

# Parkinson's Disease Glossary

A guide to the scientific language of Parkinson's disease

**Acetylcholine:** One of the chemical neurotransmitters in the brain and other areas of the central and peripheral nervous system. It is highly concentrated in the basal ganglia, where it influences movement. It is located in other regions of the brain as well, and plays a role in memory. Drugs that block acetylcholine receptors (so-called anticholinergics) are utilized in the treatment of PD.

**Acetylcholinesterase Inhibitors:** A drug that inhibits the enzyme that breaks down acetylcholine resulting in increased activity of the chemical neurotransmitter acetylcholine. Used to treat mild to moderate dementia in Parkinson's disease.

**Agonist:** A chemical or drug that can activate a neurotransmitter receptor. Dopamine agonists, such as pramipexole, ropinirole, bromocriptine and apomorphine, are used in the treatment of PD.

**Aggregate:** A whole formed by the combination of several elements. In Parkinson's disease, there is a clumping of many proteins inside neurons, including alpha-synuclein. Levy bodies are a kind of aggregate found in PD.

**Akinesia:** Literally, means loss of movement also described as a difficulty with initiating voluntary movements. It is commonly used interchangeably with bradykinesia, however bradykinesia means slow movement.

**Alpha-synuclein:** A protein present in nerve cells where it can be found in their cell body, their nucleus and their terminals. The accumulation and aggregation of this protein is a pathologic finding in PD. The first genetic mutation found in PD was discovered in the gene for alpha-synuclein (SNCA), and was called PARK1. Alpha-synuclein also accumulates in multiple system atrophy (MSA) and in Lewy Body Disease. Alpha-synuclein appears to play a key role in the pathogenesis of PD.

**Alexander Technique:** This technique is a form of complementary therapy, pioneered at the turn of the century by FM Alexander. The principal aim is to help improve health by teaching people to stand and move more efficiently.

**Amantadine:** A medication used to treat Parkinson's disease as a single therapy or with L-DOPA and other medications. It has both an anti-Parkinson's effect and an anti-dyskinesia effect.

**Aminoguanidine:** Also known as pimagedine. It acts to reduce levels of advanced glycation end products. It has been investigated as a potential treatment for diabetic nephropathy and kidney diseases and as a disease modifying therapy in PD.

**Amygdala:** An almond-shaped nucleus located deep in the brain's medial temporal lobe in animals. It is involved in fear and anxiety responses, and in the formation of memories involving emotion.

**Anticholinergics:** A type of medication that interferes with the action of acetylcholine. It is sometimes used in PD to restore the balance between dopamine and acetylcholine in the striatum.

They are not recommended for use in the elderly because they can cause confusion. Examples include:

- benztropine mesylate
- biperiden hydrochloride
- orphenadrine citrate
- procyclidine hydrochloride
- trihexyphenidyl hydrochloride.

**Anhedonia:** Decreased ability or inability to experience pleasure.

**Anosmia:** Total loss of the sense of smell. *See also Hyposmia.*

**Antagonists:** Has the opposite effect from an agonist. Antagonists block neurotransmitter receptors. Dopamine antagonists can worsen Parkinson's symptoms and can cause drug-induced Parkinsonism. Virtually all antipsychotic drugs have dopamine antagonist action.

**Apathy:** Lack of interest, enthusiasm, or concern.

**Apomorphine:** A type of dopamine agonist, which is highly powerful and effective but also causes unpleasant effects, such as nausea. A pump delivering apomorphine can be used in more advanced stages of the disease.

**Astrocytes:** They are a major support cells in the brain. Among other things, they secrete growth factors that help neurons grow and communicate. They can also pump glutamate, a neurotransmitter that, in excess, can cause neurotoxicity.

**Ataxia:** Inability to coordinate voluntary muscle movements; unsteady movements and staggering gait.

**ATP13A2 (PARK 9):** A gene that codes for a form of the ATPase enzyme. When mutated, this gene may cause a form of early onset Parkinson's.

**Autonomic Nervous System (ANS):** Part of the peripheral nervous system, consisting of sympathetic and parasympathetic nerves that control involuntary actions, in particular the heartbeat, smooth muscle (such as bladder and blood vessels), the digestive system, and glands.

**Autonomic Dysfunction:** Any abnormal functioning of the autonomic nervous system resulting in problems with bodily functions such as bowel and bladder control, blood pressure control, sweating, drooling, and so forth.

**Autophagy:** The segregation and disposal of damaged organelles within a cell. This is a normal physiological process in the body. It maintains normal functioning by protein degradation and turnover of the destroyed cell organelles for new cell formation. During cellular stress the process of Autophagy is increased. Cellular stress is caused when there is deprivation of nutrients and/or growth factors. Thus autophagy may provide an alternate source of intracellular building blocks and substrates that may generate energy to enable continuous cell survival. Dysfunctional autophagy can lead to the building of damaged organelles and misfolded proteins in the cell.

**Autosomes/autosomal:** Refers to all the chromosomes excluding the sex-related X and Y chromosomes.

**Autosomal recessive:** A mode of inheritance of genetic traits located on the autosomes that only manifests when two copies of a mutated gene (two alleles) are present. In order for a particular trait to be expressed, both parents must have the particular mutated allele or gene, and both must pass it to the offspring who then manifests the genetic disease. Some genetic forms of PD are autosomal recessive, such as from the genes known as *parkin*, *PINK1* and *DJ1*. In some cases, the gene of interest is missing. In others, there are abnormalities and if two different abnormalities of the same gene are inherited, that can result in recessive inheritance.

**Axon:** A nerve fiber that carries electrical impulses from the nerve cell body to other neurons. Thick axons tend to be through the brain and spinal cord; they are surrounded by a protective fatty sheath called myelin (in multiple sclerosis the myelin is damaged). Thin axons tend to be unmyelinated. In PD, alpha-synuclein is deposited in long, thin axons, and these are called Lewy neurites.

**Basal Ganglia:** Clusters of neurons that include the caudate nucleus, putamen, globus pallidus and substantia nigra which are located deep in the brain and play an important role in movement. Cell death in the substantia nigra contributes to Parkinsonian signs. The subthalamic nucleus is now also often considered part of the basal ganglia because it connects with other regions of the basal ganglia.

