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Abstract

Parkinson's Disease is one of the most common neurological disorders which disrupts the everyday lives of millions of people. This disease is categorized by the loss of dopamine in the brain, specifically the Substantia Nigra. People diagnosed with PD suffer from motor and cognitive impairments. While there is no one treatment which can completely cure the disease, there are many treatments available which can help alleviate symptoms. However, most of the treatments cause many negative side effects. Recently, a new physical therapy treatment, LSVT BIG has begun to show its effects. This revue describes the many factors and treatments of Parkinson's disease and explains the newly discovered treatment of LSVT BIG.

Introduction

Parkinson's disease (PD) is a progressive neurological disorder which disturbs one's motor cortex, thereby affecting one's mobility. This disorder affects over one million people in the United States alone and more than ten million across the entire world (National Parkinson's Foundation, n.d.). Unfortunately, this disease slowly worsens from the time one is diagnosed. Even more, PD has a large range of indications and effects. While many with Parkinson's disease have similar symptoms, no two individuals experience the illness in exactly the same way. If you see someone shuffling down the street taking small steps or shaking their hands quickly and repeatedly in their lap, you can suspect that this person is suffering from Parkinson's Disease. What causes this neurological disease, and what can we do to slow the progression and treat the symptoms?

Methods

The information stated in the following paper was acquired through the Touro College Library, which grants its students access to many useful databases such as ProQuest, Ebsco, PubMed and others.

Pathophysiology

Patients with Parkinson's Disease are lacking in dopamine, which is normally produced in the substantia nigra part of the brain. The thalamus must have access to the motor cortex in the brain, specifically to the basal ganglia, in order to produce movement. Within the basal ganglia there are two pathways which have opposite effects on movement. The direct loop promotes movement, while the indirect loop inhibits movement. In a healthy person, the dopaminergic pathway maintains the balance between the other two pathways, enabling the thalamus to have control over the motor cortex and over the person's movements. This dopaminergic pathway works by exciting the direct pathway, while inhibiting the indirect pathway to promote movement. This happens in two ways. First, the substantia nigra sends dopamine to the striatum which excites the striatum and causes it to inhibit the globus pallidus. Thus, the globus pallidus is unable to obstruct the thalamus. Second, the substantia nigra sends dopamine directly to the globus pallidus, inhibiting it, so it cannot prevent the thalamus from controlling the motor cortex. In those with PD, much of the dopamine in the substantia nigra is exhausted. Consequently, the globus pallidus is excited and inhibits the thalamus. Thus, the thalamus has little control over the motor cortex (Singh, 2018). See Figure 1.

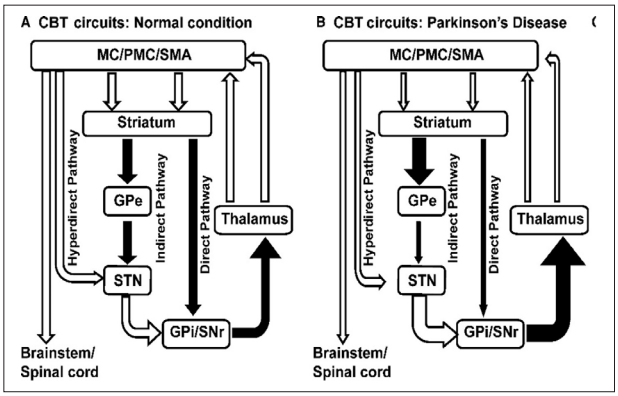

Figure 1

Figure 1: GPi = Globus Pallidus internus, GPe = Globus Pallidus externus, SNpr = Substantia Nigra, STN = Subthalamic Nucleous, MC = Motor Cortex, PMC = Pre Motor Cortex, SMA = Supplementary Motor Cortex The arrows thickness represents the amount of increase and decrease of neuronal actions. In the healthy person, the arrows of the direct and indirect pathways which are related to dopamine (explained above) are significantly thicker than the arrows in the PD patient. Furthermore, the Globus Pallidus internus has the power to inhibit the thalamus in the PD patient as demonstrated by the thickness of the arrows (Singh, 2018).

The lack of dopamine causes akinesia, bradykinesia and other motor deficits which are so commonly found in patients with PD. As the levels of dopamine decrease, the levels of Acetylcholine (Ach) increase. The increased Ach is what causes the symptoms of tremors and rigidity in PD patients. In other words, the loss of the dopaminergic system leads to disinhibition of the cholinergic system (Armstrong & Okun, 2020).

Another major marker for Parkinson's Disease is the existence of the Lewy Body. The Lewy Body is a "neuronal inclusion" which mainly contains a cluster of a-synuclein proteins (Bridi & Hirth, 2018).

