Parkinson's Disease

Hope through Research

National Institute of Neurological Disorders and Stroke
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What is Parkinson's disease?

Parkinson's disease (PD) is a degenerative disorder of the central nervous system that belongs to a group of conditions called movement disorders. It is both chronic, meaning it persists over a long period of time, and progressive, meaning its symptoms grow worse over time. As nerve cells (neurons) in parts of the brain become impaired 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 pronounced, 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.

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 genetic susceptibility and exposure to one or more unknown environmental factors that trigger the disease.

PD is the most common form of *parkinsonism*[1], in which disorders of other causes produce features and symptoms that closely resemble Parkinson's disease. While most forms of parkinsonism have no known cause, there are cases in which the cause is known or suspected or where the symptoms result from another disorder.

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[1] Words in italics appear in a Glossary at the end of this information.

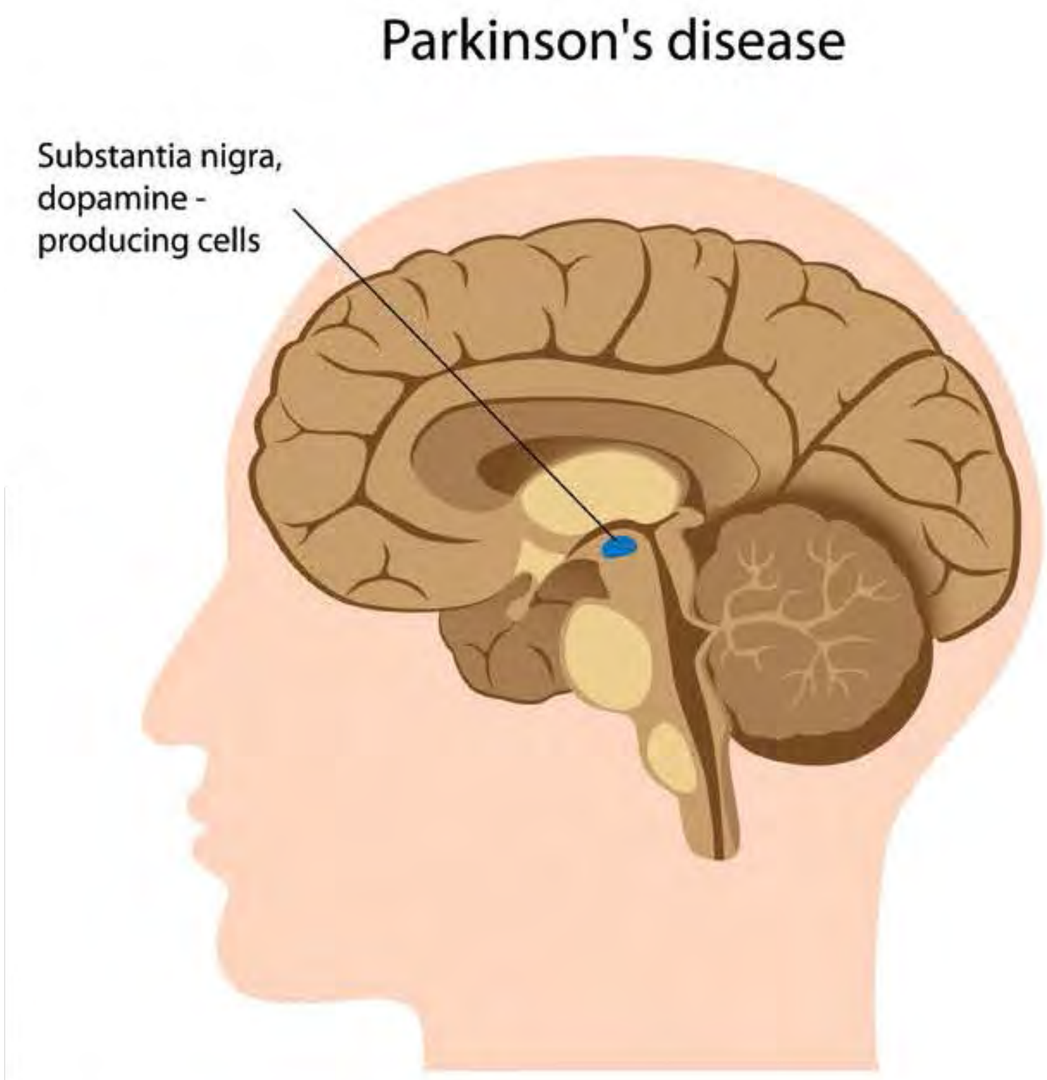
No cure for PD exists today, but research is ongoing and medications or surgery can often provide substantial improvement with motor symptoms.

What causes 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 an important brain chemical known as *dopamine*. Dopamine is a 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.

PD does not only affect the brain or the central nervous system, but the entire body. In fact, it is widely believed that the disease starts in the peripheral nervous system, in areas such as the intestine, where the nature and features of the disease can be present many years before involving the brain. The autonomic nervous system, which controls many automatic functions such as breathing and movements of the intestines, is affected, leading to characteristic signs and symptoms ranging from constipation to pain to skin changes. While the brain involvement is

responsible for the core features, other affected locations contribute to the complicated picture of PD.



The most common symptoms of PD result from the loss of neurons in a part of the brain called the substania nigra.

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. Some researchers speculate that the protein buildup in Lewy bodies is part of an unsuccessful attempt to protect the cell from the toxicity of smaller aggregates, or collections, of synuclein.

Genetics. Scientists have identified several genetic mutations associated with PD, including the alpha-synuclein gene, and many more genes have been tentatively linked to the disorder. Studying the genes responsible for inherited cases of PD can help researchers understand both inherited and sporadic cases. The same genes and proteins that are altered in inherited cases may also be altered in sporadic cases by environmental toxins or other factors. Researchers also hope that discovering genes will help identify new ways of treating PD.

Environment. Exposure to certain toxins has caused parkinsonian symptoms in rare circumstances (such

