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Shaima Shebrain

Western Michigan University, shaima.s16@gmail.com

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**The Use of Neurologic Music Therapy and Rhythmic Auditory Stimulation as Treatment
for Parkinson's Disease**

By Shaima Shebrain

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Requirements for the Lee Honors College

Thesis Chairman – Dr. Charles Ide, Department of Biological Sciences

Thesis Committee Member – Dr. Edward Roth, Music Therapy

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I. Introduction

As the aging population in the United States increases, the prevalence of neurologic disease, including Parkinson's Disease (PD), increases as well. It has been estimated that 0.6% of the general population will be affected by PD by 2050 (Kowal et al., 2013). Currently, this disease affects 50,000 people every year, which does not include those individuals whose disease goes undetected (NIH Research, 2018). Overall, 0.3% of our current population is affected by this neurodegenerative disease (Gooch et al., 2017). PD is a chronic, progressive, age-related, unfortunately incurable, neurodegenerative disease that affects neurons in the deep parts of the brain called the basal ganglia and the substantia nigra. Individuals affected by this disease are usually 50 years or older. The majority of individuals who have PD usually have idiopathic PD which accounts for 75% of the diagnosed population (Kasper et al., 2005). PD can be hereditary as well; however, only a small percentage of PD is familial, which is caused by mutations or alterations in genes (Kasper et al., 2005). Additionally, men are more susceptible to PD than women. The true reasoning behind this has not been discovered yet, but many researchers hypothesize that it may be due to toxicant exposure (which affects men more frequently than women) or head trauma; another theory suggests that abundant levels of estrogen found in women may provide protection against PD that the male hormone testosterone does not (Wooten et al., 2004).

PD affects mainly one arm of the motor system of the human body called the extrapyramidal system which controls the involuntary motor activity (Dorman, 2015). This is to differentiate it from the other motor system called the pyramidal system, which controls the voluntary movement through a direct and specific pathway between the cerebral cortex and motor neurons. Over time, individuals with PD experience tremors, rigidity, and a loss of balance. They

begin to not only go through physiological changes, but psychological changes as well, as this disease is life-changing. This thesis will explore the history of PD, its impact on affected individuals, and modalities of available therapeutic options with emphasis on the use of neurologic music as an innovative form of therapy used as a course of treatment. There are many other types of therapy that are used for treatment of PD, such as fine arts and dance; however, for the sake of this paper, music will be the focus. A literature review of cases regarding neurologic music therapy and the use of rhythmic auditory stimulation will be evaluated and analyzed in regards to how they impact the individual with PD. Moreover, this thesis will help create a better understanding of this progressive, neurodegenerative disease and the potential of neurologic music therapy as a treatment to slow the disease's progression as there is no current cure available for PD.

II. Parkinson's Disease

a. The History of Parkinson's Disease

In 1817, James Parkinson, a London doctor, was the first to medically describe a condition of “involuntary tremulous motion,” where an individual’s muscle power was reduced; thus, resulting in uncontrolled movement and posture, yet the intellect of the individuals is uninterrupted and they are fully aware of their “self” (Goetz, 2011), contrary to another neurodegenerative disease such as Alzheimer's Disease where the individual is unaware of their situation since his/her memory begins to fade. In his paper “An Essay of Shaking Palsy,” Parkinson discusses the main symptoms and development of the disease. However, it was Jean-Martin Charcot, a French neurologist, and his colleagues who were able to differentiate PD from Multiple Sclerosis (MS) and other neurological diseases. In one of his papers, Charcot discusses how patients find it challenging executing basic, everyday activities that most of us take for granted, prior to experiencing rigidity. After observing some of the patients, he noted that the problem the patients had was associated

with slowness of movement instead of actual physical weakness that would prevent them from performing the basic activities such as signing a form, fastening a seat belt, or tying shoe laces. So, the patients still have the ability to perform such activities, they just perform them slowly, while having tremors (Goetz, 2011). One of Charcot's greatest contributions to the differentiation of PD from other diseases involving tremors was reached by developing a protocol that observed the differences between tremor at rest and tremor during action (Goetz, 2011). Some of the observations he noted were that resting tremors, also known as static tremors, were associated with rigidity, soft speech, and slowed movement. On the other hand, action tremors were associated with visual disturbance, weakness, and spasticity (Goetz, 2011). Action tremors, or dynamic tremors, are more common with cerebellar diseases and usually associated with ataxia (incoordination of voluntary motor activity in absence of weakness). Charcot's findings, although there was more to discover and understand, proved to be one of the major turning points in science and medicine that paved the way for much more.

In the late 1800s, not many doctors had a definite understanding of PD and how they should treat it. At that time, some of the different types of drugs that were used to treat PD were morphine, cannabis, arsenic, and hemlock (Goetz, 2011). A few decades later, in the 1940s and 1950s, surgery was performed on individuals showing symptoms of PD that were not reduced through the use of drugs. Although surgery was shown to be effective at times by improving the conditions of patients, it was risky and resulted in deaths, especially since the knowledge of neurological disease was very limited. In the 1960s, one of the biggest advancements in PD treatment was discovered, thus transforming the understanding Parkinson's Disease (PD). Once researchers discovered that levels of a neurotransmitter called dopamine contributed to PD, the development of L-DOPA (L-3,4-dihydroxyphenylalanine), a precursor of dopamine, was introduced and found to have the

ability to cross the blood-brain barrier and perform in a way that would help reduce involuntary movement. Dopamine is responsible for movement; thus, a reduction in dopamine levels results in the reduction of smooth movement. Dopamine is released from the substantia nigra in the midbrain and is part of the basal ganglia. Basal ganglia include the caudate, putamen, and globus pallidus in the cerebrum; the substantia nigra in the midbrain; and the subthalamic nucleus. Dopamine is released by neurons onto adjacent cells and into a synapse to produce smooth and coordinated movement. When the pars compacta of the substantia nigra is degenerated, it results in the reduction of dopamine, thus producing uncoordinated movement. In PD, when the release of dopamine from the substantia nigra is decreased, the adjacent areas in the thalamus and internal globus pallidus become hyperactive and produce uncontrollable tremors. Since the reduction of dopamine was the primary cause of PD, L-DOPA was introduced as a precursor of dopamine that had the ability to increase dopamine levels. One of the major advantages of L-DOPA is that it can cross the blood-brain-barrier (which dopamine cannot do) and is then converted to dopamine inside the brain. However, over time the receptors in the brain realize that the ligand that is attaching itself to them is not true dopamine, hence the uncoordinated movements and other symptoms begin to appear again.

