

Parkinson's Disease: An Unknown World of Danger

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ABSTRACT

Parkinson's Disease is a very common disease, not only in the United States but also in the entire world. Many people are known to be affected by this disease, and just as many do not know the true extent of the disease. With the commonality of the disease, it's vital that individuals are knowledgeable about this disease. Parkinson's Disease is a neurological disorder that causes individuals affected to lose their control for movement, causing tremors throughout the face and body. This review article thoroughly examines the causes and symptoms of this disease, discusses treatments that could be provided to a suffering patient, and previews the cure that is hoped to be released in the future.

Introduction

Parkinson's Disease, or *paralysis agitans*, is a common but incredibly dangerous disease that is slow to start but packs a hard punch. This disease's symptoms are not pleasant, however mild or severe. However, the question is: what causes this disease and how are people affected by it?

Symptoms

Parkinson's Disease is a neurological disorder that affects more than half a million people in the world, though some experts estimate it to be over one million because of misdiagnosed cases. The disease causes an individual's fine motor functions to break down, which is often seen as tremors on the hands and legs that seem to be uncontrollable. Movements are slowed down, as if they require a lot more effort than normal, and even an inability to move (akinesia) can also occur. It causes unintended movements of the body, which can include shaking, stiffness, limits to the range of motion of joints in the body, and difficulty in chewing and swallowing, which leads to drooling. As it goes on, researchers have noticed that PD¹ patients also have a decreased cognitive level. These symptoms are first noticed when the unnatural movements are worse enough to cause incredible difficulty with simple tasks such as eating, speaking, and writing; this is when most individuals diagnosed visit a neurologist for the first time. PD is slow to progress, which is why most symptoms associated with it are seen in the later years of life, usually after the average age of 55.

However, some symptoms of Parkinson's Disease may show up early, known as Young Onset Parkinson's Disease (YOPD). It's rare to be diagnosed with the disease earlier than the age of 50, as they make up less than 2% of total PD cases. These patients also tend to experience more cognitive disabilities, such as dementia and memory problems. Nevertheless, YOPD patients are usually better candidates for surgery and treatments usually work more effectively than normal patients.

There are more cases of PD in men than women, which is a statistic that is deemed controversial by many researchers. This is mainly because of toxic exposure from more male-dominated areas, such as construction, and head trauma, injuries that men are more prone to than women. Some of these factors may also include mitochondrial dysfunction and other genetic factors.

As Parkinson's Disease progresses in an individual's body, they start to lose their bodily functions. In some cases the symptoms start in one part of the body, usually the extremities, and the area affected grows larger and larger until it affects the entire body. In other cases, it's one part of the body, usually a limb, that doesn't function normally. And in some cases, the disease affects the entire body. While the disease affects the human body physically, it can also greatly impact the human body mentally. Because of Parkinson's Disease, many patients are in denial that their body no longer works the way it used to, and no longer have the ability to do physical activity. This causes patients to also get diagnosed with depression.

Parkinson's Disease itself is not fatal. However, the symptoms of it can lead to death. As the brain gradually starts to lose control of the muscles, self-sufficiency is often compromised. A constant caretaker is required, and life expectancy decreases to an average of 15 years. As the disease worsens, living independently gets more difficult everyday because of deteriorating mind-muscle connection and one has to live with family or at a nursing home.

Causes

There are a large variety of reasons that can minutely or significantly influence the symptoms of Parkinson's Disease. The exact cause remains to be unknown, but there are many theories on why the disease starts to develop such as: environmental toxins, oxidative damage, brain injuries, and mutations in specific genes.

Only 15% of patients have a familial genetic history of Parkinson's Disease, and they are particularly linked to a group of genes: LRRK2, PARK2, PARK7, PINK1, or SNCA. Any of these genes, when they are inherited with a mutation, can result in catastrophic damage to the body. For example, the PARK2 gene's main function is to code for a protein called parkin, which is involved in breaking down and recycling protein. When mutated, the gene could not only denature proteins, but also other parts of the cell. A mutated LRRK2 or SNCA gene only needs to be received by one parent to inherit Parkinson's Disease, known as an autosomal dominant pattern. PARK2, PARK7, or PINK1 need to be inherited by both parents to have a likely chance to cause PD, known as an autosomal recessive pattern.

