



JADE CORNELOUP-HARCZOS

The evidence on the effectiveness of forced exercise on the symptoms of Parkinson's disease

Narrative literature review

DEGREE PROGRAM IN PHYSIOTHERAPY
2022

Author(s) CORNELOUP-HARCZOS, Jade	Bachelor's thesis	Date October 2022
	Number of pages 47	Language of publication: English

The evidence on the effectiveness of forced exercise on the symptoms of Parkinson's disease

Degree Programme: Physiotherapy

Parkinson's disease is currently one of the brain disorders with the quickest rate of growth. Although understanding regarding this condition is increasing and advances can be seen in every discipline around it, no cure is presently available. The current focus is on giving the finest care possible and developing novel methods for enhancing the patient's quality of life and autonomy.

Physiotherapy is a profession that uses a wide range of techniques to treat patients with various restrictions. In order to provide the greatest care, a physiotherapist's role is to modify their approach to the patient's needs and stay up to date on the most recent research. The use of therapeutic exercise is crucial in the field and has a variety of applications. An emerging method for managing Parkinson's disease is forced exercise. The objective of this thesis was to review the evidence on the effectiveness of forced exercise on Parkinson's disease symptoms.

For this thesis, a narrative literature review was used. The objective was to gather evidence-based information about forced exercise and how it might be used to treat Parkinson's disease. To give a more comprehensive review and reduce the likelihood of bias, a more systematized approach was adopted.

Following a review of the chosen article, the findings indicated that forced exercise has a positive impact on motor symptoms, while the findings are inconclusive or do not indicate any benefits for non-motor symptoms.

In summary, forced exercise may be helpful for certain patients, especially those with motor symptoms, but it is still an individualized approach that may not produce the same outcomes with every patient.

Keywords: Parkinson's disease, forced exercise, symptoms

CONTENTS

1 INTRODUCTION	4
2 PARKINSON’S DISEASE.....	5
2.1 Pathophysiology.....	5
2.2 Epidemiology, incidence, and prevalence.....	11
2.3 Etiology.....	12
2.3.1 Genetics.....	13
2.3.2 Environmental factors.....	13
2.4 Diagnosis.....	14
2.5 Symptoms.....	15
2.5.1 Motor.....	16
2.5.2 Non-motor.....	18
2.5.3 Stages and scales.....	24
3 PHYSIOTHERAPY INVOLVEMENT.....	25
4 THERAPEUTIC EXERCISE	28
5 HEALTH PROMOTION.....	30
6 AIM, PURPOSE, AND RESEARCH QUESTION.....	31
7 METHODS	32
7.1 Narrative literature review	32
7.2 Data collection process	32
7.3 Thematic analysis.....	38
8 RESULTS	39
8.1 Motor symptoms	39
8.1.1 UPDRS-III.....	40
8.1.2 Mobility and gait.....	41
8.1.3 Risk of falls.....	41
8.2 Non motor symptoms.....	42
8.2.1 Cognition	42
8.2.2 Depression	43
8.3 Engagement.....	43
9 DISCUSSION	44
10 CONCLUSION	47
REFERENCES	

1 INTRODUCTION

Parkinson's disease is a neurodegenerative illness that targets the neurons responsible for movement control ("What is Parkinson's?," n.d. .) Parkinson's disease is reportedly the "fastest growing brain illness in the world," (*Seven Million Cases of Parkinson's Disease - The Fastest Growing Brain Disease in the World*, 2021) with a plethora of symptoms. It is a condition that is primarily diagnosed after the age of 60, and its prevalence rises with age (Reeve et al., 2014.) The diagnosis of Parkinson's disease is quite difficult and can take a long time due to the variation in the development of symptoms and the rate of the illness in the patients. Even while some of the research has established a link between the disease and genetic and environmental factors, the reasons remain unexplained. (Keus, Munneke, Graziano et al., 2014, 20.)

The physiotherapist's involvement in Parkinson's disease is a key element of the treatment. Thanks to their training, physiotherapy will be able to slow down and even treat some Parkinson's symptoms using various approaches. (Caddick, 2020.) The involvement of the professionals in the patient's and their family's education elevates them to a significant role in treatment. Because the condition is so complicated, it is critical that physiotherapists undergo sufficient training during their studies in order to deliver the best therapy possible. (Website of *Parkinson's foundation*, 2019.)

Forced exercise is defined as a physical activity that is performed on a tandem or motorized bike in order to maintain a specific cadence and with a target heart rate that is determined with the patient's age and level of physical activity. It is a method that started to emerge in 2003 thanks to Dr Jay Alberts who then conducted a lot of research on the subject. (Forced Exercise With Theracycle Parkinson's Disease Bikes Study, 2010.)