b. Symptoms of Parkinson's Disease

PD usually appears in individuals of the age of 50 and above, thus making it an age-related, neurodegenerative disease. One of the major pathognomonic neurological findings of this disease is the lack of dopamine that can be observed when comparing a normal brain to the brain of an individual with PD. As a result, PD consists of both motor and non-motor symptoms. As the disease progresses in an individual, the symptoms become more severe and challenging to manage; unfortunately, an individual can only manage the disease as there is no cure for this disease yet.

Prior to the diagnosis of PD, individuals may experience early onset symptoms that do not appear to be as serious. Such symptoms can include a decrease of arm swing range, stooped posture, smaller handwriting than usual, and decreased rate of blinking (Kasper et al., 2005). Over time, these symptoms begin to become more aggressive and continue to progress for years. After a few months, symptoms become more evident, and the types of motor symptoms that individuals with PD experience include tremors, rigidity, bradykinesia (slowness of movement), postural instability, slurred speech, and reduced facial expressions. Tremors are usually the main indication for this disease as 85% of individuals with PD present with these tremors. Tremors that are experienced can occur at rest and/or rarely in action in the hands or other limbs. At-rest tremors usually start from the distal region of the body, such as fingers and wrists. From that region, the tremors spread to other parts of the body including the legs (Kasper et al., 2005). One of the unique features about at-rest tremors is that although they can spread to the jaw region of the face, they typically spare the head (Kasper et al., 2005). The amount of time it takes for these at-rest tremors to spread throughout the body is approximately a year, and they have a frequency of approximately 4 to 6 hertz (Hz) (Kasper et al., 2005). Rigidity is a common symptom which leads to a difficulty in standing, walking, slower and more uncoordinated movements, and a stiffness of muscles. The combination of tremors and rigidity, specifically of the orofacial musculature, can induce pain which impacts the oral health of the individual (Friedlander et al., 2009).

Usually the types of pain associated with tremors and rigidity of the orofacial musculature can be related to mandibular joint discomfort and cracked teeth. Due to the pain that is experienced, other serious issues such as prolonged food consumption time need to be considered. This becomes problematic when the individual with PD begins to lose an interest in eating because of the challenges they must endure for a basic everyday activity (Friedlander et al., 2009). The loss

of appetite is one of the primary reasons as to why most individuals with PD experience weight loss, and sometimes it is challenging for that weight to be regained. When weight is lost dramatically, that creates other problems in the individual's physical and mental health. The challenge of eating begins when tremors prevent smooth transportation of food to the mouth followed by increased difficulty in chewing, tongue movement, and swallowing. As a result of this, food is not broken down properly unless the individual can take the time to ensure proper digestion. Therefore, it is recommended that food is cut up into smaller pieces as well as modified to provide easier swallowing. Such actions may alleviate the challenges these individuals face with basic, everyday tasks. One of the most disabling symptoms is bradykinesia (slowness of movement) due to its interference with every aspect of daily life. Activities such as standing up from a seat, walking, or even turning over in bed can be impossible for those afflicted with PD (Kasper et al., 2005). Most of us take for granted our ability to easily stand up from sitting; we simply do not realize how fortunate we are to have a body that can perform such actions so smoothly. Those with PD begin to feel as though their legs and arms are too weak to support their own weight, which at times can be rather frustrating when the body cannot execute the brain's command. In regards to walking, usually those who experience bradykinesia are not able to walk normally. Rather their walks turn into short steps, even shuffles. At times, especially when the disease has advanced, the individual begins to feel as though their feet are planted into the ground and are unable to move (McNamara, 2018). Besides the inability to stand or walk easily, when the individual's ability to turn in bed is affected, that negatively impacts his/her sleep. Without adequate sleep, the body and mind are in a state of exhaustion throughout the day. Furthermore, bradykinesia affects the individual's ability to use fine motor skills to button shirts or eat with a spoon, which leads to dependence on a caregiver or family for assistance in performing these daily tasks. Sadly, many

PD patients must abandon some activities altogether once their bodies become incapable of performing certain actions.

As previously mentioned, an early-onset symptom of PD is the reduced size in handwriting; this is known as micrographia. Micrographia not only decreases one's handwriting but manual dexterity in general as well (Kasper et al., 2005). The reduction of manual dexterity prevents the ability to be meticulous, which is very problematic for those whose profession requires precise manual dexterity such as surgeons, dentists, machine operators, and many others. One way that physicians can detect if their patient is developing PD is by comparing a patient's signature from several months to a year ago to his/her current signature. The doctor may see that the current signature is smaller and not as clear as the individual's previous signature. Physicians can also observe the way in which the writing utensil is being held. Usually pen to paper contact is hindered by the instability of the individual's hand to the point that writing no longer becomes automatic. Therefore, it is recommended that the individual practices his/her penmanship in order to reinforce the hand to be able to write more clearly. If the individual begins to feel frustrated, he/she should consider drawing pictures for the sake of practicing the pen and paper contact as opposed to the precision of writing words.