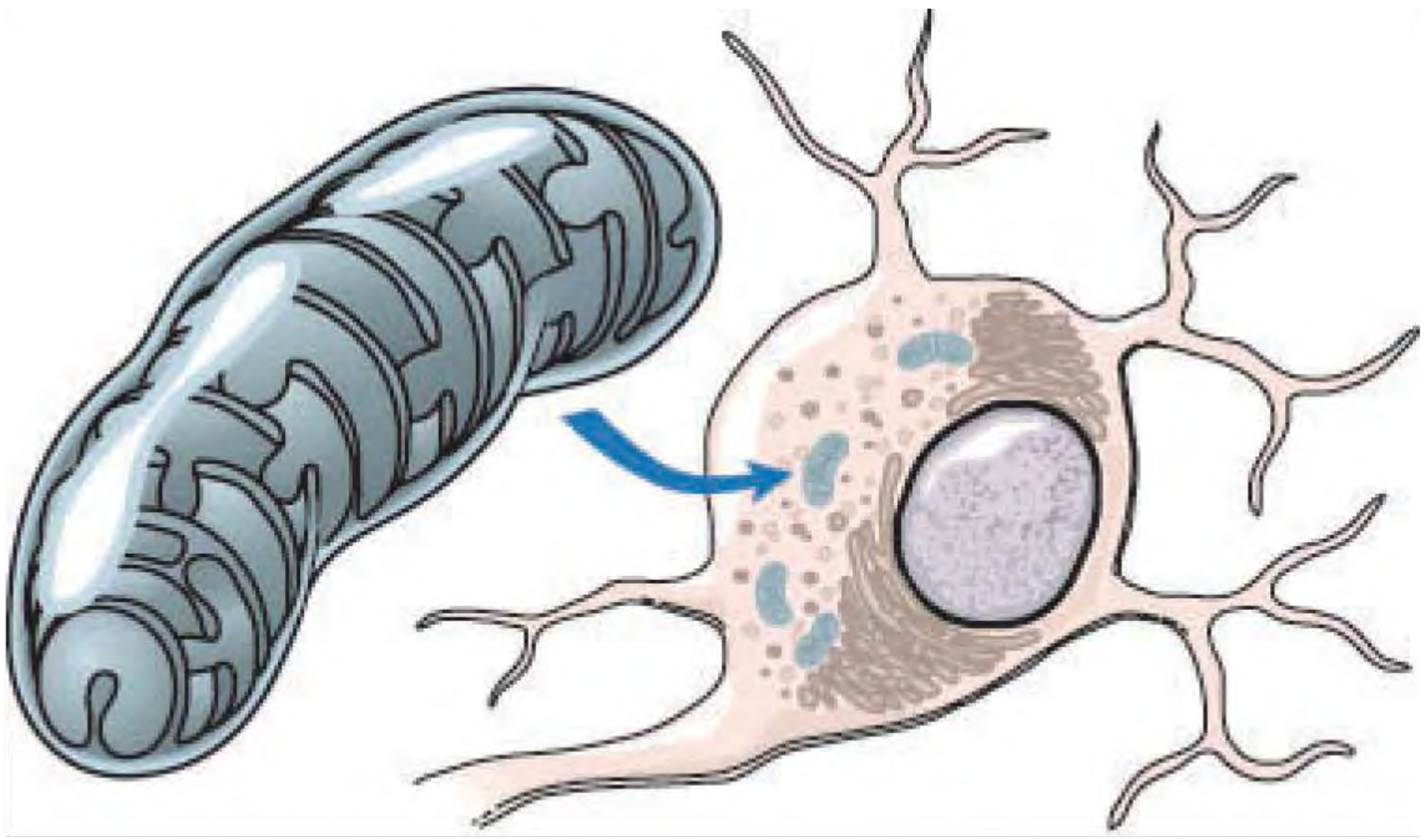
as exposure to MPTP, an illicit drug, or in miners exposed to the metal manganese). Other still-unidentified environmental factors may also cause PD in genetically susceptible individuals.

Mitochondria. Several lines of research suggest that mitochondria may play a role in the development of PD. 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.

While mitochondrial dysfunction, oxidative stress, inflammation, toxins, and many other cellular processes may contribute to PD, the actual cause of the cell loss death in PD is still undetermined.

What genes are linked to Parkinson's disease?

Several genes have been definitively linked to PD. The first to be identified was alpha-synuclein. In the 1990s, researchers at National Institutes of Health and other institutions studied the genetic profiles of a large Italian family and three Greek families with familial PD and found that their disease was related to a mutation in this gene. They found a second alpha-synuclein mutation in a German family with PD. These findings prompted studies of the role of



Some research suggests that mitochondria (shown above), the energy-producing components of a cell, may play a role in PD development.

alpha-synuclein in PD, which led to the discovery that Lewy bodies seen in all cases of PD contain alpha-synuclein protein. This discovery revealed the link between hereditary and sporadic forms of the disease.

In 2003, researchers studying inherited PD discovered that the disease in one large family was caused by a triplication of the normal alpha-synuclein gene on one copy of chromosome 4 (a chromosome is a threadlike structure of a protein and the genetic material DNA). This triplication caused people in the affected family to produce too much of the normal alpha-synuclein. This study showed that an excess of the normal form of synuclein could result in PD, just as the abnormal form does.

Other genes linked to PD include parkin, DJ-1, PINK1, and LRRK2. DJ-1 and PINK1 cause rare, early-onset forms of PD. The parkin gene is translated into a protein that normally helps cells break down and recycle proteins. DJ-1 normally

helps regulate gene activity and protect cells from oxidative stress. PINK1 codes for a protein active in mitochondria. Mutations in this gene appear to increase susceptibility to cellular stress.

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 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.

Another interesting association is with the GBA gene, which makes the enzyme glucocerebrosidase. Mutations in both GBA genes 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. Investigators seek to understand what this association can tell us about PD risk factors and potential treatments.

Who gets Parkinson's disease?

Estimates suggest that about 50,000 Americans are diagnosed with PD each year, although some estimates are much higher. Getting an accurate count of the number of cases is difficult because many people in the early stages of the disease may assume their symptoms are the result of normal aging and do not seek medical attention. Diagnosis is sometimes complicated by the fact that other conditions may produce symptoms of PD and there is no definitive test for the disease.

People with PD may sometimes be told by their doctors that they have other disorders, and people with PD-like diseases may be incorrectly diagnosed as having PD.

PD affects about 50 percent more men than women, and the reasons for this discrepancy are unclear. While PD occurs in people throughout the world, a number of studies have found a higher incidence in developed countries. Other studies have found an increased risk in people who live in rural areas with increased pesticide use. However, those apparent risks are not fully characterized.

One clear risk factor for PD is age. The average age of onset is 60 years, and the incidence rises significantly with advancing age. However, about 5 to 10 percent of people with PD have "early-onset" disease that begins before the age of 50. Some early-onset cases are linked to specific gene mutations such as parkin. People with one or more close relatives who have PD have an increased risk of developing the disease themselves, but the total risk is still about 2 to 5 percent unless the family has a known gene mutation for the disease. An estimated 15 to 25 percent of people with PD have a known relative with the disease.

PD affects both men and women; however, the disorder affects 50 percent more men than women.

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.

What are the symptoms of the disease?

The four primary symptoms of PD are:

- **Tremor**. The tremor associated with PD has a characteristic appearance. Typically, the tremor takes the form of a rhythmic back-and-forth motion at a rate of 4-6 beats per second. It may involve the thumb and forefinger and appear as a "pill rolling" tremor. Tremor often begins in a hand, although sometimes a foot or the jaw is affected first. It is most obvious when the hand is at rest or when a person is under stress. Tremor usually disappears during sleep or improves with intentional movement. It is usually the first symptom that causes people to seek medical attention.

- **Rigidity**. Rigidity, 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**. Postural instability, or impaired balance, causes affected individuals to fall easily.

PD does not affect everyone the same way, and 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. Even after the disease involves both sides of the body, the symptoms are often less severe on one side than on the other.

Friends or family members may be the first to notice changes in someone with early PD. They may see that the person's face lacks expression and animation (known as "masked face") or that the person moves more slowly.

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 and individuals may note some stiffness in addition to slowness. They may notice that they speak too softly 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.

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

As the disease progresses, the symptoms of Parkinson's disease 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).

A number of other symptoms may accompany PD, and some can be treated with medication or physical therapy.

- *Depression*. This common disorder may appear early in the course of the disease, even before other symptoms are noticed. Some people lose their motivation and become dependent on family members. Fortunately, depression typically can be treated successfully with antidepressant medications such as amytriptyline or fluoxetine.
- *Emotional changes*. Some people with PD become fearful and insecure, while others may become irritable or uncharacteristically pessimistic.
- *Difficulty with swallowing and chewing*. Muscles used in swallowing may work less efficiently 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. These problems may also make it difficult to get adequate nutrition.