Sometimes, gene variants from faulty genes cause unwanted proteins to denature. These proteins start to accumulate, resulting in damaged or dead dopamine-producing neurons. In other times, different gene variants attack the mitochondria, which is the powerhouse of the cell. When the mitochondria produce energy, they usually have a byproduct, known as free radicals, which are unstable molecules that damage the cell. Usually, cells have a counter system in place to stop these unstable molecules from destroying the cell, which are proteins built for this specific task, but these genetic mutations sabotage this process from happening. This results in the free radicals destroying the cells, resulting in Parkinson's Disease getting worse.

However significant the cause may be, for Parkinson's Disease to develop, the area of the brain that malfunctions is the substantia nigra, which is located in the midbrain posterior to the cerebral peduncle. The substantia nigra is exceptionally important in the brain as it is required for dopamine production, a chemical that the brain uses to send signals and to balance its pH. The disease is first noticed when almost 80% of the substantia nigra is almost destroyed. Through Magnetic Resonance Imaging (MRI), the substantia nigra appears white, which means that the area is dead. When most of the dopamine-producing neurons get damaged or die, the decreased amount of dopamine starts to weaken and eventually lose the communication links between the brain and the muscles. Eventually, the brain starts to lose control of the muscles. Also, the brain uses dopamine to keep a balance in its pH level and for other chemicals in the brain. For example, when alcohol is consumed, there is way too much dopamine in the brain. The brain cannot handle an excess of dopamine, causing it to lose judgement and awareness, also known as a high. When there is a lack of dopamine, the chemical balance of the brain shifts, resulting in the brain not incapable of sending signals as effectively.

Treatments

Treatments for Parkinson's disease are varied based on how fragile the body's state is as the disease progresses. These treatments can include medications, prescriptions, physical therapy, and surgery, which are aimed to reduce the symptoms of PD. However, the type and prescription of the treatment depends upon the level of intensity of the patient's symptoms.

Medications

Many drugs have been developed by researchers and they provide temporary relief from the symptoms of PD. Levodopa, considered the gold standard of treatment, is prescribed by doctors to treat Parkinson's Disease. These pills are usually given to patients when their symptoms get harder to control. Usually, clinicians use levodopa as a dopamine-replacing agent for their patients as a way of treatment. When levodopa enters the brain, it acts as a supplement for the substantia nigra. It stimulates the current neurons in the area to produce dopamine and it also gives some pre-produced dopamine. When the degeneration of the substantia nigra occurs, the nigrostriatal pathway, a path in which dopamine travels from the substantia nigra to the rest of the brain, is disconnected. Dopamine cannot but levodopa can cross the blood-brain barrier (BBB) that occurs because of the disruption of the nigrostriatal pathway. Once crossing the barrier from the periphery (the area right before the barrier), the levodopa converts to dopamine. To prevent the levodopa from converting to dopamine before it crosses the nigrostriatal pathway, several dopamine decarboxylase inhibitors, such as carbidopa and benserazide, are prescribed. This allows for more of the levodopa to cross the pathway. This increased dopamine allows the brain to become balanced with the amount of chemicals in the brain and allows it to send signals to the body efficiently, thus reducing tremors and other motor symptoms of Parkinson's Disease. It allows for the diagnosed patient to have an easier lifestyle, even though it is only a temporary fix.