Besides micrographia, one of the most classic indications of PD is an abnormal gait pattern. There are a number of distinctive features that hinder normal gait patterns for those with the disease. Those features may include, but are not limited to, the reduction in motion associated with the pelvis, trunk, and knees. In addition, poor balance, stooped posture, and increase in cadence are also common features that interfere with a normal gait pattern (Thaut & Hoemberg, 2016). The abnormal gait pattern falls under two categories: festinating and freezing gait (Kasper et al., 2005). These two types differ from one another; however, freezing gait is experienced when

the disease is more advanced. Festinating gait is what causes individuals to accelerate their pace; essentially the individual is trying to “catch up” with their center of gravity. This is a result of the reduced postural reflexes and flexed posture (Kasper et al., 2005). Freezing gait is the opposite because as the disease advances over the years, individuals experience start hesitation, a characteristic of Parkinsonism, where individuals feel as though they cannot move their feet because they are “stuck.” This is especially true if one must change directions or walk through hallways or other narrow spaces.

Along with motor symptoms, individuals with PD experience non-motor symptoms such as mood disorders, cognitive changes, and sleep and autonomic disorders (Van Laar & Jain, 2014). Individuals who suffer from PD experience mood disorders such as depression, anxiety, and irritability. One of the reasons that such conditions arise is that this disease is life-changing, and simple tasks that an individual was once able to do become more challenging, if not impossible. Furthermore, if the individual lived an independent adult life, it can make he/she feel burdensome to have to depend on others. Living with the mentality of feeling like a burden can significantly impact the individual’s mood and mental health. Cognitive changes in PD patients include language and memory difficulties, slower thought process, and the inability to focus and pay attention. Usually, individuals with PD suffer from insomnia, rapid eye movement (REM) behavior disorder, excessive daytime sleepiness (EDS), and many other sleeping disorders. Autonomic disorders include excessive sweating, constipation, hypotension, sexual dysfunction, and many more complications (Lazarus, 2018). That goes to show that this neurodegenerative disease not only challenges an individual physically but mentally as well, which takes a significant toll on the individual’s health and life.

c. Impact of Parkinson’s Disease on an Individual’s Life

Realistically, since PD greatly impacts an individual physically, it also impacts them psychologically. One of the reasons for this is that the symptoms that PD patients begin to live with are foreign to them—they have not had to live through them prior to the disease. Individuals with PD show characteristics of depression, anxiety, and irritability.

One of the most common psychological disorders associated with PD is depression, which is experienced by 50% of PD sufferers at some point in their lives. The level of depression that is experienced varies between each case. Approximately 5-20% of individuals with Parkinsonism symptoms experience major depression, while 10-30% experience minor depression (Disease Research, 2013). As the individual's mental well-being worsens, his/her physical abilities can worsen, thus decreasing quality of life. This perceived decrease in quality of life on the part of the individual with PD also increases the difficulty for the caregivers, which has a psychological impact on them, too. This demonstrates that PD not only affects the individual who suffers from it, but also the caregivers, friends, and family of those afflicted. Thus, it's important that psychological disorders are recognized and treated along with the motor aspect of this disease. Individuals with PD often feel a sense of helplessness and sadness as they may feel isolated from society due to their limited physical abilities. Over time, this can exacerbate other disorders such as anxiety.

Approximately 40% of individuals with PD suffer from anxiety. The anxiety of PD patients may be correlated to their involuntary motor function as they so often fear not being able to perform the appropriate function in a given situation. It is normal for an individual to feel some unease and apprehension; however, when excessive anxiety is experienced, it's crucial that the patient receives proper treatment. Individuals with PD can experience anxiety from being around others, specifically those who do not suffer from PD, because they feel like they draw attention to

themselves with their involuntary movements. Some individuals isolate themselves, so when they are put in a situation where they must engage with others, it can be quite uncomfortable and nerve-racking. Although it is common for individuals with PD to experience these disorders, there is treatment that can be considered to ease some of the symptoms associated with this disease.

III. Conventional Medical (Traditional) Treatments

Although there are new treatments that are being utilized, conventional treatments such as Levodopa (L-DOPA) and neurosurgical treatments, are still being used to this day. Compared to when these treatments were first used decades ago, there have been significant improvements made due to the better understanding that physicians were able to grasp over the years. Nonetheless, there is still much more to learn about treating this neurodegenerative disease.

One of the most widely used drugs for treating PD is Levodopa (L-DOPA), an amino acid that is a precursor of dopamine. This amino acid has the ability to cross the blood-brain barrier and acts like the neurotransmitter, dopamine, since dopamine itself cannot cross this barrier. When L-DOPA crosses the blood-brain barrier, it can attach itself to the dopamine receptors because these receptors are under the impression that it is actual dopamine that is being attached. Due to its ability to do so, L-DOPA can increase the deficient dopamine concentrations for individuals with PD (The Regents of the University of California, 2014).

Although L-DOPA has been used for the past few decades to control the symptoms of PD, it has its own complications which can be serious. One of the major complications of using L-DOPA is related to the individual's motor abilities. It has been stated that approximately 40% of individuals who choose this traditional and conventional route of treatment experience motor shifts within five to six years (The Regents of the University of California, 2014). Other complications associated with this treatment include dyskinesia that is induced by L-DOPA as well as the drug's

“wearing off” effect (Jankovic & Aguilar, 2008). The “wearing off” effect could be due to the striatum's inability to store L-DOPA for a long time since the dopaminergic terminals become lost as the disease progresses. To reduce the induced dyskinesia there are different options to consider such as reducing L-DOPA levels, incorporating an anti-dyskinesia drug with L-DOPA to avoid L-DOPA dosage reduction, or surgery.