Speech-language therapists, occupational therapists (who help people learn new ways to perform activities of daily living), and dieticians can often help with these problems.

- *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. A speech therapist may be able to help these individuals reduce some of these problems.

- *Urinary problems or constipation*. In some people with PD, bladder and bowel problems can occur due to the improper functioning of the autonomic nervous system, which is responsible for regulating smooth muscle activity. Medications can effectively treat some of these symptoms.

- *Skin problems*. In PD, 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. Standard treatments for skin problems can help.

- *Sleep problems*. Sleep problems are common in PD and 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

Sleep problems, which are common in PD, may include restless sleep, drowsiness, nightmares, or sudden sleep onset during the day.

"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.

- *Dementia or other cognitive problems*. Some people with PD may develop memory problems and slow thinking. Cognitive problems become more severe in late stages of PD, and a diagnosis of Parkinson's disease dementia (PDD) may be given. Memory, social judgment, language, reasoning, or other mental skills may be affected. There is currently no way to halt PD dementia, but drugs such as rivastigmine, donepezil, or memantine may help. The medications used to treat the motor symptoms of PD may cause confusion and hallucinations.

- *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. Orthostatic hypotension may improve by increasing salt intake. Physicians treating the disorder may also reduce anti-hypertension drug dosage or by prescribing medications such as fludrocortisone.

- *Muscle cramps and dystonia*. The rigidity and lack of normal movement associated with PD often causes muscle cramps, especially in the legs and toes. Massage, stretching, and applying heat may help with these cramps. 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. Management strategies may involve adjusting medications.

Exercise may help to relieve the fatigue and loss of energy that people with PD often experience.

- *Pain*. Many people with PD develop aching muscles and joints because of the rigidity and abnormal postures often associated with the disease. Treatment with levodopa and other dopaminergic drugs often alleviates these pains to some extent. Certain exercises may help.

- *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. Exercise, good sleep habits, staying mentally active, and not forcing too many activities in a short time may help to alleviate fatigue.

- *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. People should discuss these issues with their physician as they may be treatable.

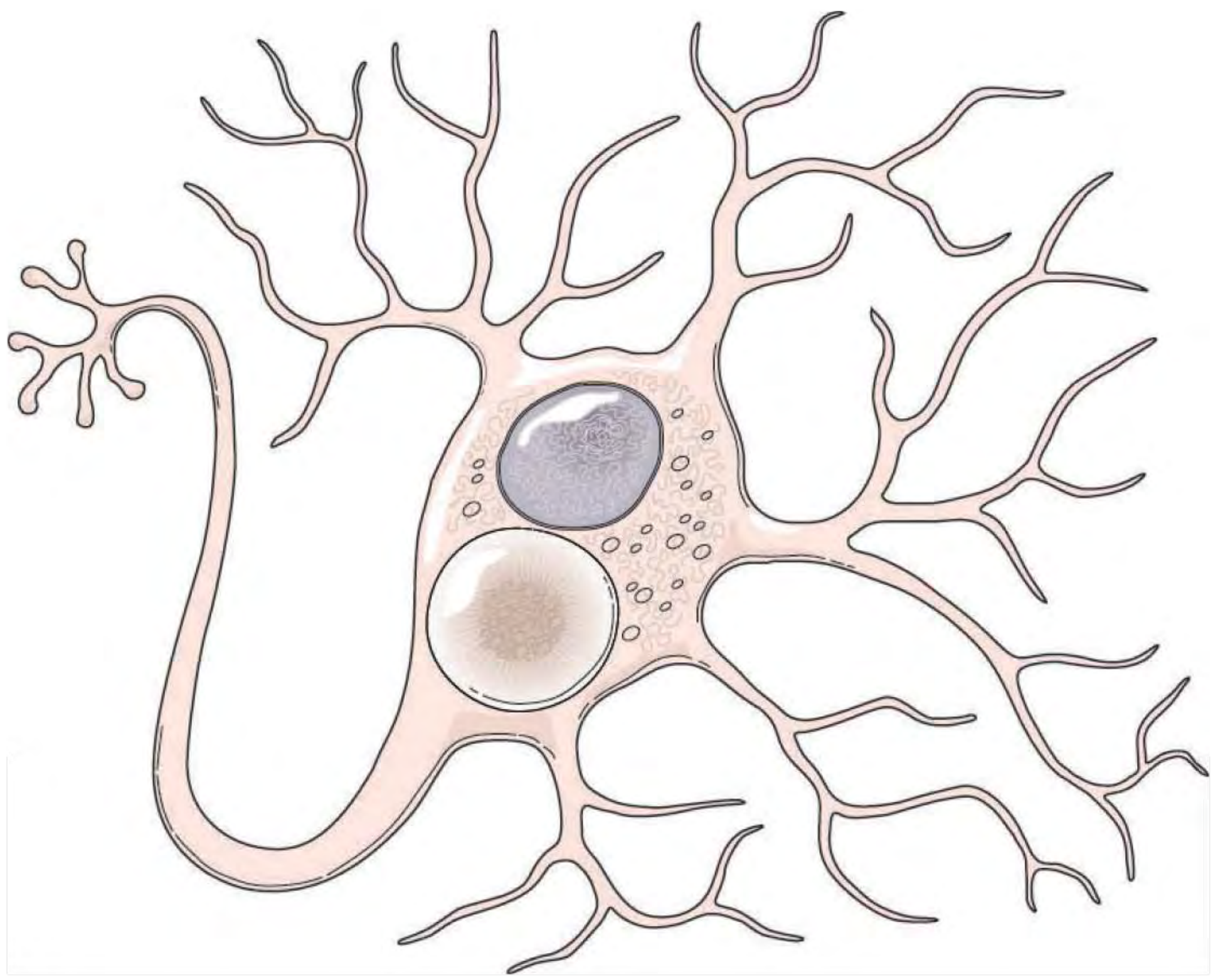
Hallucinations, delusions, and other psychotic symptoms can be caused by the drugs prescribed for PD. Reducing PD medications dosages or changing medications may be necessary if hallucinations occur. If such measures are not effective, doctors sometimes prescribe drugs called atypical antipsychotics, which include clozapine and quetiapine. The typical antipsychotic drugs, which include haloperidol, worsen the motor symptoms of PD and should not be used.

What other diseases and conditions resemble Parkinson's disease?

A number of disorders can cause symptoms similar to those of PD. People with symptoms that resemble PD but that result from other causes are considered to have parkinsonism. Some of these disorders include:

- **Multiple system atrophy**. Multiple system atrophy (MSA) refers to a set of slowly progressive disorders that affect the central and autonomic nervous systems. In MSA, the protein alpha-synuclein forms harmful filament-like aggregates in the supporting cells in the brain called

oligodenreoglia. 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. Other symptoms may include swallowing difficulties, male impotence, constipation, and urinary difficulties. The disorder previously called Shy-Drager syndrome refers to MSA with prominent orthostatic hypotension—a fall in blood pressure every time the person stands up. MSA with parkinsonian symptoms is sometimes referred to as MSA-P (or striatonigral degeneration), while MSA with poor coordination and slurred speech is sometimes called MSA-C (or olivopontocerebellar atrophy). Unfortunately, many of the symptoms of MSA either do not respond to PD medications or the response is minimal or short-lived.