**Big data:** A term for data sets that are so large or complex that traditional data processing applications are inadequate.

**Biomarker:** An early indicator that a person may have a disease, such as Parkinson's. A biomarker, if present, could indicate that the person has a disease before symptoms of that disease appear. There is a search for biomarkers for PD. Biomarkers could be a chemical, clinical, or imaging finding.

**Blood brain barrier:** The separating membrane between the blood and the brain; a tight physical barrier that normally keeps immune cells, and some chemicals and drugs out of the brain.

**Braak Staging:** A method to classify the degree of pathology in Parkinson's disease on brain autopsy, based on the idea that more brain regions contain alpha-synuclein pathology as Parkinson's disease progresses over time. There is also a (different) Braak staging for Alzheimer's disease.

**Bradykinesia:** Literally, means slowness of movement. It is commonly (but erroneously) used synonymously with akinesia and hypokinesia. Bradykinesia is a clinical hallmark of Parkinsonism.

**Bradypnea:** Slowness of thought common to many brain disorders.

**Brain stem:** The part of the brain between the cerebral hemispheres and the spinal cord. The three parts of the brain stem are the medulla oblongata, pons, and midbrain. The brain stem is a vital structure that is a passageway between the brain and spinal cord, and it contains neurons involved in sleep and wakefulness, as well as the main centers that command vital functions such as respiration and heart function. The substantia nigra, which is damaged in Parkinson's, is located in the midbrain of the brain stem.

**C-Abl:** A gene implicated in the processes of cell differentiation, cell division, cell adhesion, and stress response.

**Calcium:** An essential mineral. Calcium is important for neurological "signaling" and is involved in many chemical reactions within neurons and in mitochondria function. Calcium overload in substantia nigra has been postulated as one mechanism that could contribute to death of these neurons.

**Carbidopa:** A drug given with levodopa. Carbidopa blocks the enzyme dopa decarboxylase, thereby preventing levodopa from being metabolized to dopamine. Because carbidopa does not penetrate the blood brain barrier, it only blocks levodopa metabolism in the peripheral tissues and not in the brain, thereby reducing side effects, but increasing the effectiveness of levodopa.

**Carer/ Care Partner:** A name used to describe anyone who provides help or support of any kind to a relative or friend.

**Caudate nucleus:** A nucleus located in the basal ganglia important in learning and memory. It is one component of the basal ganglia called the striatum. The other component is the putamen.

**Cerebellum:** Part of the hindbrain; controls smooth movements. When damaged, it results in ataxia.

**Cerebrospinal fluid (CSF):** A watery fluid generated within the brain's ventricles. CSF circulates to bathe the brain and spinal cord to cushion these from physical impact. Small amounts can be harvested in humans by lumbar puncture to measure chemicals coming from the brain.

**Chemokines:** Signaling proteins that are part of the Cytokines family. They are named for their ability to induce movement in an organism in response to chemical stimulus.

**Chronic:** (opposite: acute) Chronic diseases are of long duration. Chronic diseases are typically of subtle onset and slow worsening over time. The term does not imply anything about the severity of a disease.

**Clinical Trials:** Refers to those research studies that involve human volunteers and are conducted to add to our understanding of certain diseases or to determine whether a drug may be effective in treating a disease.

**Central Nervous System (CNS):** consists of the brain, brain stem and spinal cord.

**Coenzyme Q10:** An antioxidant studied in Parkinson's disease to slow down disease progression, but with little proven benefit so far.

**Cognition:** Mental processes including attention, remembering, producing and understanding language, solving problems and making decisions.

**Cognitive:** Relating to mental activity such as thinking, reasoning, making judgments and remembering.

**Cogwheel:** Stiffness of the muscles characterized by jerky movements when arms and legs are moved against a resistance.

**Complementary therapies:** These are non-medical treatments, which many people use in addition to conventional medical treatments, such as the Alexander technique, acupuncture, aromatherapy, music and art therapies, reflexology, and osteopathy.

**Computed tomography (CT):** A medical imaging method employing computer processing to produce images seen as slices through the tissue. This presentation of images is known as tomography.

**COMT Inhibitor:** A drug used to treat Parkinson's symptoms. It works by inhibiting COMT thereby preventing the breakdown of dopamine resulting in increased levels of this neurotransmitter.

**COMT (catechol-O-methyltransferase):** One of the enzymes that break down dopamine, adrenaline (also called epinephrine) and noradrenaline (also called norepinephrine).

**Continuous Dopaminergic Stimulation (CDS):** A therapeutic concept for the management of Parkinson's disease that proposes that continuous (as opposed to discontinuous or pulsatile) stimulation of striatal dopamine receptors will delay or prevent the onset of levodopa-related motor complications.

**Controlled Release Drugs:** These are special preparations of drugs that release the drug into the body slowly and steadily rather than all at once. They keep the amount of the drug in the bloodstream at a steadier level than the 'ordinary' version of the same drug.

**Cytokines:** A family of small proteins that are secreted by specific cells of the immune system and carry signals locally between cells, and thus have an effect on other cells.. Unlike growth factors, they have no specific role in cell proliferation and are primarily linked to blood and immune cells. Some cytokines are "pro-inflammatory, which is beneficial against infections ut may also cause death of cells in the body whereas others are "anti inflammatory" and may be beneficial in stopping inflammation. Higher levels of pro-inflammatory cytokines are found in Parkinson's brains.

**DaTscan:** a type of neuroimaging that can be used to differentiate between Parkinson's disease and conditions that look similar, by evaluating the brain's dopamine system.

**Deep Brain Stimulation (DBS):** A surgical treatment that involves the implantation of a medical device (electrical stimulator) that acts as a brain pacemaker sending electrical impulses to the specific area in which the electrode was inserted. In Parkinson's patients, the device is typically inserted in either the subthalamic nucleus or the globus pallidus, less often in the thalamus or pedunclopontine nucleus, depending upon the specific problem.

**Dementia:** A decline in cognitive function due to damage or disease in the brain beyond what might be expected from normal aging. Areas particularly affected include memory, attention, judgment, language, planning and problem solving.