As a result of these complications, it is important for physicians to decide the best time to start the patient on L-DOPA (Jankovic & Aguilar, 2008). Thus, time of admission of this drug varies between each individual, and physicians must be able to carefully create a treatment plan that is unique to each patient. In order to ensure an accurate diagnosis, doctors must first determine the level of impairments of the patient, both physically and mentally (Jankovic & Aguilar, 2008). Following this, the patient must be notified about the circumstances, educated about the disease by the physician and reliable sources, and informed of the importance of treatment options. Once the different options of treatment have been researched, the physician must choose the most appropriate treatment without taking away the autonomy of the patient. During this part, both the physician and patient must work together to determine what the patient is most comfortable with and what the physician deems best for this particular patient. The final step would be to customize the chosen treatment for the patient for the best results possible. Although L-DOPA is still being used, there are physicians that advocate the use of other forms of therapy and delaying the use of L-DOPA since there are motor complications associated with the therapy. As previously mentioned, L-DOPA acts as dopamine, so to ensure that the drug does not break down too quickly, an inhibitor is used at the same time (The Regents of the University of California, 2014). This inhibitor is known as catechol-o-methyl-transferase (COMT) inhibitor which functions to prolong

the job of L-DOPA. It is important that both L-DOPA and COMT inhibitors are taken together, especially when patients begin to experience the “wearing off” effects of the treatment.

Another conventional treatment used to treat tremors, rigidity, and other disabling neurological symptoms of PD is neurosurgery. One of the most well-known types of neurosurgeries for this disease is known as deep brain stimulation (DBS) which was first approved in 1997 to treat the present tremors because medications were not working properly for certain patients (Spears, 2018). In 2016, DBS was then approved for early stages of PD as opposed to just tremors and advanced stages. In DBS, only the problem areas are targeted, thus avoiding any of the healthy tissues, which is crucial because tampering with healthy parts of the brain can create other problems for the patient. These problem areas that have been approved by the FDA include the globus pallidus, thalamus, and subthalamic nucleus. The problem areas are targeted by the insertions of an electrode, a thin insulated wire, through a small opening in the skull with the use of an MRI and brain recordings for accuracy (Spears, 2018). For effective and efficient performance, the tip of the electrode would have to be properly placed within the target area. Once the electrode is set in place, an impulse generator battery (IPG), equipment that functions as a pacemaker, is placed under the skin near the collarbone or near the abdomen.

Although DBS is not a cure for PD it does allow the patient with some motor control to turn the device on and off. However, this treatment is seen as the last option, when medication and L-DOPA therapy fail to work. Nonetheless, individuals with PD differ from one another. So, even if medication does not work, surgery may not be successful either; therefore, looking into other forms of therapy is ideal. For those who are qualified for DBS, the surgery would not necessarily slow down the progression of the disease and would not improve some of the motor complications that are associated with PD such as swallowing, gait patterns, and other complications of that

nature since the focus of DBS is treating tremors and rigidity by creating electrical signals that interfere with abnormal signaling patterns in the brain. Furthermore, DBS can reduce medication dosages, which can lead to a reduction in medication side effects.

DBS does possess a low but significant risk, at about 1 to 3 percent, that physicians must explicitly explain to their patients. Such complications include, but are not limited to, infections, cranial bleeding, reduction of cognitive ability, and stroke (Parkinson's News Today, 2018). Furthermore, there is much more to learn about these types of surgeries and their target areas. As previously mentioned, there are three target areas, and the physician must carefully analyze the test results of the patient to ensure that the correct target area is chosen. For instance, not all patients have a problem in their thalamus, so the electrode would either be placed in the subthalamic nucleus or globus pallidus, depending on what the physician finds.

IV. Neurologic Music Therapy

PD's main feature is diminished dopamine as the neurotransmitter in the basal ganglia (the caudate, putamen, and globus pallidus in the cerebrum; the substantia nigra in the midbrain; and the subthalamic nucleus). In addition to the conventional therapy, there have been new non-conventional modalities in use over the last few decades such as music therapy. Before discussing the effect of this modality, I will discuss the basal ganglia and their networking that have interplay in the pathophysiology of PD.

a. The Basal Ganglia

The brain is very intricate and one of the most fascinating organs of the human body. It is the main source of people's ability to move and prevent unwanted movement in a way that is seamless. It is able to communicate with the skeletal and muscular system in order to execute movements. This all leads back to the basal ganglia, an area of the brain deep within the cerebral

hemisphere that consists of the caudate and putamen, which together form the striatum. Three other structures that make up the basal ganglia include the globus pallidus, substantia nigra, and the subthalamic nucleus. These structures and the thalamus are what allow the brain to control movement, thus communication between them through pathways is crucial. Essentially, neurons play a vital role in pathways as they are constantly communicating with other neurons at the synapse of the presynaptic and postsynaptic neuron. From this, neurons can receive the information through their projecting dendrites and then transmit that information along the axon and to the terminals. At the synapse, the presynaptic neuron conveys neurotransmitters to the postsynaptic neuron; however, the action from the postsynaptic neuron depends on the type of neurotransmitter that is released. For instances, one of the main neurotransmitters is Gamma-Aminobutyric Acid (GABA), which possesses inhibitory effects that act as brakes and reduce the activity of neural cells in the central nervous system. On the other hand, glutamate, an excitatory neurotransmitter, excites the postsynaptic neuron activity.