Dementia with Lewy bodies is a neurodegenerative disorder associated with the same abnormal protein deposits, called Lewy bodies, found in Parkinson's Disease. The drawing above shows a Lewy body.

- **Dementia with Lewy bodies**. Dementia with Lewy bodies is a neurodegenerative disorder 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. Visual hallucinations are often one of the first symptoms, and individuals may suffer from other psychiatric disturbances such as delusions and depression. Cognitive problems also occur early in the course of the disease. Levodopa and other antiparkinsonian medications can help with the motor symptoms of Dementia with Lewy bodies, but they may make hallucinations and delusions worse, and affected individuals may require treatment with atypical antipsychotic medications.

- **Progressive supranuclear palsy**. Progressive supranuclear palsy (PSP) is a rare, progressive brain disorder that causes problems with control of gait and balance. The symptoms of PSP are caused by a gradual deterioration of cells in the brain stem. People often tend to fall early in the course of PSP. One of the characteristic features of the disease is an inability to move the eyes properly, which some people describe as having blurred vision. People with PSP often show alterations of mood and behavior,

including depression and apathy as well as mild dementia. PSP is often misdiagnosed because some of its symptoms are much like those of PD, Alzheimer's disease, and other brain disorders. PSP symptoms usually do not respond to medication, or the response is minimal and short-lasting. PSP is characterized by aggregation of a protein called tau.

- **Corticobasal degeneration**. 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 are similar to some of the features found in PD, including rigidity, impaired balance, and problems with coordination. Often there is dystonia affecting one side of the body. Other symptoms may include 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). Unlike PD, CBD usually does not respond to medication. Like PSP, it 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.

Parkinsonism resulting from neurological disorders

- **Arteriosclerotic parkinsonism**. Sometimes known as pseudoparkinsonism, vascular parkinsonism, or atherosclerotic parkinsonism, arteriosclerotic parkinsonism involves damage to the brain due to multiple strokes. Tremor is rare in this type of parkinsonism, while dementia and difficulties with gait are common. Antiparkinsonian drugs are of little help to people with this form of parkinsonism.

- **Post-traumatic parkinsonism**. Also known as post-traumatic encephalopathy or "punch-drunk syndrome," parkinsonian symptoms can develop after a severe head injury or frequent head trauma associated with boxing or other activities. This type of trauma can also cause a form of dementia called chronic traumatic encephalopathy.

Post-traumatic parkinsonism occurs when parkinsonian symptoms develop after a severe head injury or frequent head trauma associated with boxing or other activities.

- **Essential tremor**. Sometimes called benign essential tremor or familial tremor, this common condition tends to run in families and progresses slowly over time. The tremor is usually equal in both hands and increases when the hands are moving. It may involve the head but usually spares the legs. Essential tremor is not the same as Parkinson's disease and does not usually lead to it, although in some cases the two conditions may overlap in one person. People with essential tremor have no other parkinsonian features. Essential tremor does not respond to levodopa or to most other PD drugs, but there are medications to treat it.

- **Normal pressure hydrocephalus**. Normal pressure hydrocephalus (NPH) is an abnormal increase of cerebrospinal fluid (CSF) in the brain's ventricles, or cavities. This causes the ventricles to enlarge, putting pressure on the brain. Symptoms include problems with walking, impaired bladder control leading to increased urinary frequency or incontinence, and progressive mental impairment and dementia. The person may also have a general slowing of movements or may complain that his or her feet feel "stuck." These symptoms may sometimes be mistaken for PD. They do not respond to Parkinson's medications. Brain scans, intracranial pressure monitoring, and other tests can help to diagnose NPH. NPH can sometimes be treated by surgically implanting a CSF shunt that drains excess cerebrospinal fluid into the abdomen, where it is absorbed.

- **Parkinsonism accompanying other conditions**. Parkinsonian symptoms appear in individuals with other, clearly distinct neurological disorders such as Wilson's disease, Huntington's disease, Alzheimer's disease, spinocerebellar ataxias, and Creutzfeldt-Jakob disease. Each of these disorders has specific features that help to distinguish it from PD.

Environmental causes

- **Postencephalitic parkinsonism**. Just after the first World War, the viral disease encephalitis lethargica affected almost 5 million people throughout the world, and then suddenly disappeared in the 1920s. Known as sleeping sickness in the United States, this disease killed one-third of its victims and led to post-encephalitic parkinsonism in many others. This resulted in a movement disorder that appeared sometimes years after the initial illness. (In 1973, neurologist Oliver Sacks published *Awakenings*, an account of his work in the late 1960s with surviving post-encephalitic patients in a New York hospital. Using the then-experimental drug levodopa, Dr. Sacks was able to temporarily "awaken" these individuals from their statue-like state). In rare cases, other viral infections, including western equine encephalomyelitis, eastern equine encephalomyelitis, and Japanese B encephalitis, have caused parkinsonian symptoms.

Many disorders can cause symptoms similar to those of Parkinson's disease.

- **Drug-induced parkinsonism.** A reversible form of parkinsonism sometimes results from use of certain drugs, such as chlorpromazine and haloperidol, which are typically prescribed for patients with psychiatric disorders. Some drugs used for stomach disorders (metoclopramide), high blood pressure (reserpine), and others such as valproate can cause tremor and bradykinesia. Stopping the medication or lowering the dosage of these medications usually causes the symptoms to go away.

- **Toxin-induced parkinsonism.** Some toxins can cause parkinsonism by various mechanisms. The chemical MPTP also causes a permanent form of parkinsonism that closely resembles PD. Investigators discovered this reaction in the 1980s when heroin addicts in California who had taken an illicit street drug contaminated with MPTP began to develop severe parkinsonism. This discovery, which showed that a toxic substance could damage the brain and produce parkinsonian symptoms, led to a dramatic breakthrough in Parkinson's research.

- **Parkinsonism-dementia complex of Guam.** This disease occurs among the Chamorro populations of Guam and the Mariana Islands and may be accompanied by a motor neuron disease resembling amyotrophic lateral sclerosis (Lou Gehrig's disease). The course of the disease is rapid, with death typically occurring within 5 years.

How is Parkinson's disease diagnosed?

There are currently no blood or laboratory tests that diagnose sporadic PD. Therefore the diagnosis is based on medical history and a neurological examination. In some cases PD can be difficult to diagnose accurately early on in the course of the disease. Early signs and symptoms of PD may sometimes be dismissed as the effects of normal aging. Doctors may sometimes request brain scans or laboratory tests in order to rule out other disorders. However, computed tomography (CT) and magnetic resonance imaging (MRI) brain scans of people with PD usually appear normal. Since many other diseases have similar features but require different treatments, making a precise diagnosis is important so that people can receive the proper treatment.

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. One commonly used scale neurologists use for describing how the symptoms of PD have progressed in a patient is the Hoehn and Yahr scale.

Hoehn and Yahr Staging of Parkinson's Disease

Stage one – symptoms on one side of the body only.

Stage two – symptoms on both sides of the body. No impairment of balance.

Stage three – balance impairment. Mild to moderate disease. Physically independent.

Stage four – severe disability, but still able to walk or stand unassisted.

Stage five – wheelchair-bound or bedridden unless assisted.