- Alzheimer's disease dementia: The most common form of dementia, typically presents with difficulty in remembering names and events. May also initially include apathy and depression, and later impaired judgment, disorientation, confusion, behavior changes and

difficulty speaking, swallowing and walking. Associated with abnormal deposits of the protein fragment beta-amyloid (plaques) and twisted strands of the protein tau (tangles) as well as brain nerve cell damage and death.

- **Dementia with Lewy bodies (DLB):** Similar, but not identical, symptoms as in Alzheimer's dementia. DLB commonly has a greater occurrence of sleep disturbances, well-formed visual hallucinations, and muscle rigidity. Associated with aggregation of alpha-synuclein in the cerebral cortex. Lewy bodies are also a pathologic hallmark in Parkinson's disease. The relationship of DLB and PD remains to be resolved.
- **Parkinson's dementia:** Presents similarly to Alzheimer's dementia or dementia with Lewy bodies, but is typically preceded by clinical Parkinson's disease. Associated with alpha-synuclein aggregates that more likely begin in the brain stem, including the substantia nigra.

**Dendrites:** (from Greek meaning, "tree") Nerve fibers that project from the nerve cell body. Branches of dendrites are the receiving fibers of signals coming to the neuron from other neurons and convert these chemical signals into electrical ones to the nerve cell body.

**Depression:** Causes feelings of sadness and/or a loss of interest in activities once enjoyed. It can decrease one's ability to function in daily activities. Depression can be a clinical symptom of PD.

**Disease modification:** Treatments or interventions that affect the underlying pathophysiology of the disease and have a beneficial outcome on the course of a disease, for example Parkinson's.

**Disequilibrium:** Another word for unsteadiness or balance problems.

**DJ-1:** Mutations in this gene cause an autosomal recessive form of Parkinson's disease. The function of the DJ-1 protein appears to reduce oxidative stress.

**Dopa decarboxylase inhibitors:** Drugs (such as carbidopa) that inhibit the metabolism of levodopa to form dopamine. By inhibiting dopa decarboxylase only in the peripheral organs (not the Central Nervous System), levodopa concentration is increased and more can enter the brain. These drugs are particularly useful in Parkinson's when used with levodopa.

**Dopamine:** A small chemical molecule that is one of the brain's neurotransmitters. Among other brain regions, it is found in cells within the substantia nigra. These cells project to the striatum in the basal ganglia. Deficiency of dopamine in the striatum due to the death of cells in the substantia nigra causes symptoms of Parkinsonism.

**Dopamine agonist:** A compound that activates dopamine receptors, other than dopamine. Examples include, bromocriptine mesylate (Parlodel), pergolide (Permax), pramipexole (Mirapex), ropinirole hydrochloride (Requip), piribedil, cabergoline, apomorphine (Apokyn), rotigotine (Neupro patch) and lisuride. These act like dopamine, but are not actually dopamine. They can be used in both the early and late stages of Parkinson's disease. They are the second most powerful type of anti-Parkinson medication after levodopa. They can cause side effects such as sleepiness, sleep attacks, ankle swelling, hallucinations and impulse control problems, more commonly than levodopa does.

**Dopaminergic pathways:** Neural pathways in the brain which utilize dopamine as their neurotransmitter. There are four major groups: the nigrostriatal, mesocortical, mesolimbic and tuberoinfundibular pathways.

- **Nigrostriatal:** Connects the substantia nigra to the striatum. Involved heavily in Parkinson's.
- **Mesocortical:** Connects the ventral tegmental area (adjacent to the substantia nigra) to the cerebral cortex. Closely associated with the mesolimbic pathway. Can cause hallucinations and schizophrenia if not functioning properly.
- **Mesolimbic:** Connects ventral tegmental area to nucleus accumbens, amygdala & hippocampus and prefrontal cortex. Along with the mesocortical pathway, is involved in memory, motivation, emotional response, reward and addiction.
- **Tuberoinfundibular:** from hypothalamus to pituitary gland involved in hormonal regulation, maternal behavior (nurturing), pregnancy and sensory processes.

**Drug Repurposing:** Repurposing generally refers to studying drugs that are already approved to treat one disease or condition to see if they are safe and effective for treating other diseases.

**Duodopa:** Advanced Parkinson's therapy. It is a new means of delivering the current gold-standard via pump directly in the small intestines.

**Dysarthria:** Impaired speech function.

**Dyskinesia:** Abnormal involuntary movements; also sometimes called hyperkinesia.

**Dysphagia:** Difficulty in swallowing.

**Dystonia:** Characterized by persistent or intermittent contractions of opposing muscles causing abnormal movements or postures. It should not be confused with dyskinesia.

**Embryonic stem (ES) cells:** *See stem cells.*

**Encephalitis:** Inflammation of the brain. *See neuroinflammation.*

**Entacapone:** A Parkinson's drug that is used alongside levodopa and carbidopa. It inhibits the enzyme COMT, decreasing the breakdown of levodopa.

**Exosomes:** Small ball-like structures produced by the cells and which can be found in all sorts of body fluids such as blood, urine, and CSF and cultured medium of cell cultures. They are formed inside the cell and during this process they engulf bits of the cellular fluid and contents.

**Executive Dysfunction:** A deficit in executive functioning that may occur in Parkinson's dementia. Executive functioning allows the completion of tasks using higher level mental skills such as planning, organization, memory, flexible thinking, and self-regulation.

**Festination:** An involuntary quickening of the gait; the acceleration of gait noted in Parkinsonism and similar disorders, literally means "chasing the center of gravity".

**Freezing of Gait (FOG):** The sudden brief inability to walk or to continue walking.

**Functional magnetic resonance imaging (fMRI):** An imaging technique designed specifically for the brain. It measures the rate at which oxygen is removed from the blood to the cells, therefore suggesting the activity of a particular area of the brain.

**GABA (gamma amino butyric acid):** The principal inhibitory neurotransmitter in human brain. GABA neurons are rich in the striatum, globus pallidus, substantia nigra and cerebellum.

