including dyskinesia (difficulty controlling intended muscle movement), as well as tremor, dystonia (involuntary muscle contractions), freezing of gait (inability to start walking), and other motor complications become evident as PD progresses; these symptoms are often difficult to treat. NINDS scientists have studied the safety and effectiveness of drugs and interventions in alleviating motor symptoms in persons with PD. For example, basic research using adenosine found it could improve motor complications associated with PD. A current NINDS clinical study of motor complications is testing an at-home device to evaluate PD movement symptoms while performing different tasks.

Exercise: Exercise routines are often recommended to help individuals with PD maintain movement and balance necessary for everyday living. Research continues on the role of exercise in slowing the decline of motor function and modifying the course of PD.

Neuroprotective Drugs. NINDS supports basic, clinical, and translational research aimed at protecting nerve cells from the damage caused by PD. The NINDS-funded NeuroNext Network is designed to test new therapies and to validate biomarkers in a number of neurological disorders, including Parkinson's disease.



Current PD research includes genetic studies to gain a better understanding of genetic risk factors that may play a critical role in the mechanisms of the disease.

Parkinson's Disease Clinical Studies offer an opportunity to help researchers find better ways to safely detect, treat, or prevent PD and therefore hope for individuals now and in the future. Current studies include:

- genetics and PD
- the search for PD biomarkers
- experimental therapies
- diagnostic imaging
- deep brain stimulation
- cognition in PD.

NINDS conducts clinical studies on Parkinson's disease at the NIH research campus in Bethesda, Maryland, and supports PD studies at medical research centers throughout the United States. But studies can be completed only if people volunteer to participate. By participating in a clinical study, healthy individuals and people living with Parkinson's disease can greatly benefit the lives of those affected by this disorder. Talk with your doctor about clinical studies and help to make the difference in improving the quality of life for all people with Parkinson's disease. For more information about

NINDS clinical trials on PD, see www.clinicaltrials.gov and search for “Parkinson AND NINDS.”

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute’s Brain Resources and Information Network (BRAIN) at:

BRAIN

P.O. Box 5801
Bethesda, MD 20824
800-352-9424
www.ninds.nih.gov

Information also is available from the following organizations:

American Parkinson Disease Association

135 Parkinson Avenue
Staten Island, NY 10305-1425
718-981-8001 or 800-223-2732
www.apdaparkinson.org

Bachmann-Strauss Dystonia & Parkinson Foundation

P.O. Box 38016
Albany, NY 12203
212-509-0995
www.dystonia-parkinsons.org

Davis Phinney Foundation

357 McCaslin Boulevard, Suite 105
Louisville, CO 80027
303-733-3340 or 866-358-0285
www.davisphinneyfoundation.org

Michael J. Fox Foundation for Parkinson's Research

Grand Central Station

P.O. Box 4777

New York, NY 10163

800-708-7644

www.michaeljfox.org

Parkinson Alliance

P.O. Box 308

Kingston, NJ 08528-0308

609-688-0870 or 800-579-8440

www.parkinsonalliance.org

Parkinson's Foundation

1359 Broadway, Suite 1509

New York, NY 10018

800-473-4636

<https://parkinson.org>

The Parkinson's Institute and Clinical Center

2500 Hospital Drive

Building 10, Suite 1

Mountain View, CA 94040

408-734-2800 or 800-655-2273

www.thepi.org

Parkinson's Resource Organization

74090 El Paseo, Suite 104

Palm Desert, CA 92260

760-773-5628 or 877-775-4111

www.parkinsonsresource.org

Lewy Body Dementia Association

912 Killian Hill Road, SW

Lilburn, GA 30024

404-935-6444

www.lbda.org



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