Another commonly used scale is the Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS). This four-part scale measures motor movement in PD: non-motor experiences of daily living, motor experiences of daily living, motor examination, and motor complications. Both the Hoehn and Yahr scale and the MDS-UPDRS are used to describe how individuals are faring and to help assess treatment response.

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. The first category includes 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.

The second category of PD drugs affects 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.

The third category of drugs prescribed for PD includes 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.

- **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.) 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. It allows the majority of people with PD to extend the period of time in which they can lead active, productive lives.

Although levodopa/carbidopa helps most people with PD, not all symptoms respond equally to the drug. Levodopa usually helps most with bradykinesia and rigidity. Problems with balance may not respond.

People often see noticeable improvement in their symptoms after starting levodopa/carbidopa therapy. However, they may need to increase the dose gradually for maximum benefit. Levodopa is often so effective that some people may not show symptoms during the early stages of the disease as long as they take the medicine. But levodopa is not a cure. Although it can reduce the symptoms of PD, it does not replace lost nerve cells and it does not stop the progression of the disease.

Levodopa/carbidopa can have a variety of side effects. The most common initial side effects include nausea, low blood pressure, and restlessness. The nausea and vomiting caused by levodopa are greatly reduced by the right combination of levodopa and carbidopa. The drug also can cause drowsiness or sudden sleep onset, which can make driving and other activities dangerous. Long-term use

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.

of levodopa sometimes causes hallucinations and psychosis.

Dyskinesias, or involuntary movements such twisting and writhing, commonly develop in people who take levodopa over an extended period. These movements may be either mild or severe. Some doctors start younger individuals with PD on drugs that act directly like dopamine itself and add levodopa later in the course of the disease. The dosage of levodopa is sometimes reduced in order to lessen these drug-induced movements. The drug amantadine may help control dyskinesias but if dyskinesias are severe, surgical treatment such as deep brain stimulation may be considered (see description in "Surgery").

Other difficulties may be encountered later in the disease course. People with PD may begin to notice more pronounced symptoms before their first dose of medication in the morning 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.

In addition to levodopa/carbidopa, there are other available treatments:

- **Dopamine agonists**. These drugs, which include apomorphine, pramipexole, ropinirole, and rotigotine, mimic the role of dopamine in the brain. They 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.

- **MAO-B inhibitors**. These drugs inhibit 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. 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. It should not be taken with the antidepressant fluoxetine or the sedative meperidine, because combining

selegiline with these drugs can be harmful. The drug rasagiline is used in treating the motor symptoms of PD with or without levodopa. Whether rasagiline slows progression of PD is still controversial.

- **COMT inhibitors**. COMT stands for catechol-O-methyltransferase, another enzyme that breaks down dopamine. The drug 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. The most common side effect is diarrhea. The drugs cause 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 is often used alone in the early stages of the disease. It may also 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, benztropine, and ethopropazine, decrease the activity of the neurotransmitter acetylcholine and can be

particularly effective for tremor. 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.

Medications to Treat the Motor Symptoms of Parkinson's Disease

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)	Benztropine Ethopropazine Trihexyphenidyl	Cogentin Parsidol Artane
Drugs with an unknown mechanism of action for PD	Amantadine	Symmetrek

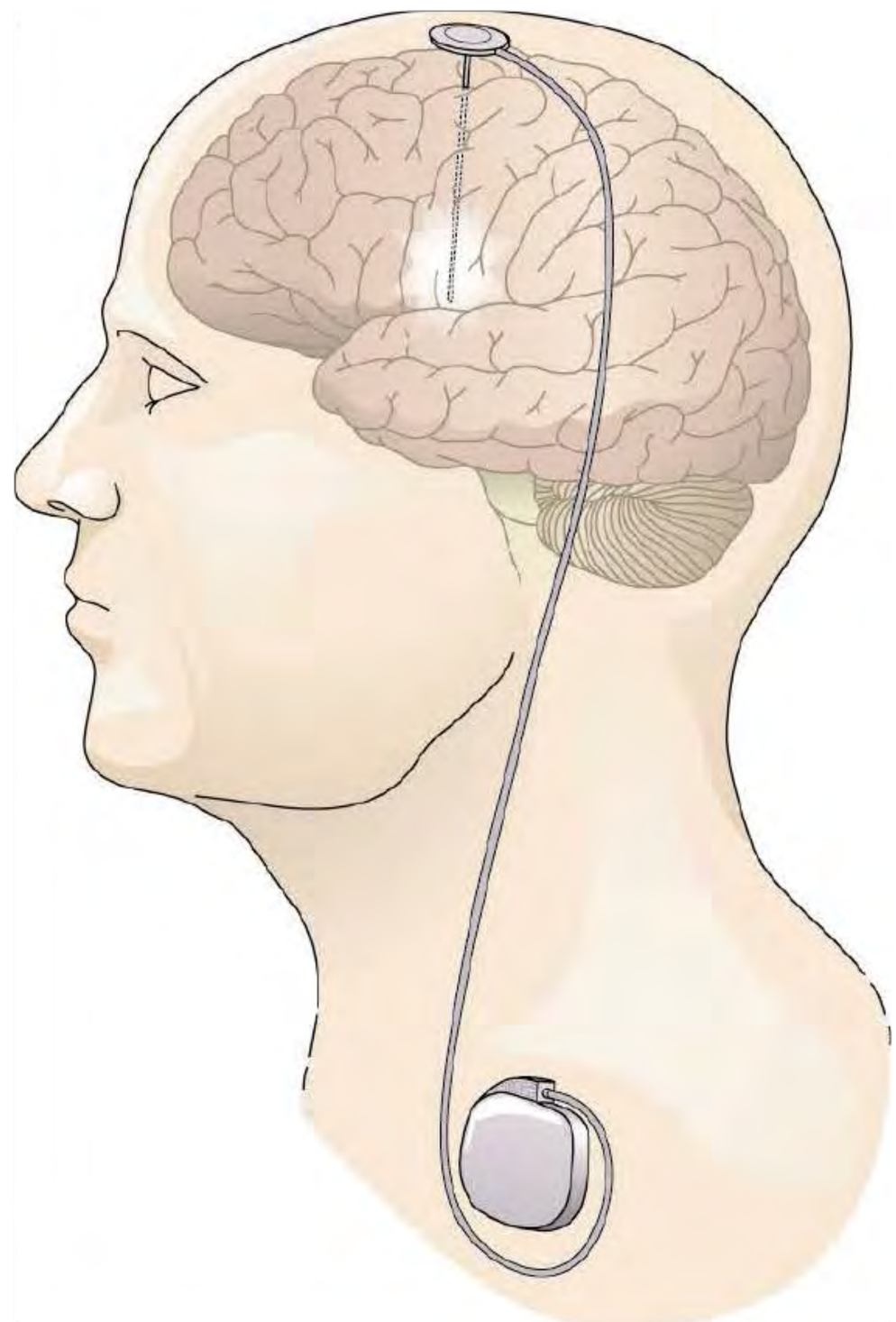
Surgery

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.

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 new 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. 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 can be used on one or both sides of the brain. If it is used on just one side, it will affect symptoms on the opposite side of the body. 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.

People who initially responded well to treatment with levodopa tend to respond well to DBS. 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.

One advantage of DBS compared to pallidotomy and thalamotomy is that the electrical current can be turned off using a handheld device. The pulse generator also can be externally programmed.