Causes of Parkinson Disease

PD is believed to be an idiopathic disease being that scientists are unable to find one definitive cause of this Parkinson's disorder. However, there are factors that increase one's likelihood of developing Parkinson's disease. First, there are those who have a genetic predisposition. The most established or proven genetic cause of Parkinson's is mutations in what is known as the Parkin gene (Park2) (Shadrina, et al., 2007) or the PINK1 gene (PARK6) as they both inhibit normal mitochondrial function (Seirafi, et.al. 2015). Additionally, people who experience a head injury are at a greater risk for developing PD. High milk and dairy intake and exposure to pesticides can also increase one's risk for developing PD. Interestingly, research has found that there are certain steps one can take in order to reduce his/her risk of developing the disease, such as cigarette smoking and consumption of coffee or other caffeinated drinks (Ascherio & Schwarzchild, 2016).

Symptoms of Parkinson's Disease

PD is a progressive disorder, meaning there is no cure and the disease slowly worsens over time. Most people consider PD a disease which only affects movement, however this is not the case. Rather, Parkinson's causes a large range of symptoms and affects different systems in the body. Individuals suffering from PD perceive the world as much smaller than healthy individuals. Therefore, many of the symptoms are correlated to this viewpoint. For example, when a PD patient shuffles, one thinks that s/he is walking normally. (Fox, et.al. 2011).

Motor Symptoms

There are two groups of symptoms caused by PD. First, and more well recognized, are motor symptoms. Up to 80% of dopamine in the Substantia Nigra is depleted before these motor symptoms become noticeable. However, in order to be diagnosed with PD, people must demonstrate some symptoms. First, they must exhibit slow movement and low amplitude of everyday movements (shuffling of gait), otherwise known as bradykinesia. Then, they must also display one additional cardinal sign of Parkinson's, which include rigidity, akinesia or unable to initiate movement, lack of balance or tremors. As mentioned above, about 80% of PD patients suffer from limb tremors, usually concerning the hand, which is caused by increased levels of Ach. Furthermore, several years after initial symptoms, 25% -60% of patients with PD exhibit frozen movements, while 40% – 80% of PD patients have swallowing issues and 25% drool. Additionally, more than 50% suffer from speech impairments including quiet and hurried speech (Sveinbjornsdottir, 2016). Additionally, those with PD display a masked expression, also known as bradykinesia of the face. This happens because when a person is suffering from Parkinson's Disease, all movements slow down including facial movements. The delay of the facial muscles is what causes PD patients to lose their ability to express themselves via facial expressions (Bologna, et al., 2013).

Non-Motor Symptoms

Contrary to popular belief, Parkinson's is not just a movement disease, rather it affects non-motor abilities as well. Even before the motor symptoms start and the person is diagnosed, patients may experience a variety of non-motor symptoms. These symptoms can be divided into three sections: autonomic function disturbances, sleep disturbances and neuropsychiatric symptoms (Sveinbjornsdottir, 2016).

Autonomic Function Disturbances

Those with PD often experience rapid drops in blood pressure causing dizziness, visual troubles and weakened cognition which can ultimately cause loss of consciousness. Furthermore, the movement of the gastrointestinal tract slows down. This can cause overstuffed feelings, gastric retention and constipation. Constipation occurs in over 75% of PD patients. Also, those with Parkinson's suffer from an inability to control their urinary frequency and urgency. About 60% of PD patients display frequent nocturia, needing to wake up several times throughout the night to use the bathroom (Sveinbjornsdottir, 2016).

Sleep Disturbances

Roughly two thirds of PD patients suffer from an assortment of sleep disorders. This can be due to physical or cognitive limitations of the disease itself, or due to the different medications and treatments which are being used to treat the patient's symptoms. The most common ailment is fractionated sleep. Studies show that PD patients sleep lighter and have regular interruptions throughout the night. This fractionated sleep can also be a result of other PD sleep disorders such as frequent nocturia, difficulties with moving in bed and nocturnal tremors. Depression caused by Parkinson's can also disturb a patient's sleep throughout the night. Additionally, about

50% of people diagnosed with Parkinson's undergo extreme daytime sleepiness. Some say that this is somewhat caused by the dopaminergic drugs. Even more, 27-32% of PD patients kick and smack while dreaming and others uncontrollably jerk while sleeping (Sveinbjornsdottir, 2016).

Neuropsychiatric Symptoms

Many with PD suffer from various Neuropsychiatric Symptoms. The earliest indications consist of executive functioning issues, visuospatial disfunction, weakened speech fluency and memory loss. Additionally, in more than a third of PD patients experience hallucinations and illusions. Also, as the disease progresses some develop paranoia, particularly feeling suspicious towards their spouse. Moreover, dementia is also common in those with Parkinson's. Other common Neuropsychiatric symptoms include depression and anxiety. One third of PD patients have clinically diagnosed depression and 17% were confirmed to have a major depressive disorder (Sveinbjornsdottir, 2016). All symptoms, whether they are movement related or not, adversely affects the lives of PD patients.