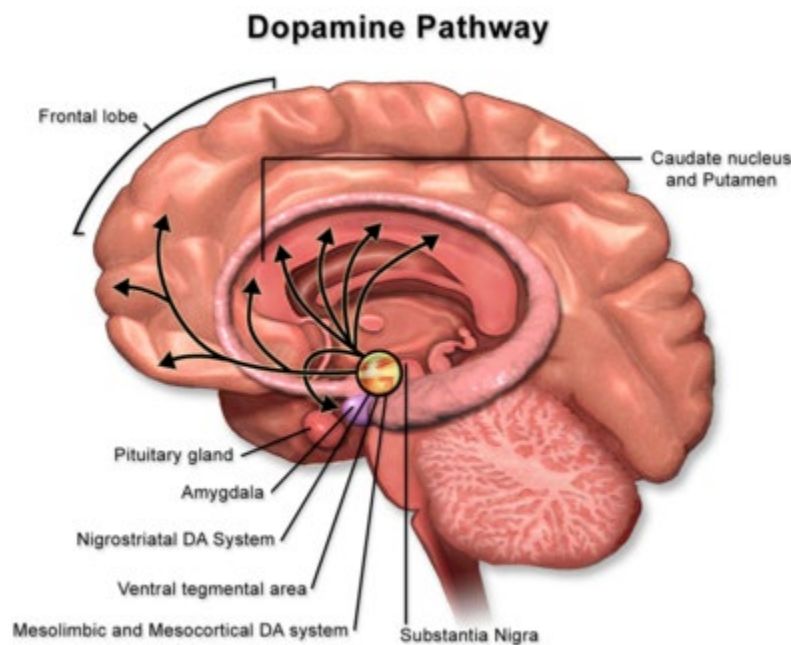


Figure 1. A diagram of the brain showing the substantia nigra (most bottom right label) and the nigrostriatal system (3rd label in bottom left). This shows the pathway dopamine takes when leaving the substantia nigra.

Surgery

There are several types of surgery available for a patient. The objective of the procedure is to reduce the symptoms of Parkinson's Disease without harmful side effects, which allows the patient undergoing surgery to return to a lifestyle that isn't completely run by Parkinson's Disease. Some of these surgeries include ablative surgery, deep brain stimulation (DBS), and transplantation surgery. These surgeries are only available for people who qualify for them, which is usually only about 10% of all candidates. These eligible candidates are usually for people whose prescribed medication is ineffective.

Ablative Surgery

An ablative surgery's objective is to remove the area of the brain that causes the unnatural tendencies and symptoms of Parkinson's Disease. Most ablative surgeries are performed on the globus pallidus region of the brain. First, an MRI is taken to locate the exact area that causes the uncontrollable tremors of the face and limbs. During the surgical procedure, surgeons target, locate, and then destroy that lesion of the brain. They use an MRI-guided probe to locate the area and then destroy it using lasers and heat and then remove the dead cells. This makes it so that the part that produces the abnormal chemicals or improper electrical impulses does not affect the patient any more. However, this isn't a complete cure, but instead is a major temporary stop against the disease. As time goes on, more cells in the area start to die, which revamps the problems again.

Deep Brain Stimulation (DBS)

This is the most popular surgery used to treat Parkinson's Disease, as it is the procedure with the most effective and profound results. In the surgery, a patient (can stay awake or can be put into general anesthesia) allows the surgeon to efficiently drill a hole through the skull for the brain tissue to receive the signal. A small device, which can be called a deep brain stimulator or a neurostimulator, which is an extremely small and innovative device, is inserted into the brain and is attached to the motor cortex of the brain. A second wire is run through up from the collarbone, with a battery attached to it and placed deeper than the clavicle. When it is fully set up, there are two wires running from the top of the cranium to underneath the clavicle, and they connect to the neurostimulator. The neurotransmitter works by sending electrical impulses into the brain. When the deep brain stimulator senses that the motor cortex starts to send out signals that cause the uncontrollable tremors, it instantly sends an electrical impulse. This causes the motor cortex to temporarily disable, stopping the tremors.