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. After a few months, the number of medical visits usually decreases significantly, though individuals may occasionally need to return to the center to have their stimulator checked. Currently, the battery for the pulse generator must be surgically replaced every three to five years. DBS does not stop PD from progressing, and some problems may gradually return. DBS is not a good option for everyone. It is generally appropriate for people with levodopa-responsive PD who have developed dyskinesias or other disabling "off" symptoms despite drug therapy. It is not generally an option for people with memory problems, hallucinations, severe depression, poor health, or a poor response to levodopa. 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.

As with any brain surgery, DBS has potential complications, including stroke or brain hemorrhage. These complications are rare, however. There is also a risk of infection, which may require antibiotics or even replacement of parts of the DBS system.

Complementary and Supportive Therapies

A wide variety of complementary and supportive therapies may be used for PD. Among these therapies are standard physical, occupational, and speech therapy techniques, which can help with such problems as gait and voice disorders, tremors and rigidity, and cognitive decline. Other types of supportive therapies include:

Diet. At this time there are no specific vitamins, minerals, or other nutrients that have any proven therapeutic value in PD. An NINDS clinical study of the dietary supplement coenzyme Q10 was stopped in 2011 when results from an interim analysis showed active treatment with the supplement was unlikely to demonstrate a statistically significant difference than from a placebo. The 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. While there is currently no proof that any specific dietary factor is beneficial, 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, highlighting the importance of the timing of medications.

Exercise. Exercise can help people with PD improve their mobility and flexibility. Some doctors prescribe physical therapy or muscle-strengthening exercises to tone muscles and to put underused and rigid muscles through a full range of motion. The effects of exercise on disease progression are not known, but it may improve body strength so that the person is less disabled. Exercises also improve balance, helping people minimize gait problems, and can strengthen certain muscles so that people can speak and swallow better. Exercise can improve emotional well-being and general physical activity, such as walking, gardening, swimming, calisthenics, and using exercise machines, can have other benefit. An NINDS-funded clinical trial demonstrated the benefit of tai chi exercise compared to resistance or stretching exercises.[2] People with PD should always check with their doctors before beginning a new exercise program.

Other complementary and supportive therapies that are used by some individuals with PD include massage therapy, yoga, hypnosis, acupuncture, and the Alexander technique, which optimizes posture and muscle activity.

Another important therapeutic approach involves speech and swallowing evaluation and therapy. Certain techniques can help with the low voice volume that individuals with Parkinson's often experience.

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[2] Li, F. et al. "Tai chi and postural stability in patients with Parkinson's disease." ***New England Journal of Medicine***. February 9, 2012. Volume 366(6), pages 511-9.

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

How can people cope with Parkinson's disease?

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.

Can scientists predict or prevent Parkinson's disease?

In most cases, there is no way to predict or prevent sporadic PD. However, researchers are looking for a biomarker—a biological abnormality that all people with PD might share—that could be detected by screening techniques or by a simple chemical test given to people who do not yet have any parkinsonian symptoms. This could help doctors identify people at risk of the disease. It also might allow them to find treatments that will stop the disease process in the early stages. Studies demonstrated that synuclein builds up in nerve cells years before symptoms occur. Loss of a sense of smell, constipation, restless legs, and REM sleep disorder are potentially caused by these early changes.

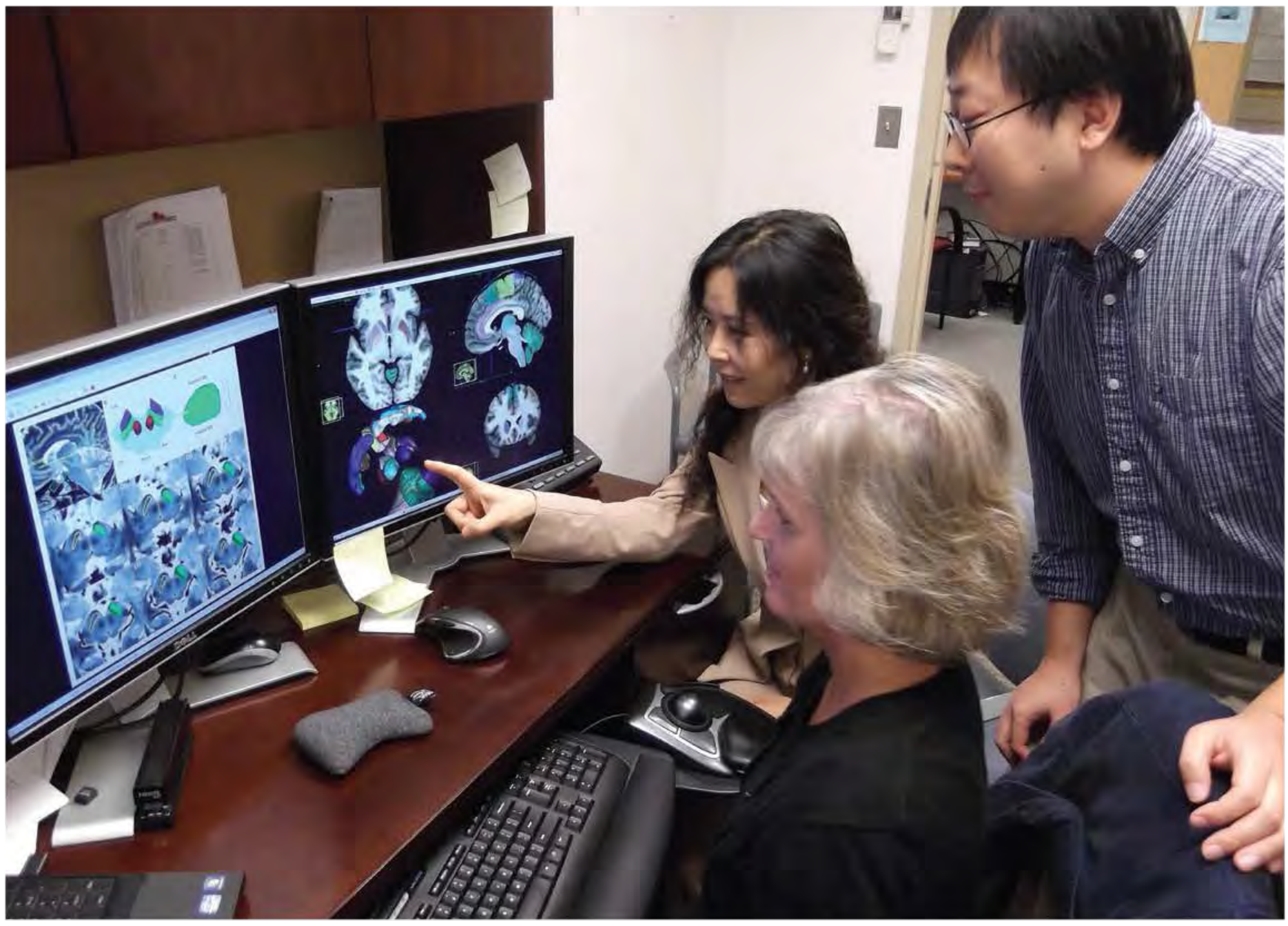
One important area of research in this domain involves imaging techniques, such as special MRI techniques or nuclear imaging techniques currently under study at the National Institutes of Health and elsewhere.