**GBA (Glucocerebrosidase):** An enzyme found within the lysosome of cells. Mutations in the GBA gene are associated with Parkinson's disease.

**GDNF:** Glial Cell line derived nerve growth factor. *See growth factors.*

**Gene therapy:** The insertion of genes into an individual's cells and tissues to treat hereditary diseases where deleterious mutant alleles can be replaced with functional ones. The genes are usually placed within a non-pathogenic virus, which serves as the vector to penetrate the cells. Gene therapy can also be used to correct non-genetic deficiencies such as the loss of dopamine in Parkinson's, to modify the function of a group of cells (e.g. convert an excitatory structure to one that is inhibitory) or to provide a source of growth factors.

**Genotype:** The collection of genetic material in an organism that gives rise to its characteristics.

**Glia (Glial cells):** Non-neural cells, commonly called neuroglia or simply glia (Greek for "glue"), that maintain homeostasis, form myelin, and provide support and protection for the brain's neurons. Astrocytes are one kind of glial cells.

**Globus pallidus:** A major part of the basal ganglia involved in movement control. It is split into two main parts: the internal globus pallidus (GPI), and the external globus pallidus (GPe). Deep brain stimulation of the GPI causes an increase in motor function in Parkinson's patients. Often patients also show a reduction in dyskinesia, probably because they require less levodopa.

**Glucose:** A simple sugar that is an important energy source in living organisms and is a component of many carbohydrates.

**Glutamate:** An amino acid and the main excitatory neurotransmitter in the human brain. The major input to the striatum is from the cerebral cortex and uses glutamate as a neurotransmitter. Excess glutamate can occur if the neurotransmitter is not well regulated and may cause cell death.

**Glycation:** The bonding of a sugar molecule to a protein or lipid molecule without enzymatic regulation.

**Glycosylceramide:** A type of cerebroside. Cerebroside is an important component in muscle and nerve cell membranes.

**Growth factors:** Naturally occurring substances (usually proteins) that help maintain the health of neurons and encourage cell growth, proliferation and differentiation. Some growth factors are being looked at to try to promote the survival of the neural cells that are degenerating in Parkinson's.

- Glial cell line derived nerve growth factor (GDNF): Thought to promote the health of dopamine neurons.
- Brain-derived nerve growth factor (BDNF): Also supports dopamine neurons.
- Fibroblast growth factor (FGF): Studies have found a possible genetic link to Parkinson's disease on the FGF20 gene.

- Vascular endothelial growth factor-B (VEGF-B): May have neuroprotective affects in Parkinson's disease.

**Gut microbiome:** The complex community of microorganisms that live in the digestive tracts of humans and other animals.

**Heterogeneity:** Lacking uniformity in composition or character (as opposed to homogeneity, which is uniformity in composition or character).

**Hippocampus:** A complex neural structure (shaped like a sea horse) located in the temporal lobes of the brain; involved in memory storage, motivation and emotion as part of the limbic system.

**Hoehn and Yahr scale:** A commonly used system for describing how the symptoms of Parkinson's disease progress. The higher the stage, the more advanced the disease.

- Stage 0: No signs of disease.
- Stage 1: Unilateral symptoms only.
- Stage 1.5: Unilateral and axial (midline) involvement.
- Stage 2: Bilateral symptoms. No impairment of balance.
- Stage 2.5: Mild bilateral disease with recovery on pull test.
- Stage 3: Balance impairment. Mild to moderate disease. Physically independent.
- Stage 4: Severe disability, but still able to walk or stand unassisted.
- Stage 5: Needing a wheelchair or bedridden unless assisted.

**Hyperkinesia:** An abnormal increase in movement and/or muscle activity; sometimes used synonymously with dyskinesia.

**Hypokinesia:** Literally means reduced amplitude of movement. It is commonly used synonymously (but erroneously) with akinesia and bradykinesia.

**Hypothalamic pituitary adrenal axis (HPA):** The three primary components of the endocrine system. Made up of the hypothalamus, pituitary gland and the adrenal cortex, the HPA has a wide range of functions from stimulating the stress response to controlling digestion, the immune system, mood, sexuality and energy storage and consumption.

**Hypothalamus:** A brain region that links the limbic system to the pituitary gland and is a master area for the autonomic nervous system.

**Idiopathic:** Arising from an unknown cause.

**Idiopathic Parkinson's disease:** This term is used to describe the common type of Parkinson's disease to distinguish it from other forms of Parkinsonism (also termed "Sporadic PD").

**Impulse control disorder (ICD):** A set of psychiatric disorders characterized by an inability to control one's actions, in particular those that might bring harm to oneself or others. Common ICDs

in patients receiving dopamine agonists are pathologic gambling, compulsive eating, compulsive shopping and hypersexuality.

**Interdisciplinary care:** Multiple healthcare professionals collaborating to provide care with a common perspective, often involving joint consultations.

**iPS Cells:** Stem cells that can be generated directly from adult cells. *See stem cells.*

**Learned voluntary movements:** Movements that we learn to do, like walking and talking.

**Leucine rich repeat kinase 2 (LRRK2):** A protein created by the LRRK2 gene which when mutated can lead to Parkinson's. Several different mutations in the LRRK2 gene have been found to cause Parkinson's disease, but there may also be variants within the general population that do not necessarily cause disease.

**Levodopa (L-DOPA):** A chemical that is the precursor to dopamine. It can pass through the blood-brain barrier (whereas dopamine cannot). Once it has entered the central nervous system, L-dopa is converted into dopamine by aromatic L-amino acid decarboxylase (DOPA decarboxylase/DDC). L-DOPA is also converted into dopamine within the peripheral nervous system, but this is usually blocked by employing peripherally-active dopa decarboxylase inhibitors to avoid unwanted effects.

**Lewy bodies:** A pathologic hallmark of Parkinson's disease and dementia with Lewy bodies. First described by Frederic Lewy, Lewy bodies are seen microscopically as inclusions in neurons in several brain regions, including the substantia nigra and locus ceruleus. One protein seen is alpha-synuclein in an aggregated form. Aggregates of this protein in axons are called Lewy neurites.