The basal ganglia have two types of pathways—one to control moving (direct) and one to inhibit unnecessary movement (indirect). The goal of the direct pathway is to alleviate the normal inhibition state of the thalamus so that it can communicate with the motor cortex. By communicating with the motor cortex, glutamate, an excitatory neurotransmitter, is sent to the striatum. There the excitatory neuron synapses with an inhibitory neuron from the striatum to the internal globus pallidus (Gilles, 2015). Following this is the release of GABA, an inhibitory neurotransmitter, to the internal globus pallidus where it is further inhibited in order to activate the thalamus. Without GABA being transmitted to the internal globus pallidus, the thalamus would have been inhibited because the job of the globus pallidus is to keep the thalamus suppressed. Since the thalamus is no longer suppressed, it is able to transmit excitatory signals to the motor

cortex, thus initiating muscle movement. As previously mentioned, there are four parts to the basal ganglia, and the two structures that are important for making the small but necessary adjustments are the subthalamic nucleus and substantia nigra. Compared to the other structures, these two work more behind than scenes; nonetheless, without them, the pathways would not be sufficient. The substantia nigra contains dopamine neurons that synapse with the inhibitory neurons that are found in the striatum. Dopamine binds with the dopamine receptors that are found in the neurons of the striatum which continues to excite these inhibitory neurons resulting in further suppression of the internal globus pallidus for further excitatory activity of the thalamus. The subthalamic nucleus functions to excite the substantia nigra through the transmission of excitatory signals through the neurons that are found there. This allows the substantia nigra to continue releasing dopamine to the striatum; however, when the excitatory signals are no longer needed, the substantia nigra communicates that to the subthalamic nucleus. By doing this, the thalamus will eventually become less excited and return to its normal state of suppression; thus, it will no longer communicate with the motor cortex, and no more movement will occur.

As stated previously, the thalamus is known as the relay station because it is the part of the brain that can transfer information from the basal ganglia to the motor cortex to the muscles. It is important that thalamus can be suppressed at times to prevent certain movements from occurring—this is where the internal globus pallidus comes into play. The internal globus pallidus is key in the indirect pathway as it acts as a tether for the thalamus which is why the thalamus is suppressed only until excitatory signals excite it. Without the internal globus pallidus, the thalamus would cause uncontrolled amounts of movement that will eventually cause muscle fatigue. However, the tether from the internal globus pallidus to the thalamus does have some leniency by communicating with some of the other structures in the basal ganglia—the substantia nigra and

subthalamic nucleus. When the basal ganglia want more movement, the internal globus pallidus reduces the number of inhibitory signals to the thalamus so the motor cortex doesn't become as active. To cause less movement, the internal globus pallidus is instructed to increase the inhibitory signals to the thalamus to prevent further communication with the motor cortex. For the indirect pathway to be successful, there are certain communications that take place. First off, the striatum becomes stimulated as the motor cortex transmits excitatory signals to that location. Due to the increase in activity, the inhibitory neurons in the striatum release inhibitory signals to the external globus pallidus, reducing its activity. This reduction of activity increases the activity of the subthalamic nucleus because the external globus pallidus is no longer able to suppress that structure. Since the subthalamic nucleus is more active than usual, it stimulates the inhibitory neurons that are found from the internal globus pallidus to the thalamus. This tightens the tether that the internal globus pallidus has on the thalamus which ensures suppression and lack of communication of the thalamus, thus any unwanted movement is prevented.

Furthermore, just as the direct pathway contained behind-the-scenes structures, there are two structures that allow for flexibility; those are the subthalamic nucleus and substantia nigra. Essentially, the activity of the substantia nigra increases due to the excitatory signals that are sent from the subthalamic nucleus. This increase in activity allows dopamine to be transmitted from the substantia nigra to the striatum. Unlike in the direct pathway, the dopamine here binds to the D2 receptor found in inhibitory neurons, preventing the external globus pallidus from being inhibited (Gilles, 2015). Since the external globus pallidus is not able to excite its inhibitory neurons that cause the internal globus pallidus to become more inhibited than before, the tether attached to the thalamus is loosened. Therefore, the thalamus is able to have a minimal amount of communication with the motor cortex but not significant enough to result in unwanted movements.

It is evident that the substantia nigra plays a vital role in preventing and limiting unwanted movement; therefore, its deterioration is very problematic for those with PD.

Neurologic music therapy is known to be a form of treatment that involves the use of music interventions. In the case of PD, some of the main goals of this type of therapy are to strengthen one's voice, breaths, and motor movements (both fine and gross). Individuals with PD experience the loss of their internal rhythm and tempo. As a result of this loss, the individuals affected are either going too fast or too slow compared to normal rhythm. It is important to select music with a consistent rhythm for this type of therapy. This allows the individual the ability to be in sync with the music as they are walking, dancing, and/or exercising. If the music of choice lacks consistency in rhythm and tempo, it can be difficult to sync movement with the music; therefore, rhythm is a crucial aspect. Depending on the actions that the individual is performing, the type of music selection may vary. For instance, if an individual is exercising, he/she may listen to something upbeat and at a semi-fast pace. On the other hand, an individual who is walking from point A to point B may listen to something softer. The use of music allows rhythmic stimulations which trigger parts of the brain into doing what it usually would do if dopamine was not lacking. Thus, individuals with PD can achieve some control over their movement through auditory signals and rhythmic stimulants as an alternative route.



Figure 1

This diagram represents the direct pathway (green) and the indirect pathway (red) and how the basal ganglia (orange) communicates with one another and with nearby structures of the brain such as the thalamus and motor cortex. As the different parts of the brain work with one another, the information is then relayed to the muscles which results in the stimulations and/or inhibition of movement. (Shebrain, 2018).

b. Influence of Music on the Basal Ganglia

As previously mentioned, the basal ganglia links different parts of the brain together, and they are primarily the targeted areas of the brain that are associated with PD. Based on studies that

have been conducted, there is data indicating that there are positive effects of music, an external auditory stimulus, on individuals with PD, especially on their gait pattern. One of the fascinating aspects of music is that it produces feelings that can be shared among individuals from all different backgrounds and cultures, thus making it a universal phenomenon. Both music and dance go hand in hand with one another; meaning that a person can never make a sound without moving and a person can never move without making sound. This complementation is what makes music and PD an interesting match as music is demonstrated to provoke the production and absorption of dopamine.