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.

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. The NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world. The 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 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.

A long-term NINDS research and planning strategy led to the NINDS-hosted January 2014 conference, "Parkinson's Disease 2014: Advancing Research, Improving Lives," at which neuroscientists, physicians, public and private organization representatives, and people with Parkinson's disease discussed the highest research priorities, ranging from lab discoveries to developing new therapies for PD (see **www.ninds.nih.gov/research/parkinsonsweb/PD2014/**).



Scientists involved in the Parkinson's Disease Biomarkers Program hope that finding characteristics that may indicate risk of the disease will speed the development of new PD therapeutics.

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 to track the progression of the disease. Identifying biomarkers (signs that may indicate risk of a disease and improve diagnosis) will speed the development of novel therapeutics for PD. Projects are actively recruiting volunteers at sites across the U.S. The 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 PDPB 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—a central component of NINDS PD research—was established in 1997 to find the fundamental causes of PD and better diagnose and treat people with PD. The NINDS currently funds 10 Udall Centers across the country, where researchers are examining PD disease mechanisms, the genetic contributions to PD, and potential therapeutic targets and treatment strategies. To learn more about the NINDS Udall Centers, see **www.ninds.nih.gov/udall**.

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. 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." Current studies include genetics and PD, search for PD biomarkers, experimental therapies and other treatment options, diagnostic imaging, brain control and movement disorders, DBS, and exercise and PD.

Animal models: These are valuable tools for scientists studying disease mechanisms to develop new treatments for people with PD. For example, a study of the drug isradipine—which had been shown in animal models to have a protective effect on dopaminergic neurons—is being tested for a similar neuroprotective effect in humans.

Cognition and Dementia: Mild cognitive impairment is common in PD, sometimes in its early stages, and some people develop dementia in the disease's later stages. The NINDS has funded research using neuroimaging to predict which individuals with PD might develop cognitive impairment.

Deep Brain Stimulation (DBS): NINDS has been a pioneer in the study and development of DBS, which is now considered a standard treatment option for some people living with PD whose symptoms no longer respond to PD medications. While NIH supported research on brain circuitry was critical to the development of DBS, NINDS research continues to fine-tune the optimal site within the brain to implant the DBS electrode to help even more people with PD regain function.

Researchers are continuing to study DBS and to develop ways of improving it. A two-part study funded by the NINDS and the Department of Veterans Affairs first compared bilateral DBS to best medical therapy, including medication adjustment and physical therapy. Bilateral DBS showed overall superiority to best medical therapy at improving motor symptoms and quality of life. The second part of the study, involving nearly 300 patients, compared subthalamic nucleus (STN)

DBS to globus pallidus interna (GPI) DBS. The two groups reported similar improvements in motor control and quality of life in scores on the Unified Parkinson's Disease Rating Scale. On a variety of neuropsychological tests, there were no significant differences between the two groups. However, the STN DBS group experienced a greater decline on a test of visuomotor processing speed, which measures how quickly someone thinks and acts on information. Also, the STN DBS group had slight worsening on a standard assessment of depression, while the GPI DBS group had slight improvement on the same test.

Other clinical studies hope to determine the best part of the brain to receive stimulation and to determine the long-term effects of this therapy. In addition, NINDS-supported researchers are developing and testing improved implantable pulse generators and conducting studies to better understand the therapeutic effect of neurostimulation on the brain.

For more information about current studies on deep brain stimulation and Parkinson's disease, see **www.clinicaltrials.gov** and search for "deep brain stimulation AND Parkinson AND NINDS."

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 before age 50. For example, NINDS-funded researchers analyzed the occupational histories of twins in which one of the pair developed PD.

In a recent study to evaluate three forms of exercise, researchers found that tai chi led to the greatest overall improvements in balance and stability for people with mild to moderate PD.

Based on estimates of exposure to six chemicals previously linked to PD, the researchers concluded that two of the common solvents were significantly linked to development of PD. (See **www.ninds.nih.gov/news_and_events/news_articles/solvents_PD_twins.htm**)

Exercise: Exercise routines are often recommended to help individuals with PD maintain movement and balance necessary for everyday living. A recent NINDS-funded study evaluated three different forms of exercise—resistance training, stretching, and tai chi—and found that tai chi led to the greatest overall improvements in balance and stability for people with mild to moderate PD. A current trial is studying the effects of two levels of exercise in people who have been recently diagnosed with PD. For more information, see **www.ninds.nih.gov/disorders/clinical_trials/NCT01506479.htm**.

Genetic studies: A better understanding of genetic risk factors is playing a critical role in elucidating PD disease mechanisms. A 2011 NINDS workshop led to an analysis of data from PD genome-wide studies around the world, to correlate genetic variants and common traits among people with PD. The workshop contributed to the development of NeuroX, the first DNA chip that can identify genetic

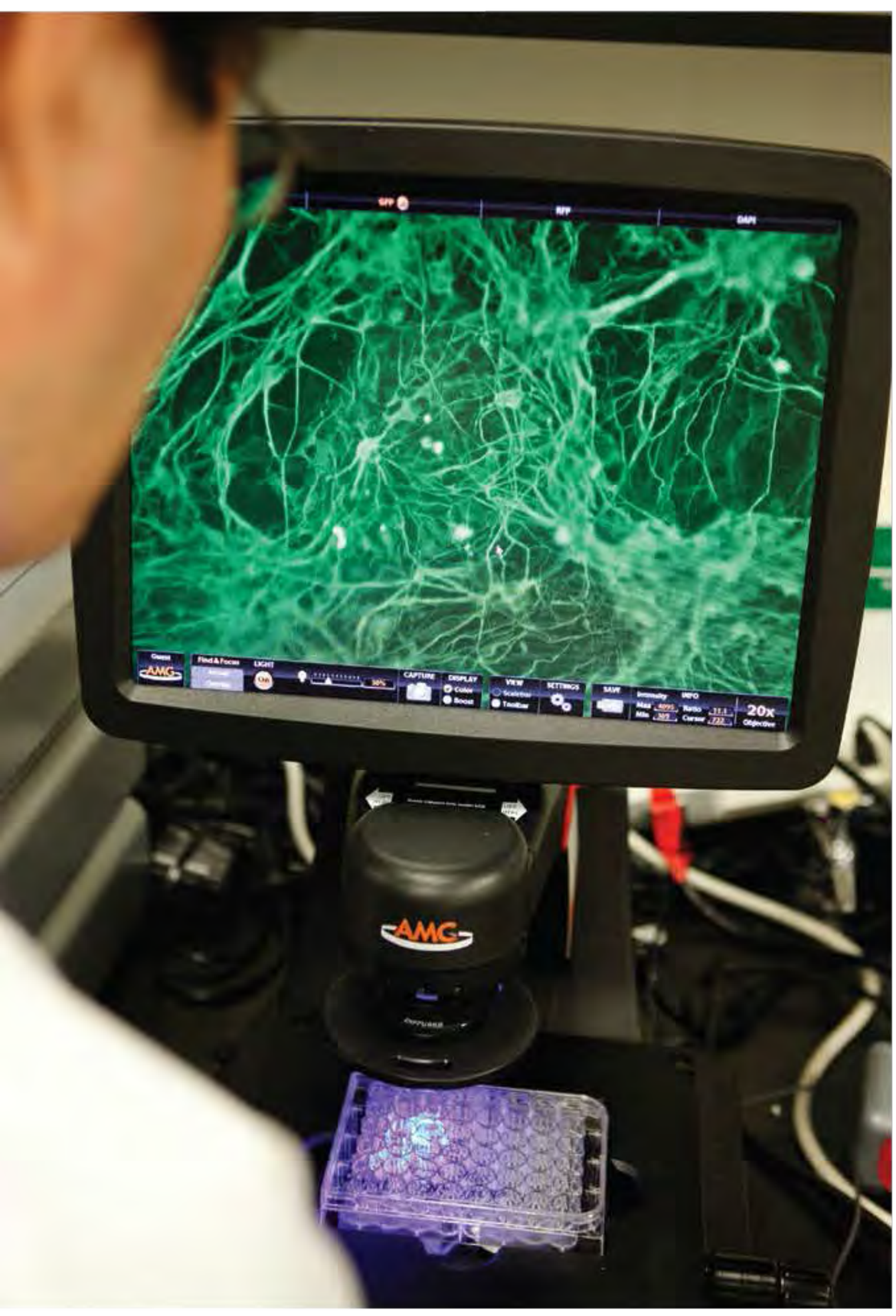
changes in persons at risk for a number of late-onset neurodegenerative diseases, including PD. Another NINDS collaborative, the Consortium On Risk for Early-onset Parkinson's Disease (CORE PD), hopes to identify the genetic factors that contribute to the development of early-onset PD. Current clinical 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. For more information on these studies, see **www.clinicaltrials.gov** and search for "gene AND NINDS AND Parkinson."