**Magnetic resonance imaging (MRI):** A noninvasive medical imaging technique to visualize detailed internal structure and limited function of the body. MRI provides much greater contrast between the different soft tissues of the body than computed tomography (CT), making it especially useful in neurological (brain), musculoskeletal, cardiovascular and oncological (cancer-related) imaging.

**MAO (monoamine oxidase):** A family of enzymes with two subtypes: MAO-A and MAO-B. These catalyze the oxidation of amine molecules (replacing the amine group with an oxygen molecule.)

- MAO A inhibitors: Drugs that inhibit the MAO-A enzyme, which is responsible for the metabolism of dietary tyramine. MAO-A inhibitors can cause tyramine-induced hypertension, the so-called "cheese effect" because tyramine can be found in high concentrations in some soft cultured cheeses.
- MAO B inhibitors: These drugs (e.g. selegiline, rasagiline) inhibit the breakdown of dopamine via MAO-B enzyme and do not cause the "cheese effect" of hypertension.

**MPTP (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine):** A neurotoxin precursor of MPP+ that is taken up in dopamine nerve terminals. MPP+ damages the dopamine cells. MPTP is catalyzed to MPP+ by MAO-B. MPTP has been widely used to create an animal model of Parkinsonism by depleting substantia nigra dopamine neurons.

**Microbiome:** The collection of microbes (bacteria, viruses, fungi) and their genetic material that live outside an area of the human body. *See gut microbiome.*

**Microglia:** A type of glial cell; it provides the first immune defense mechanism in the brain and central nervous system.

**Micrographia:** The tendency to have very small handwriting due to difficulty with fine motor movements in Parkinson's disease.

**Mild Cognitive Impairment (MCI):** A decline in memory or intellectual functioning that is not as severe as that found in dementia.

**Mitochondria:** A spherical or elongated organelle in the cytoplasm of nearly all eukaryotic cells, containing genetic material and many enzymes important for cell metabolism, including those responsible for the conversion of food to usable energy. It consists of two membranes: an outer smooth membrane and an inner membrane arranged to form cristae.

**Mitophagy:** The selective degradation of mitochondria by autophagy. *See Mitochondria and Autophagy.*

**Motor skills:** The degree of control or coordination provided by brain control of the skeletal muscles.

**Motor symptoms:** Symptoms that involve movement, coordination, physical tasks or mobility. These include, among others: resting tremor, bradykinesia, rigidity, postural instability, freezing, micrographia, mask-like expression, unwanted accelerations, stooped posture, dystonia, impaired motor dexterity and coordination, speech problems, difficulty swallowing, muscle cramping, and drooling of saliva. *See non-motor symptoms.*

**Movement Disorder Specialist (MDS):** A neurologist that has special interest in and extra training and experience with movement disorders such as Parkinson's disease.

**Multidisciplinary care:** Care given by multiple healthcare professionals each approaching the patient from their professional perspective, often involves separate, individual consultations.

**Multiple System Atrophy (MSA):** A less common degenerative neurological disorder that causes symptoms similar to Parkinson's disease but with more widespread damage to the central nervous system. Other systems involved besides the basal ganglia include the cerebellum and autonomic systems.

**Neuroinflammation:** The swelling of the tissue in the nervous system. It could be initiated in response to a number of things including infection, traumatic brain injury, toxic metabolites, or autoimmunity. Microglia are the immune cells activated in response to these cues.

**Neurology:** A branch of medicine dealing with the diagnosis and treatment of disorders of the nervous system.

**Neuromelanin:** The dark pigment made from oxidized metabolites of monoamine neurotransmitters including dopamine and norepinephrine, found in neurons enriched with these amines, namely the substantia nigra and locus ceruleus, respectively. Neuromelanin gives the substantia nigra (Latin for "black substance") its black appearance.

**Neuromodulator:** A chemical substance other than a neurotransmitter, released by a neuron at a synapse and either enhances or dampens their activities.

**Neurological conditions:** Disorders caused by damage or malfunctioning of the brain or nervous system.

**Neurologist:** A doctor who specializes in the diagnosis, care and treatment of disorders of the brain or nervous system.

**Neuroplasticity:** The ability of the brain to change and form new connections even with aging. It involves neurons regenerating anatomically or functionally after partial injury, or changing (such as by making more numerous or more effective connections) in response to training and experience.

**Neuron:** A nerve cell that is the fundamental unit of the brain and nervous system. Neurons transmit information through electrochemical signals.

**Neuroprotection:** Mechanisms within the nervous system that would protect neurons from dying due to a degenerative disease or from other types of injury.

**Neuroprotective:** Serving to protect neurons from injury or degeneration or an effect that may result in salvage, recovery or regeneration of the nervous system, its cells, structure and function.

**Neuropsychology:** The study of how the structure and function of the brain influence behavior and cognition.

**Neuroscience:** The scientific study of the nervous system that deals with the anatomy, biochemistry, molecular biology, and physiology of neurons and neural circuits.

**Neurotransmitter:** A chemical messenger in the nervous system that permits communication between two neuronal cells, often but not always across a synapse. The neurotransmitter is usually released from the nerve terminals on the axons. Examples of neurotransmitters include dopamine, acetylcholine, adrenaline, noradrenaline, serotonin, glutamate, and GABA.

**Neurotrophic factors:** A family of biomolecules that support the growth, survival, and differentiation of both developing and mature neurons.

**Nicotine:** A stimulant that acts as an agonist at nicotinic receptors, which are one kind of receptors for acetylcholine. Nicotine is present in cigarette smoke and has been proposed to decrease chances of developing Parkinson's disease, but this remains controversial and the mechanism of the relationship is not well understood.

**Non-motor symptoms:** Symptoms that do not involve movement, coordination, physical tasks or mobility, including impaired sense of smell, constipation, sleep disturbances, mood disorders, orthostatic hypotension, bladder problems, sexual problems, excessive saliva, weight loss or gain, vision and dental problems, fatigue, depression, fear and anxiety, skin problems, and cognitive issues. *See motor symptoms.*

**Objective measurements:** The repetition of a unit amount that maintains its size, within an allowable range of error, no matter which instrument, intended to measure the variable of interest, is used and no matter who or what relevant person or thing is measured.