One of the primary influences of music's influence on rhythm is through a process called audio-spinal facilitation (Thaut, 1999). This process uses the sound that is perceived in the auditory field to excite the nerve cells in the spinal cord to initiate movement. The sound which acts as an external stimulus is processed upstream and downstream simultaneously which has an evolutionary purpose to it so a person can move away from loud, dangerous sounds before he/she are consciously aware of what he/she is moving away from. This process happens so fast that it is below the threshold of consciousness since movement is occurring before a person makes the conscious decision to do so. A second process that is important to note is the use of physiological entrainment which is a process by which sound that is repeated over time, such as a repeated beat in music, sets up this process that allows a person to not just synchronize his/her movements to the sound that is being heard but it becomes embedded into the central nervous system that even when the sound is turned off, the person will continue to walk in that same pace in the absence of the sound (Thaut, 1999). Often times when people hear music, they automatically have the urge to coordinate their body movements with the tune and beat of the stimulus. Most of the time people do not think much about it because it is natural for them to hear a music stimulus and synchronize

their movements—to the best of their ability. For instance, when sitting in the waiting room of a dental office, it is not uncommon to see people synchronize their foot tapping with the music being played. This involuntary body movement indicates that the basal ganglia is under the influence of music and can validate the use of music as a means of treatment for PD.

These process that help facilitate the mechanism are fascinating and hold a level of complexity that requires more research in order to fully grasp music's positive effects on PD. Some may argue that one possible reason behind music's positive effects may be due to its ability to directly trigger emotional responses more effectively and efficiently than other stimuli such as visual stimuli (Brodal et al., 2017). More specifically, music has the ability to excite the basal ganglia through these emotion stimulating sounds. However, the facilitated mechanism is not mainly due to the pleasure that a person draws from music. Rather, the pleasure allows the person to do their therapy and is motivating because sometimes therapy can be unamusing because brain plasticity is driven by repetition. Therefore, doing something over and over can be dull but when a person does it with music, especially one that he/she likes, it adds a pleasurable aspect to it but the actual mechanism is due to audio-spinal facilitation and physiological entrainment.

c. Use of Nonconventional Interventions

Although there are conventional interventions that can help those with PD, there is an increasing amount of interest in nonconventional interventions. One of the preeminent reasons is due to the limited ability of conventional therapeutic interventions to improve motor impairments that are associated with this disease. Conventional interventions such as the use of L-DOPA and deep brain stimulations have the risk of damaging cognitive function and result in disorders that can create further involuntary movement. Over the past few decades, there have been studies showing the positive outcomes of using music-based interventions for improving motor activity,

gait patterns, and the overall mobility of individuals with PD. These nonconventional interventions prove to be safe and non-invasive unlike some of the conventional interventions. Moreover, they are accessible to many affected individuals in many different countries besides the United States (Kabra et al., 2018). The risks that nonconventional interventions hold are rather minimal compared to conventional interventions, which is another reason why some people show an interest in them.

d. Rhythmic Auditory Stimulations

One of the most successful nonconventional interventions is known as RAS, which is short for rhythmic auditory stimulation. RAS is a technique used to create and maintain the biological rhythms of movement, specifically gait, as the patterns become abnormal for those with PD (Thaut & Hoemberg, 2016). However, RAS can be used on individuals with other diseases or health issues such as Multiple Sclerosis, traumatic brain injury, and more. Although gait may seem to be simple since it is done unconsciously, it is a complex process as well because, once it is altered, it interferes with an individual's activities. A normal gait pattern is comprised of alternating cycles. The first phase is known as the stance phase which accounts for 60% of the cycle, while the remaining 40% account for the swing phase (Thaut & Hoemberg, 2016). In this cycle there is a period in which both feet are planted on the ground, which accounts for 20% of the cycle or 10% per foot. This 20% is where the problem can be seen in those with an abnormal gait pattern because this percentage is increased. One of the reasons for this increase is because individuals with PD feel like they are rooted to the ground and that is also a way for them to reduce their chances of falling.

RAS was first conducted two decades ago, and the results have been promising. The obtained results have indicated that RAS was highly efficient in improving gait patterns, stride length, and

gait timing of individuals with PD. Based on the research that has been conducted and collected over the years, RAS is effective, mainly for those with PD, in two ways. The technique can either be effective in providing rhythmic cues as the individual is moving, or it can help achieve a less abnormal gait pattern (Thaut & Hoemberg, 2016). It was also concluded that a focus on the auditory system was more rewarding and beneficial than other systems for several reasons. One of the main reasons pertains to the precision of the auditory system compared to the somatosensory and visual system. This system has the ability to detect certain patterns both quickly and efficiently, which allows for effective interactions between the auditory and motor systems considering that these two systems complement one another.