Unified Parkinson's Disease Rating Scale

For any disease, when testing a new treatment, or tweaking a current treatment, there must be a way to measure the success. Specifically for Parkinson's disease, there are different ways of measuring the severity of PD symptoms, thereby displaying the treatments progress. Most frequently used is the Unified Parkinson's Disease Rating Scale (UPDRS). This rating tool is used to determine the severity of the PD patient's symptoms. It is divided into four sections which evaluate the symptoms' severity on a 0-4 scale. First, UPDRS I measures non-motor daily behaviors such as sleep, mood and brain activity. Second, UPDRS II assesses the patient's motor abilities for daily living, such as speech, chewing, handwriting, walking and drooling. Third, UPDRS III is the section which includes motor evaluation such as rigidity, gait and tremors. Last, UPDRS IV calculates treatment complications such as pain (Kleiner-Fisman, et.al. 2010).

Brief Overview of PD treatments

Although there is not a single cure for PD, there are different treatments which target specific symptoms of the disease. This includes both motor symptoms and non-motor symptoms. Furthermore, there are three types of treatments used to improve PD patient's way of life. There are medicinal treatments, surgical intervention and physical therapies.

Drug Therapy

Many of the medicinal treatments for Parkinson's Disease patients target the dopaminergic pathway, working to increase the dopamine in the patient's brain. While some medicines work better than others, no drug cures symptoms completely. The most commonly used drug is levodopa which increases the dopamine in the brain. Primarily, levodopa targets the movement disorders of PD. Although levodopa is still considered the most effective treatment, about 40% of patients develop motor complications after 4-6 years of levodopa treatments. There are other drugs taken to combat the side effects of levodopa (Dong, et.al. 2016). Another commonly used drug is amantadine. Many clinical trials have proved that amantadine can lessen the dyskinesia side-effect of the levodopa drug. It was also found to reduce the severity of freezing gait. Thus, improving PD patients' abilities to perform daily activities. Additionally, there are less frequently used drugs such as anticholinergic drugs. These drugs help by restoring the balance between dopamine and acetylcholine. Anticholinergic drugs are mostly used at the onset of the disease, when the primary symptom is tremors. The use of this type of medication is very limited, as there are many side-effects which some believe outweigh the benefits (Dong, et.al. 2016). Side-effects include decreased cognitive function, especially in older PD patients, constipation, blurred vision and tachycardia (Lertxundi, et al., 2015).

Surgical Treatments

There are many surgical interventions which were proven to be beneficial for PD patients. One such method is called Deep Brain Stimulation (DBS). This surgery places electrodes at certain places in the brain which control movements. They are either placed in the subthalamic nucleus (STN), the globus pallidus interna (GPi), or the ventralis intermedius (VIM) nucleus of the thalamus. DBS improves patients' movement abilities and may lessen tremor severity. Yet, unlike other pharmaceutical drugs, DBS has demonstrated little to no side-effects (Chou, Grube, & Patil, 2012, p. 15). Another surgical treatment is cell transplantation. This treatment has proven to be effective on motor symptoms of PD. This works as the transplanted stem cells can "infiltrate and integrate with diseased tissue, differentiate into dopaminergic neurons to replace damaged cells and reconstruct neuronal circuits to restore nerve function (Li, 2012)."

Physical Therapy

A major issue with medication for PD patients is that the effectiveness of the medicinal drugs decreases over time.

As a result, the creation of different exercises and physical therapies have also proven to be an effective way of combating Parkinson's disease. First, basic exercises lessen the motor and even non-motor symptoms of those with PD. Exercise increases mitochondrial respiration and arouses neuroplasticity. Furthermore, recent clinical trials recommend aerobic exercises. They claim that these exercises improve gait, physical performance and balance. They also state that they impact fatigue, depression and improve cognitive ability. Additionally, a Chinese exercise called Tai Chi, through breathing exercises combined with slow movements, has improved the balance of PD patients (Dong, et.al. 2016). Finally, LSVT BIG, a relatively new approach to physical therapy in PD, has begun to show its effectiveness.

What is LSVT BIG?

LSVT Big was created based on the success of a treatment called LSVT Loud. First introduced in 1995, LSVT Loud was proven to be an effective way of improving the strength and loudness of the voice of PD patients. LSVT Loud is a treatment which focuses on how one feels and sounds when talking loudly. Unlike many speech treatments which target many different speech systems, LSVT Loud primarily focuses on increasing movement in the respiratory and laryngeal systems. Currently, after conducting many studies and experiments, LSVT Loud was proven to be a successful treatment (Fox, et.al. 2011). After the success of LSVT-Loud, in 2005 LSVT-BIG was first introduced (McDonnell, et al., 2017).