**Occupational therapist:** Occupational therapists are concerned with assessing a person's home or work situation and then devising ways to make them more manageable and less hazardous. They can also advise on aids and equipment and leisure activities.

**Olfactory dysfunction:** An impaired ability to detect odors, impaired sense of smell. Thought to be an early sign of Parkinson's disease but can occur in many situations not related to Parkinson's.

**On and Off:** The clinical states of PD while being treated with levodopa, which commonly causes clinical fluctuations after a few years of treatment. The "on" state is when the PD symptoms and signs are reduced by levodopa. The "off" state is when the benefit has been reduced or lost. The most common type of "off" is wearing-off, due to the levodopa's benefit not lasting more than 4 hours after a dose. Sudden and unpredictable "off" states can also occur, but are less common. "Off" states usually will respond to another dose of levodopa. Clinical fluctuations are considered a complication of levodopa therapy.

**Organoid:** A miniature, simplified version of an organ that shows realistic micro-anatomy. They are derived from tissue, embryonic stem cells, or induced pluripotent stem cells.

**Orthostatic hypotension:** A drop in blood pressure when a person is standing. It can be a complication of medications, but can sometimes be due to Parkinson's itself.

**Oxidative stress:** *See Reactive Oxidative Species.*

**Paradoxical kinesia:** The ability to move as a response to an unexpected stimulus, occurring in a person who previously could not move so easily. Paradoxical kinesia can occur in Parkinson's disease.

**Parkin:** A protein that is generated by the Parkin gene. With homozygous (both alleles affected) Parkin mutations (PARK2 gene), Parkinson's disease develops. It is the most common cause of juvenile onset PD.

**Parkinson-plus syndromes:** A group of neurodegenerative diseases featuring the classical features of Parkinsonism (rigidity, akinesia/ bradykinesia, postural instability and less commonly tremor) with additional features that distinguish them from typical Parkinson's disease. Parkinson-plus syndromes include multiple system atrophy (MSA), progressive supranuclear palsy (PSP), and corticobasal degeneration (CBD).

**Parkinsonism:** A group of neurological diseases whose features include slowness and paucity of spontaneous movement (bradykinesia), rest tremors, rigidity of the muscles, loss of postural reflexes, flexed posture and freezing of gait.

**Parkinsonian gait:** With bradykinesia, gait is slow, short paced and with a tendency to shuffle, associated with decreased arm swing. Freezing of gait can also occur in Parkinsonism.

**Pathogenesis:** The underlying biologic mechanism responsible for a disease.

**Peripheral Nervous System:** The nervous system outside the brain and spinal cord.

**Phenotype:** The observable characteristics of an organism or person, such as appearance, development and behavior. Determined by the interaction between the genotype and the environment.

**Phosphorylation:** A process that modifies proteins by adding one or more phosphates. For proteins that function as enzymes, this results in activating or deactivating their function.

**Pill-rolling tremor:** A characteristic tremor in Parkinson's patient where the thumb and forefinger involuntary move in a way that resembles rolling a small object such as a pill.

**PINK-1:** An abbreviation for the name of a gene that encodes a particular serine/threonine kinase found in mitochondria that stops stress related cell destruction. With homozygous (both alleles affected) *PINK-1* mutations, juvenile or early onset Parkinson's disease can develop. Lack of PINK-1 causes an overload of calcium in mitochondria and indirectly cell death. The substantia nigra is particularly sensitive to PINK-1 mutations.

**Physiotherapist:** Physiotherapists use physical means such as exercise and manipulation to help prevent or reduce stiffness in joints and restore muscle strength. They can also advise on aids and equipment to help with movement problems.

**Placebo:** A simulated or inert form of treatment without known proven benefit on a symptom or a disease. A pill serving as a placebo is colloquially called a "sugar pill." Placebos are employed in controlled clinical trials along with the active drug being tested; patients and health professionals involved in the trial do not know who receives the placebo or the drug. The difference in responses between the two drugs is considered the true effect of the active drug. Surgical trials can also utilize a placebo arm in which sham or simulated surgery is performed in the control group. Sometimes placebos provide benefit; it is called a placebo effect. The mechanism of how placebos provide benefit may be associated with release of dopamine in the brain when patients believe that they receive an effective drug.

**Positron emission tomography (PET):** A medical imaging technique in which radioactive isotopes that emit gamma rays are used. The radioactive substance is incorporated into a chemically active compound (a radiotracer, which could be a substrate for an enzyme or a ligand that binds to neurotransmitter receptors) utilized by an organ in the body. The emitted gamma rays are detected by a special camera/scanner. These radioactive strikes on the camera are analyzed by a computer to produce an image to localize where that ligand is located in the organ being studied. Fluorodeoxyglucose (FDG) measures regional metabolism of glucose (sugar); fluorodopa (F-DOPA) is taken up in dopamine nerve terminals. The amount of uptake serves as a measure of the integrity of these nerve terminals. Other radiotracers may bind to neurotransmitter receptors (including those for dopamine) or to inflammatory cells, etc.

**Postural instability:** Difficulty with balance.

**PPMI - Parkinson's Progression Markers Initiative:** a study launched in 2010 by Michael J Fox Foundation to find biomarkers for PD; s a landmark observational clinical study to comprehensively

evaluate people with Parkinson's disease and those at greater risk of developing the disease, as well as healthy controls.

**Prodromal:** Referring to the period before the classic manifestation of a disease leading to diagnosis.

**Progressive Supranuclear Palsy (PSP):** A rare degenerative brain disorder that causes serious and progressive problems with control of gait and balance, along with complex eye movement and thinking problems. A classic manifestation of the disease is the inability to move the eyes properly. PSP is one of the Parkinson-plus syndromes.

**Proteostatis:** A combination of the words protein and homeostasis. It is the concept that there are biological pathways within cells that control the creation, folding, tracking, and degradation of proteins present within and outside the cell.

**Protesomes:** Protein complexes which degrade unneeded or damaged proteins.

**Protein:** 1. A class of food necessary for the growth and repair of the body tissues—sources of proteins include fish, meat, eggs and milk. 2. Large biomolecules or macromolecules consisting of long chains of amino acid residues. Within organisms, proteins catalyze metabolic reactions (enzymes), replicate DNA, and transport molecules.