Mitochondria: These cellular energy factories may play a central role in PD. NINDS-funded scientists have found that hundreds of genes involved in mitochondrial function are less active in people with PD. Drugs that target genes involved in mitochondrial function could perhaps slow progression of the disease.

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. For more information, see **www.clinicaltrials.gov/ct2/show/NCT01905839**.

Nerve growth factors: Growth factors are proteins involved in nervous system formation and are of interest to researchers studying neurodegenerative diseases. One small clinical trial will assess the safety, tolerability, and potential clinical effects of gene therapy with Glial Derived Neurotrophic Factor (GDNF)—a protein that may help protect dopamine-producing nerve cells. This trial for individuals with advanced PD is based on NINDS-sponsored research showing that an advanced viral technique for delivery of the GDNF gene into the brain improves the health and function of the dopamine neurons in animal models of PD. For more information, see **www.clinicaltrials.gov/ct2/show/NCT01621581**.



Scientists are looking at various types of cells, including stem cells, as opportunities for PD drug discovery.

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. For more information, see **http://www.neuronext.org/**.

Stem cells: Scientists are exploring various types of cells, including induced pluripotent

stem cells (iPSCs), as opportunities for PD drug discovery. iPSC technology is used to define disease mechanisms and discover the most promising treatments for sporadic PD. To pursue this area of research, NINDS established a PD cell research consortium in 2009 in collaboration with the Michael J. Fox Foundation and the Parkinson's Disease Foundation. For more information, see **www.ninds.nih.gov/news_and_events/news_articles/pressrelease_nih_stem_cells.htm** or **http://stemcells.nih.gov/**.

Where can I go for 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
http://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
800-223-2732
Young Onset Center 877-223-3801
http://www.apdaparkinson.org

The Bachmann-Strauss Dystonia & Parkinson Foundation
Fred French Building
551 Fifth Avenue, Suite 520
New York, NY 10176
212-682-9900
http://www.dystonia-parkinson.org

The Michael J. Fox Foundation for Parkinson's Research
Grand Central Station
P.O. Box 4777
New York, NY 10163-4777
212-509-0995
800-708-7644
http://www.michaeljfox.org

National Parkinson Foundation
200 SE 1st Street, Suite 800
Miami, FL 33131
800-473-4636
http://www.parkinson.org

Parkinson Alliance
P.O. Box 308
Kingston, NJ 08528
609-688-0870
800-579-8440
http://www.parkinsonalliance.org

Parkinson's Action Network
1025 Vermont Avenue, NW, Suite 1120
Washington, DC 20005
202-638-4101
800-850-4726
http://www.parkinsonsaction.org

Parkinson's Disease Foundation
1359 Broadway, Suite 1509
New York, NY 10018
212-923-4700
800-457-6676
http://www.pdf.org

Parkinson's Institute and Clinical Center
675 Almanor Avenue
Sunnyvale, CA 94085
408-734-2800
800-655-2273
http://www.thepi.org

Parkinson's Resource Organization
74-090 El Paseo, Suite 104
Palm Desert, CA 92260
760-773-5628
877-775-4111
http://www.parkinsonsresource.org

Davis Phinney Foundation
1772 14th Street, Suite 150
Boulder, CO 80302
303-733-3340
866-358-0285
http://www.davisphinneyfoundation.org

Tuchman Foundation
4422 Route 27
P.O. Box 582
Kingston, NJ 08528
609-924-6006

Glossary

akinesia **—** trouble initiating or carrying out movements.

anticholinergic drugs **—** drugs that interfere with production or uptake of the neurotransmitter acetylcholine.

bradykinesia **—** gradual loss of spontaneous movement.

corpus striatum **—** a part of the brain that helps regulate motor activities.

deep brain stimulation **—** a treatment that uses an electrode implanted into part of the brain to stimulate it in a way that temporarily inactivates some of the signals it produces.

dopamine **—** a chemical messenger, deficient in the brains of people with PD, that transmits impulses from one nerve cell to another.

dyskinesias **—** abnormal involuntary twisting and writhing movements that can result from long-term use of high doses of levodopa.

dystonia **—** involuntary muscle contractions that cause slow repetitive movements or abnormal postures.

neurotransmitters **—** chemicals which carry messages from one nerve cell, or neuron, to another.

pallidotomy **—** a surgical procedure in which a part of the brain called the globus pallidus is lesioned in order to improve symptoms of tremor, rigidity, and bradykinesia.

parkinsonian gait **—** a characteristic way of walking that includes a tendency to lean forward; small, quick steps as if hurrying forward (called festination); and reduced swinging of the arms.

parkinsonism **— a term referring to a group of conditions that are characterized by four typical symptoms—tremor, rigidity, postural instability, and bradykinesia.**

"Parkinson's-plus" **— a group of diseases that includes corticobasal degeneration, progressive supranuclear palsy, and multiple system atrophy. These diseases cause symptoms like those of PD in addition to other symptoms.**

postural instability **— impaired balance that causes a tendency to lean forward or backward and to fall easily.**

rigidity **— a symptom of the disease in which muscles feel stiff and display resistance to movement even when another person tries to move the affected part of the body, such as an arm.**

substantia nigra **— movement-control center in the brain where loss of dopamine-producing nerve cells triggers the symptoms of PD; substantia nigra means "black substance," so called because the cells in this area are dark.**

thalamotomy **— a procedure in which a portion of the brain's thalamus is surgically destroyed, usually reducing tremors.**

tremor **— shakiness or trembling, often in a hand, which in PD is usually most apparent when the affected part is at rest.**

wearing-off effect **— the tendency, following long-term levodopa treatment, for each dose of the drug to be effective for shorter and shorter periods.**

Credits

Illustrations and photos:

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Bob Stockfield, for National Center for Complementary and Integrative Health—Page 42

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