LSVT-BIG was created to combat the hypokinesia or reduced amplitude movements which interfere with the everyday lives of people with PD. The goal of the treatment is to revise the way the patient perceives movement performance. LSVT BIG therapy includes four consecutive, one on one, 60-minute sessions per week in addition to one (on treatment day) or two (non-treatment days) 15 to 20-minute home sessions per day. When performing any action, patients are told to conduct large amplitude movements. The beginning of each out-session includes seven whole-body exercises such as reaching in more than one direction, weight shifting and stepping. Next, the patient works on five every-day movements, such as shifting positions, rolling over in bed and any others that the patient requests to improve. Third, the patient practices walking with larger amplitude, while standing straight. At the end of the session, the patient works on more complicated tasks which are directly related to his/her goals and abilities. Later in the treatment, this final segment would increase in difficulty by either adding an additional task or by enhancing the existing mission (Isaacson, et.al. 2018).

Experiments Conducted

To prove the effectiveness of LSVT-BIG, there were numerous studies and experiments done on all different types of people at all stages of Parkinson's disease. One such experiment performed, compared the results of 41 patients involved in general exercise to 43 patients participating in the LSVT-BIG program. After sixteen weeks, they found the motor function of the LSVT-BIG patients to have improved significantly more than the other 41 patients. Additionally, it was found that those participating in the program increased their speed of moving. Another study found that LSVT-BIG helped decrease response time when prompted (McDonnell, et al., 2017).

Another study was done to see if LSVT-BIG also impacted the duration of a patient's 'off time,' meaning the time of day where one feels at his/her low. Eight patients participated in the study. Before starting treatment, each patient was required to report their 'on' and 'off' durations for three days. Then they were evaluated under the UPDRS III scale on motor ability. Then they began treatment. The changes were measured every four weeks by ministering different tests. The results proved that LSVT-BIG therapy does lessen the duration of 'off' time as it did significantly improves the UPDRS III scores (Ueno, et al., 2017).

In addition, a non-controlled study was performed which examined the effects that LSVT BIG had on eighteen PD patients. It was found that after just four weeks of therapy, the participants experienced a 12-14% increase in walking and walking rate (Fox, et.al. 2011).

A different blind study was done which took sixty people suffering from Parkinson's disease and randomly assigned them to one of three therapies, LSVT BIG, Nordic Walking in a group setting, or regular exercise with no therapist. After four months of treatment, the average improvement of the scores on the UPDRS III on patients receiving LSVT BIG therapy was 5.05, while the scores of those undergoing Nordic Walking or domestic training worsened. This amount of scaled motor increase clinically proves that LSVT BIG does improve the symptoms of PD patients (Fox, et.al. 2011).

Another case study included twelve idiopathic PD patients who underwent LSVT BIG therapy treatment. There were also two control groups: one with eight PD patients who did not undergo any physical therapy and the other included fourteen healthy individuals who experienced the same experiment as the case study. The PD LSVT BIG patients were given sixteen sessions, four sessions per week for four weeks. Each session was an individualized meeting with a licensed LSVT BIG therapist and lasted one hour each morning. Each appointment began with

using the patient's entire body including "BIG" amplitude exercises and "repetitive multidirectional movements." The second half of the meeting included daily activities according to what the patient wished to focus on such as buttoning shirts and putting on a coat. The results showed the gait speed and the step length of patients undergoing LSVT BIG increased. Furthermore, the LSVT BIG patients displayed better functional mobility as they were able to transition from sitting to standing faster and more often. The LSVT BIG patients' improvements were significantly greater than the PD control group (Flood, et al., 2020).

Each of the experiments described above prove the effectiveness of LSVT BIG therapy. There were countless of other case studies conducted whose results were similar to the outcomes stated previously. Thus, it is safe to conclude that LSVT BIG is an effective way of treating Parkinson's disease.

Conclusion

Parkinson's Disease is a neurological disorder which affects tens of millions of people across the world. Primarily, the disease is associated with progressive loss of dopamine in the brain. People with PD are affected in many different areas of life including motor skills and cognitive abilities. Unfortunately, researchers have not found one perfect solution to completely cure Parkinson's Disease. Rather, there are only palliative solutions, treatments which either ease the symptoms or slow the progression of the disease however, doctors don't often give patients medication for two reasons. Often, many of the commonly used medicinal treatments can cause difficult side effects. Secondly, as time progresses, the impact the medicine has on the body weakens as the patient becomes accustomed to the drug. Therefore, doctors and therapists are beginning to use more non-invasive treatments such as exercise and Physical Therapy. Recently, there has been a new treatment, LSVT BIG, which targets the amplitude of the PD patients. This treatment has continuously proved itself effective and worthwhile. Every Parkinson's patient should have the opportunity to undergo LSVT BIG treatment.

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