**PwP:** Person with Parkinson's.

**Reactive oxygen species (ROS):** Chemically-reactive molecules containing oxygen that may trigger cell death. These are also called oxyradicals. These molecules are a cause of oxidative stress that may play a role in the pathogenesis of cell death of dopamine neurons. Oxyradicals are formed during regular cellular and mitochondrial metabolism. Defense mechanisms include naturally occurring reducing agents to neutralize the oxyradicals.

**Receptor:** A protein structure typically embedded in the cell membrane with which neurotransmitters and drugs interact.

**REM (rapid eye movement) sleep behavior disorder (RBD):** A sleep disorder that involves movement and abnormal behavior during the sleep phase with rapid eye movements - the stage of sleep in which dreaming occurs. In normal sleep, muscles are paralyzed during dreaming, except for the eye movements. In RBD, muscles are not paralyzed so that the dreamer acts out his or her dreams. RBD is common in people with Parkinson's disease or Multiple System Atrophy.

**Restless leg syndrome (RLS):** A neurological disorder characterized by unpleasant sensations in the legs, like the feeling of ants crawling underneath the skin. These sensations usually occur in the late evening and during sleep. Walking around relieves the sensation, hence the term "restless legs." RLS interferes with sleep and is common in people with PD. Medications, such as dopamine agonists, levodopa and opioids, can be effective treatments.

**Rigidity:** A special type of muscle stiffness, which is one of the main symptoms of Parkinson's disease. The muscles tend to pull against each other instead of working smoothly together.

**Schwab and England Activities of Daily Living (ADL) Scale:** An estimation of the abilities of a person's degree of independence. The person (or a family member) can self-assess this as:

- 100% - Completely independent. Able to do all chores without slowness, difficulty or impairment.
- 90% - Completely independent. Able to do all chores with some slowness, difficulty or impairment. May take twice as long to complete.
- 80% - Independent in most chores. Takes twice as long. Conscious of difficulty and slowing.
- 70% - Not completely independent. More difficulty with chores. 3 to 4 times longer to complete chores for some. May take large part of day for chores.
- 60% - Some dependency. Can do most chores, but very slowly and with much effort. Errors, some impossible.
- 50% - More dependent. Help with 1/2 of chores. Difficulty with everything.
- 40% - Very dependent. Can assist with all chores but few alone.
- 30% - With effort, now and then does a few chores alone or begins alone. Much help needed.
- 20% - Nothing alone. Can do some slight help with some chores. Severe invalid state
- 10% - Totally dependent, helpless.
- 0% - Vegetative functions such as swallowing, bladder/bowel function are not functioning. Bedridden.

**Senescence:** A process in cells that stops them from dividing. It gets activated when certain types of damage occur.

**Serotonin:** A neurotransmitter that regulates mood, appetite, and sleep. It also has some cognitive functions, including memory and learning. The serotonin-containing neurons are in the brain stem. Serotonin is reduced in PD.

**Shaking palsy:** Prior term for Parkinson's disease.

**Side effects:** A reaction to drugs, which is additional to the intended therapeutic actions. These unwanted extra effects are called side effects. Side effects vary in their severity from person to person, and often disappear when the body becomes used to a particular drug.

**Single photon emission computed tomography (SPECT):** A nuclear medicine tomographic imaging technique using gamma rays and able to provide 3D information, for instance on brain chemistry.

**Sleep apnea:** A sleep disorder characterized by abnormal pauses in breathing or instances of abnormally low breathing during sleep.

**Sodium channel:** Voltage gated channels in nerve cell membranes that allow the generation of action potentials. Sodium ions are important in generating the electrical impulses that travel down the dendrites and axons. After sodium enters the cell during this process, it needs to be pumped back out, via the so-called sodium-pump, a process that requires the utilization of cellular energy. Sodium channels may be a target for new drugs in Parkinson's.

**Stem cells:** Biological cells found in all multicellular organisms, that can divide (through mitosis) and differentiate into diverse specialized cell types and can self-renew to produce more stem cells.

They are a potential line of treatment in Parkinson's, either by directly replacing the old nigrostriatal neuronal cells or by creating growth factor releasing cells. Problems have arisen due to the inability to stop growth, which may cause tumor growth.

**Striatum:** A large cluster of nerve cells that are part of the basal ganglia. The striatum consists of two sectors: the caudate nucleus and the putamen. It controls movement, balance, and walking; the striatum receives nerve inputs from many parts of the brain including dopamine neurons from the substantia nigra and glutamate neurons from the cerebral cortex. Acetylcholine and GABA neurons are located within the striatum. GABA neurons also send signals outside the striatum. The striatum contains the largest concentration of dopamine and acetylcholine in the brain.

**Substantia nigra:** (Latin for black substance). A brain structure located in the midbrain that plays an important role in movement. Parts of the substantia nigra appear darker than neighboring areas due to high levels of neuromelanin in dopaminergic neurons. The substantia nigra is the site of the brain's major collection of dopamine neurons, which project their axons to the striatum, the so-called nigrostriatal pathway. These neurons slowly die in PD. The substantia nigra is part of the basal ganglia; the other parts of the basal ganglia include the striatum (caudate nucleus, putamen), globus pallidus, and subthalamic nucleus. The substantia nigra is made up of two parts: the pars compacta and the pars reticulata.

- Pars compacta: The part of the substantia nigra primarily involved in Parkinson's. It contains dopamine neurons, and it is black due to the high concentration of neuromelanin within these neurons. (Parkinson's disease is characterized by the death of dopaminergic neurons in the substantia nigra pars compacta.)
- Pars reticulata: Part of the substantia nigra that serves both as the location of dendrites from the pars compacta, receiving nerve signals to the substantia nigra and also as an output, conveying signals to numerous other brain structures. These output neurons are mainly GABAergic neurons.