i. Rhythmic Auditory Stimulations & Motor Functions

A study found in the *Journal of Neurology, Neurosurgery, and Psychiatry* explored RAS on gait patterns in 31 patients with PD. The 31 individuals were divided into two groups: “ON” and “OFF” group. The “ON” group consisted of 21 individuals who were on medication for the disease. The “OFF” group had 10 individuals who were off medication. The control group of the study contained 10 healthy individuals that did not have this disease. The methods for this study were very simple and broken into four parts. The first of four parts required all three groups to walk as fast as they could for 30 meters without the use of rhythmic auditory simulations. In this part, the results indicated abnormal gait patterns which are expected in individuals with PD. However, there was a difference in gait pattern between the “ON” and “OFF” groups. Although both groups experienced a decrease in stride length and velocity, the OFF group showed lower numbers as well as asymmetry in strides. A normal, healthy individual takes approximately 113 steps per minute; however, the individuals who have PD and are on medication took 98 steps per minute, while the OFF group took 91 steps per minute. The second part required them to walk the

same distance of 30 meters with the use of RAS that matched their baseline from the first part of the study. During the RAS matching, the majority of the individuals in each of the groups were able to maintain synchronization. Only three of the “OFF” group were not in sync because they were either going too fast or too slow compared to their baseline. The third part used RAS, but it was adjusted to be 10% faster than the individuals’ baseline. There were two individuals in the “ON” group that were not able to perform this matching task successfully. However, the rest of the “ON” group were able to match to the 10% increase. In the OFF group, 2 were slightly ahead of their baseline and another individual was 25% faster than the RAS frequency. The control group did not find it challenging, which is to be expected as they do not suffer from the symptoms associated with this disease. Finally, the last part of the study was to see the overall effect of RAS when individuals walked 30 meters without external rhythm, thus solely relying on their internal rhythm. In all the groups, results showed that the carryover of RAS was limited as it did not hold a long-term effect.

ii. Rhythmic Auditory Stimulations & Non-Motor Functions

Although music therapy has been shown to improve motor functions that are compromised in individuals with PD, there have been studies that show the effects of music-based interventions for non-motor symptoms that are associated with this disease (Koshimori & Thaut, 2018). Individuals with PD experience cognitive impairment which can be associated with the frontal lobe of the brain (Goldman, 2018). The frontal region of the human brain has an important role in controlling cognitive skills including language, memory, emotions, and expressions.

There was a study conducted to demonstrate the use of music therapy for both motor and non-motor symptoms caused by PD (Spina et al., 2016). The study had a total time period of 12 months and involved 25 individuals who had this disease. The criteria for these individuals consisted of

them not undergoing treatment for dementia, depression, or anything that would interfere with the study. To keep the study unbiased, the individuals were randomly assigned to receiving music therapy or no music therapy. Those who did not receive music therapy were used as the control group to be compared with the other group. Individuals who received music therapy had to attend one session every week for 90 minutes. These sessions were not only limited to music but included singing and dancing as well. After the first 6 months of this study the individuals were evaluated. The evaluation consisted of examinations on their motor skills, language, and quality of life. After the first evaluation, the individuals were re-evaluated after another 6 months, but this time, without a music therapy session to see if there was a difference in their quality of life. At the end of this study, the data obtained was analyzed, and it indicated that there was an improvement of the frontal lobe function with an increase in processing speed, memory, and other cognitive skills using music therapy. Not only was there improvement in that region of the brain, but the overall quality of life for these individuals improved significantly as well. Their well-being improved as they were more comfortable being out in public, interacting with people, and doing everyday activities. Although there were improvements with the use of music therapy, the study did indicate that this treatment is effective during interventions. During the second evaluation, 6 months after the end of the program, the data indicated a decrease in improvements as the effects were wearing off. This decrease suggested that music therapy should be extended for a longer period since its effects are beneficial for the individual with PD.

Not only has rhythmic intervention helped alleviate motor and non-motor impairments, but it has proven to alleviate speech impairments as well (Koshimori & Thaut, 2018). Those with PD experience the inability to speak as efficiently and easily as before. Just like any symptom associated with a disease, this secondary motor symptom is not experienced in the same way by

all PD individuals. Those that have speech impairment can experience the inability to communicate, which can be very troublesome. It is already common for people with PD to become self-conscious about their involuntary movements, thus the added stress and anxiety of not being able to communicate can lead to emotional and psychological problems. A lack of interest in interacting with others and going out in public to perform basic, everyday activities can result from this. Due to the speech impairment, individuals with PD can find it challenging to be part of conversations, especially if they are rapidly paced conversations.

Individuals with PD may gradually develop speech deficiencies such as slurred, monotoned, and softer speech than usual. These changes in speech are characterized by hypophonia (soft speech) and tachyphemia (rapid speech). Dysarthria is one type of disorder that affects the muscles that are used for speech, and often times hypophonia and tachyphemia are associated with it (Downward, 2017). Hypophonia is a result of weakened muscles, thus speech is softer due to the lack of coordination in speech muscles. In a normal individual, there are small muscle contractions even when relaxed in order to prevent things from going down. However, the weakened speech muscle that individuals with PD experience is slightly different. Muscles are regulated by the central nervous system, thus when there is damage to the brain, a decrease in muscle tone can result (Downward, 2017). Unlike hypophonia, tachyphemia, also known as cluttering, makes it difficult for those with PD to be understood by others as their speech is fast with poor rhythm and grammar. In healthy individuals, facial muscles and muscles found in the throat help with speech; however, that is not the case for individuals with PD since they experience rigidity in those muscles. Although the speech muscles are greatly affected, the primary source of speech impairment is found in the brain, specifically in the substantia nigra pars compacta (Downward, 2017). Thus,

individuals in advanced stages of PD experience a decrease in speech muscle functionality compared to those in the early stages.

V. Conclusion

Over the past decades, physicians' and therapists' understanding of PD being a progressive dopaminergic depletion disease, has allowed for the creation of neurologic music therapy as a form of treatment alongside the traditional L-DOPA and DBS treatments. Through the use of rhythmic auditory stimulation (RAS) there is evidence indicating noninvasive yet positive effects on individuals with PD. It has been shown to improve abnormal gait patterns and timing, other motor impairments, and non-motor impairments better than normal physical therapy due to the addition of rhythm. Nonetheless, although there is a substantial number of studies supporting the use of neurologic therapy, there is a considerable amount to be discovered regarding PD. Specifically, further research on the neural mechanisms and the neurochemical processes that occur.