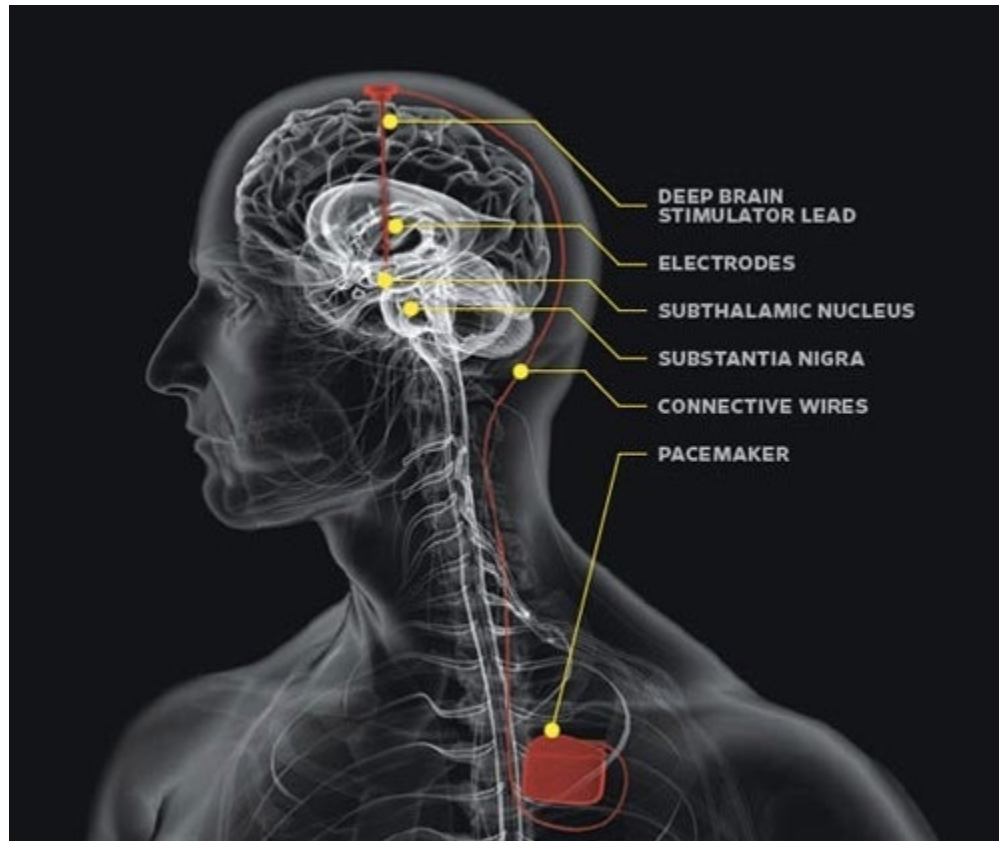


Figure 2. A diagram of where a neurostimulator from a DBS surgery is placed within the body.

Transplantation Surgery

This surgery is completed by transplanting stem cells from donors to eligible PD surgical patients. Stem cells are base model cells, in which they can be molded into any other cell of the body. They are the basic building blocks in which all other cells, such as RBCs, WBCs, neurons, etc. are fashioned after. Researchers hope to take these stem cells and allow them to grow into a dopamine-producing neuron for the substantia nigra, the nigrostriatal pathway, and the globus pallidus. When these stem cells are added, those respective areas of the brain can start to function as if they hadn't ever changed, and can even continue to grow in those areas. However, unlike the other two surgeries stated above, this procedure is not yet cleared for operating on PD surgical patients. It is still being researched by neurosurgeons on how best to perform the surgery without causing any safety issues or other side effects.

Conclusion

Though the cause of Parkinson's Disease isn't completely confirmed, everyone can be sure to know that this disease isn't one to take lightly as it can cause incredibly dangerous problems for the diagnosed. It can cause patients to lose control over their own body, resulting in a feeling of danger, depression, and an inability to reestablish control. Though it isn't fatal, the symptoms and the actions that follow after may be. There are many treatments that reduce the symptoms of Parkinson's Disease and increase lifestyle, but they aren't cures. Researchers are searching for a cure, and they hope they can find one with transplantation surgery. What we can do as citizens of the world is to help raise awareness for this issue is to educate ourselves about this disease and give donations to different research centers so that a cure can come out as quickly as possible.

Acknowledgments

I would like to thank my advisor, Ms. McIntyre, for taking the time to read this extensive review paper. She has given me exceptional feedback and helpful criticism that has made my paper more professional and distinguished like no other. Also, I would like to thank my family because they have helped and supported me in every way possible. It would be completely impossible to accomplish this significant paper without them.

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