**Subthalamic nucleus (STN):** A small lens-shaped nucleus involved in movement control. As suggested by its name, the subthalamic nucleus is located below the thalamus. It is part of the basal ganglia. It receives input from the cerebral cortex and from the globus pallidus interna. It sends its output mainly to the globus pallidus externa and substantia nigra pars reticulata. It is a component of the "indirect pathway" within the basal ganglia. It is "overactive" in PD due to loss of inhibitory incoming fibers. It is a common target in deep brain stimulation for PD.

**Shuffling gait:** Refers to short, slow steps, with feet close to the ground or dragging along the ground. This gait is often seen in people with advanced Parkinson's disease.

**SWEDD- Scans Without Evidence of Dopamine Deficit:** When individuals with early-stage Parkinson's disease have normal dopaminergic functional imaging scans, these are called Scans Without Evidence of Dopamine Deficit.

**Synapse:** The narrow space between two neurons (axon to dendrite) or between a neuron and a muscle. Axons release neurotransmitters at the nerve terminal. The neurotransmitter crosses the synapse to activate or inhibit another nerve cell by acting on a receptor on the dendrite.

**Synaptic plasticity:** The ability of synaptic activity to modify and adapt to changes.

**Syndrome:** A group of symptoms that tend to occur together and which reflect the presence of a specific disorders or diseases. Parkinson syndrome, also called Parkinsonism, comprise a group of disorders with symptoms and signs in common, such as bradykinesia, rigidity, tremor, loss of postural reflexes, flexed posture and freezing of gait. A person with Parkinsonism does not need to have all of these but must have bradykinesia according to one diagnostic criterion. Disorders that fall within Parkinson syndrome include Parkinson's disease, atypical Parkinsonism, Parkinson Plus Syndromes, drug-induced Parkinsonism, and normal pressure hydrocephalus.

**Synucleinopathy:** A class of neurodegenerative disease resulting from pathological accumulation of alpha-synuclein in neurons (Parkinson's, Lewy Body Dementia) or a kind of glia cells called oligodendrocytes (Multiple System Atrophy).

**Tau proteins:** Proteins that stabilize microtubules, which are structural entities in axons. They are abundant in neurons in the central nervous system and are less common elsewhere. When tau proteins are defective and no longer stabilize microtubules properly, they can result in dementia (including Alzheimer's disease).

**Tauopathies:** A class of neurodegenerative diseases resulting from the pathological aggregation of tau protein in so-called neurofibrillary tangles (NFT) in the human brain. Besides Alzheimer's, this is commonly seen in Pick's disease, progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD).

**Thalamotomy:** A now uncommon surgical procedure used to treat Parkinson's tremor in which a small portion of the brain area called the thalamus is destroyed.

**Thalamus:** A midline paired symmetrical structure situated between the cerebral cortex and brain stem, both in terms of location and neurological connections. It is composed of many regions with distinct functions. For example, some thalamic regions relays sensory signals to the cerebral cortex, other relay signals from the basal ganglia to the cerebral cortex, and others relay motor signals from the cortex to the spinal cord and brain stem.

**Toxicity:** The degree to which a chemical substance or a particular mixture of substances can damage an organism.

**T.R.A.P.:** Acronym for four primary Parkinson's disease symptoms:

- Tremor: Shaking of limb (usually hands) while they are at rest.
- Rigidity: Muscle stiffness and resistance to movement.
- Akinesia/bradykinesia: Difficulty initiating voluntary body movements/Slowed ability to start and continue movements.
- Postural instability: Loss of postural stability can cause falls and produce a feeling of unsteadiness.

**Transcranial Magnetic Stimulation:** A method in which a changing magnetic field is used to cause electric current to flow to a small region of the brain.

**Transcription factors:** Proteins in eukaryotes (cells which contain complex membrane-bound structures within the cell) that regulate the transcription (i.e. the expression) of genes.

**Translation:** A step in protein biosynthesis wherein the genetic code transferred from DNA to messenger RNA (mRNA) is decoded to allow the formation of a protein molecule. The process is preceded by transcription of the DNA into the mRNA.

**Tyramine-induced hypertension:** High blood pressure caused by an increase in tyramine in the blood, which forces noradrenaline/norepinephrine out of vesicles and into circulation. This is the so-called "cheese effect" because some fermented cheeses (and other foods) contain high concentrations of tyramine. Normally, tyramine is broken down in the gut by MAO-A. When this enzyme is inhibited, the tyramine in food is able to enter the blood stream and produce its hypertensive crisis.

**Tyrosine:** An amino acid used by cells to synthesize proteins. It is also the precursor of dopamine.

**Ubiquitin:** A small regulatory protein that is composed of 76 amino acids. It is involved in the degradation of damaged proteins. In Parkinson's disease, it is believed that accumulation of damaged proteins "choke" the cell, leading to the eventual death of the cell.

**Unified Parkinson's Disease Rating Scale (UPDRS):** A rating scale used to measure the severity of Parkinson's disease. The UPDRS can follow a person's worsening over time and also measure improvement with various treatments. The UPDRS is made up of the following sections:

- Part I: Evaluation of mentation, behavior, motivation and mood
- Part II: Self-evaluation of the activities of daily life (ADLs) including speech, swallowing, handwriting, dressing, hygiene, falling, salivating, turning in bed, walking, cutting food
- Part III: Clinician-scored motor evaluation
- Part IV: Measures some of the adverse effects (such as motor complications of "off" states and dyskinesias) of levodopa therapy in Parkinson's disease

The UPDRS has been modified by the Movement Disorder Society to include more non-motor features of PD. This new version is called MDS-UPDRS.

**Ventral Tegmental Area (VTA):** A group neurons located in the midbrain next to the substantia nigra and involved in cognition and motivation, including reward and addiction.

**Vesicle:** An organelle in a cell that separates some molecules from the rest of the cell. In nerve terminals, the vesicles are called synaptic vesicles. They store neurotransmitters, which are released into the synapse when the nerve fires.

**Wearable devices:** Devices worn on the body, incorporating computers, electronics, software and/or sensors, often used to measure some aspect of function or physical manifestation, for example: activity trackers, accelerometers, gyroscopes, etc.

**Wearing Off:** The loss of the effectiveness of Parkinson's medication between doses resulting in the return of symptoms.