Mari Törne and the degree program of physiotherapy are ordering this thesis.

2 PARKINSON'S DISEASE

Parkinson's illness was named after James Parkinson, a British doctor who published a medical essay called "An essay on shaking palsy" in 1817. It was not until 1861 that French neurologist Jean-Martin Charcot began to research the disease and discovered two stages: tremor and rigidity. He is also the one who suggested using James Parkinson's name for the condition because he recognizes that Parkinson's patients have something other than a regular shaking palsy. Parkinson had already hypothesized that the condition was caused by a malfunction in the medulla region of the brain. (Goetz, 2011; McCoy & Bass, 2016.) The purpose of this section will be to first determine what brain activity is required to create a voluntary or controlled movement, and then to comprehend the impact of the disease on the brain that causes those motions to be disrupted.

2.1 Pathophysiology

The cerebellum, cerebrum, and brainstem are typically seen as the three components of the brain. Each of those regions contributes in some way to the creation of a voluntary movement. The greatest portion of the brain is called the cerebrum. It is made up of white matter in the cerebrum's center and grey matter on the cerebrum's periphery. Each of the two hemispheres of the cerebrum contains four lobes. These are the frontal, parietal, occipital, and temporal lobes. (Image 1) (Lobes of the Brain, 2022)

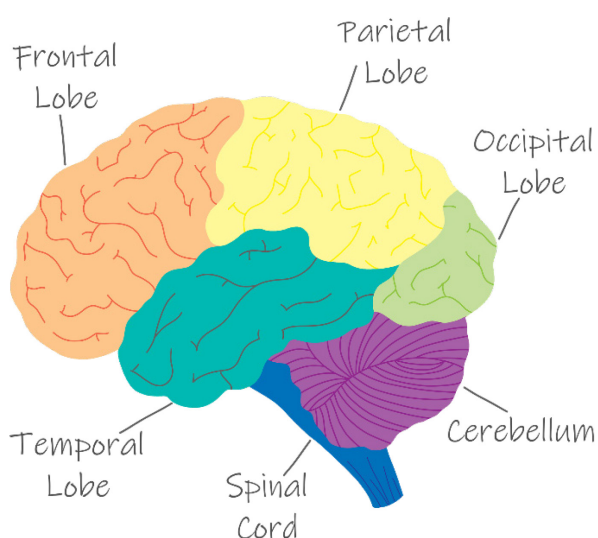


Image 1 Lobes of the brain

There is a region called the motor cortex located near the back of the frontal lobe. The motor cortex is divided into three regions which are essential in motor control: the premotor cortex, the supplementary motor cortex, and the primary motor cortex. (Image 2) (Regions of the Motor Cortex, n.d.)

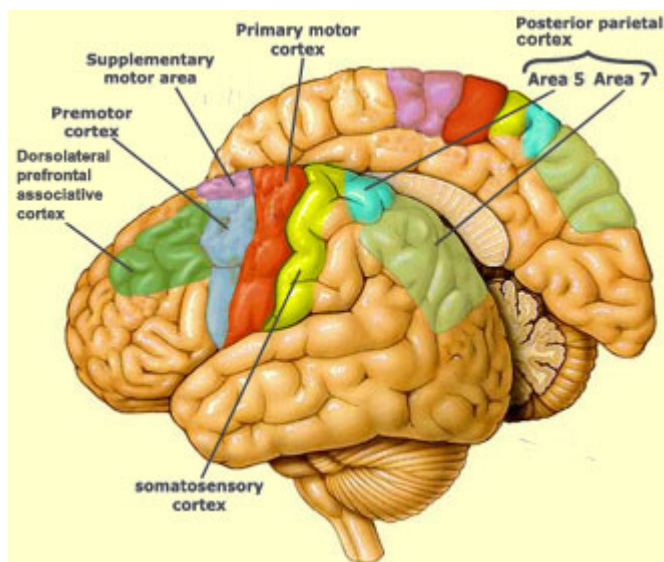


Image 2 Main regions of the motor cortex

To produce a simple movement of one body component, the primary motor cortex requires less activation. Both the premotor and supplementary motor systems require greater stimulation, which leads to more intricate movements and coordinated use of several body parts. Since the motor cortex is somatotopically arranged, distinct parts of the motor cortex oversee controlling the movement of specific parts of the body. The bodily components associated with more specialized, delicate, or precise motions are having a larger influence in the depiction known as the homunculus. (Knierim, 2020b.) (Image 3) (The Relative Homuncular Representation of the Primary Motor Cortex, n.d.)