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VII. References

1. Brodal, H. P., Osnes, B., & Specht, K. (2017). Listening to Rhythmic Music Reduces Connectivity within the Basal Ganglia and the Reward System. *Frontiers in neuroscience*, 11, 153. doi:10.3389/fnins.2017.00153
2. Disease Research, & Education. (2013). Parkinson's Disease Research, Education and Clinical Centers. Retrieved from <https://www.parkinsons.va.gov/index.asp>
3. Dorman, D. (2015). The Handbook of Clinical Neurology. *ScienceDirect*. Retrieved from <https://www.sciencedirect.com/topics/neuroscience/extrapiramidal-system>
4. Downward, E. (2017). Symptoms – Speech difficulties or changes. *ParkinsonsDisease.net*. Retrieved from <https://parkinsonsdisease.net/symptoms/speech-difficulties-changes/>
5. Friedlander, A. H., Mahler, M., Norman, K. M., & Ettinger, R. L. (2009). Parkinson disease systemic and orofacial manifestations medical and dental management. *Journal of the American Dental Association*, 140 (6), 658-669.
6. Giles, E. (2015). The basal ganglia - The direct pathway. Retrieved from <https://www.khanacademy.org/science/health-and-medicine/nervous-system-diseases/parkinsons-disease/v/the-basal-ganglia-the-direct-pathway>
7. Giles, E. (2015). The basal ganglia - Details of the indirect pathway. Retrieved from <https://www.khanacademy.org/science/health-and-medicine/nervous-system-diseases/parkinsons-disease/v/the-basal-ganglia-details-of-the-indirect-pathway>

8. Goetz, C. (2011). The history of Parkinson's disease: early clinical descriptions and neurological therapies. *Cold Spring Harbor Perspectives in Medicine*, 1(1), a008862.
9. Goldman, J. G. (2018). Cognitive changes. American Parkinson Disease Association. Retrieved from <https://www.apdaparkinson.org/what-is-parkinsons/symptoms/cognitive-changes/>
10. Jankovic, J., & Aguilar, L. G. (2008). Current approaches to the treatment of Parkinson's disease. *Neuropsychiatric Disease and Treatment*, 4(4), 743–757.
11. Kabra, A., Sharma, R., Kabra, R., & Baghel, U. S. (2018). Emerging and Alternative Therapies For Parkinson Disease: An Updated Review. *Current Pharmaceutical Design*, 24(22), 2573-2582. doi:10.2174/1381612824666180820150150
12. Kasper, D. L., Fauci, A. S., Longo, D. L., Braunwald, E., Hauser, S. L., & Jameson, J. (2005). *Harrisons principles of internal medicine* (16th ed.). New York: McGraw-Hill.
13. Koshimori, Y., & Thaut, M. H. (2018). Future perspectives on neural mechanisms underlying rhythm and music based neurorehabilitation in Parkinson's disease. *Ageing Research Reviews*, 47, 133-139. doi:10.1016/j.arr.2018.07.001
14. Kowal, S. L., Dall, T. M., Chakrabarti, R., Storm, M. V., & Jain, A. (2013). The current and projected economic burden of Parkinsons disease in the United States. *Movement Disorders*, 28(3), 311-318. doi:10.1002/mds.25292
15. McIntosh, G. C., Brown, S. H., Rice, R. R., & Thaut, M. H. (1997). Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinsons disease. *Journal of Neurology, Neurosurgery & Psychiatry*, 62(1), 22-26. doi:10.1136/jnnp.62.1.22

16. McNamara, P. (2018). Bradykinesia in Parkinson's Disease: Slowed movement that affects both fine and gross motor control. *Very Well Health*. Retrieved from <https://www.verywellhealth.com/bradykinesia-2612077>
17. NIH Fact Sheets - Parkinson's Disease. (2018). Retrieved from <https://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=109>
18. Parkinson's Disease Clinic and Research Center. (2014). Retrieved from <http://pdcenter.neurology.ucsf.edu/patients-guide/parkinson's-disease-medications>
19. Parkinson's News Today. (2018). Surgical treatments for Parkinson's Disease. Retrieved from <https://parkinsonsnewstoday.com/parkinsons-disease-treatments/surgical-treatments/>
20. Smith, D. (2011). Mental and physical exercise: Alternative to dopamine treatment in Parkinson's Disease. *Brain Study*. Retrieved from <https://brainstudy.wordpress.com/tag/basal-ganglia/>
21. Spears, C. (2018). Deep brain stimulation (DBS). *Parkinson's Foundation*. Retrieved from <http://www.parkinson.org/Understanding-Parkinsons/Treatment/Surgical-Treatment-Options/Deep-Brain-Stimulation>
22. Spina, E., Barone, P., Mosca, L. L., Davanzati, R. F., Lombardi, A., Longo, K., Lavarone, A., & Amboni, M. (2016). Music Therapy for Motor and Nonmotor Symptoms of Parkinsons Disease: A Prospective, Randomized, Controlled, Single-Blinded Study. *Journal of the American Geriatrics Society*, 64(9). doi:10.1111/jgs.14295
23. Thaut, M.H., (1999). *Training manual of Neurologic Music Therapy*. Colorado State University: Center for Biomedical Research in Music.

24. Thaut, M. H., & Hoemberg, V. (Eds.). (2014). Handbook of neurologic music therapy. New York, NY, US: Oxford University Press.
25. Van Laar, A. D., & Jain, S. (2004). Parkinson disease: an update. *The Neurologist*, 10(4), 185-94.
26. Wooten, G., Currie, L., Bovbjerg, V., Lee, J., & Patrie, J. (2004). Are men at greater risk for Parkinson's Disease (PD) than women? *Journal of Neurology, Neurosurgery, and Psychiatry*, 75(4), 637–639. <http://doi.org/10.1136/jnnp.2003.020982>