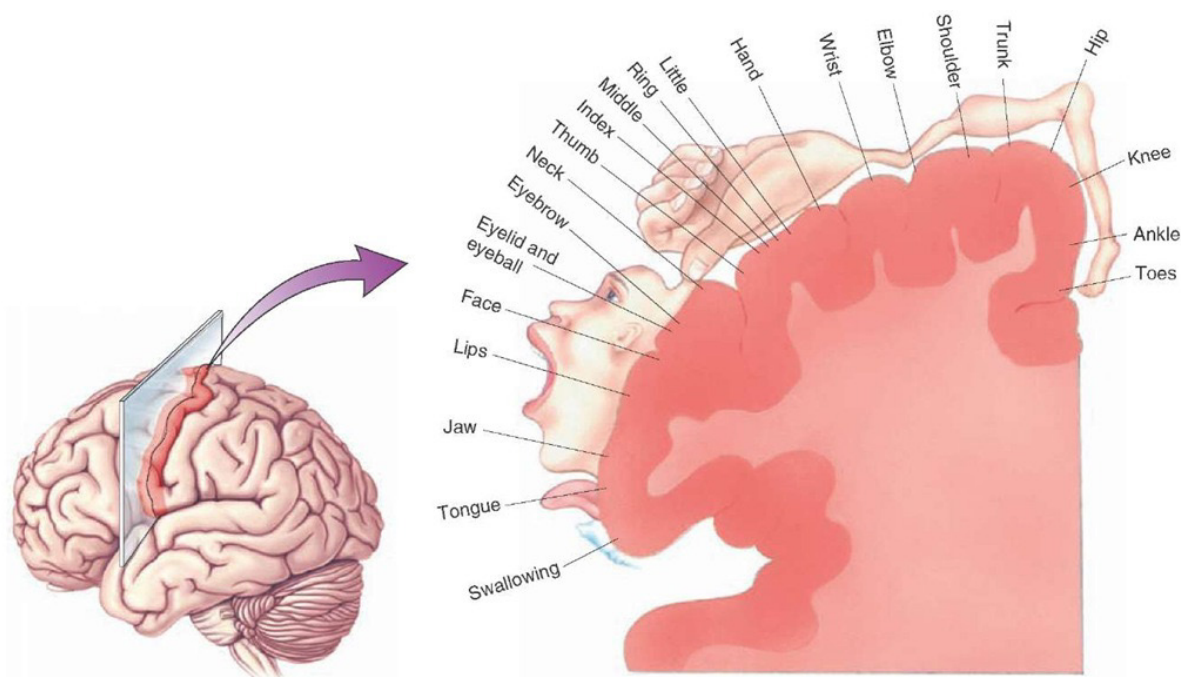


Image 3 Penfield's Homunculus

Signals are sent to the basal ganglia by the motor cortex when a voluntary movement is initiated. In response, the motor cortex will receive information from the basal ganglia via the thalamus. The motor cortex must then communicate a movement command to the muscle via the spinal cord to complete the movement. (ArmandoHasudungan, 2016.)

In the center of the brain, there is a collection of structures known as the basal ganglia. The caudate putamen, two globus pallidus (one external and one internal), the subthalamic nucleus, the nucleus accumbens, and the substantia nigra (that has two parts the pars compacta and the pars reticula) make up this structure. Under a different name, some of these structures are clustered together. The striatum, also known as the neostriatum, is made up of the caudate putamen, caudate nucleus, and nucleus accumbens. The corpus striatum is created when the globus pallidus is combined with the preceding group. (Knierim, 2020a.) The connections between the structures are made using two different neurotransmitters, glutamate (GluT), which has an excitatory effect, and gamma aminobutyric acid (GABA), which has an inhibitory effect. The basal ganglia coordinates acquired movement patterns and controls muscle tone, but it does not initiate controlled movements; rather, it aids in their production. Input refers to the signal transmitted from the motor cortex to the basal ganglia, and output refers

to the signal sent from the basal ganglia to the motor cortex. (ArmandoHasudungan, 2016.)

There are two paths that are processing the motor cortex's signals in the basal ganglia. These two paths are referred to as direct and indirect pathways. The direct pathway will produce a movement and the indirect pathway will stop the movement or a competing movement. (Knierim, 2020a.)

The direct pathways begin with the motor cortex providing glutamate-based excitatory signals to the striatum. The striatum is stimulated by the glutamate neuron. The GABAergic neuron in the striatum will instantly inhibit the GABAergic neurons in the globus pallidus interna (GPi) and the substantia nigra. The GABAergic neuron in the GPi normally inhibits the thalamus, but because the striatum is inhibiting the GPi, it no longer does so. The thalamus will be able to communicate excitatory signals to the motor cortex and permit movement via the corticospinal tract as a result of the thalamic neuron's disinhibition. (ArmandoHasudungan, 2016; Knierim, 2020a.) (Image 4) (Direct and Indirect Pathways of the Basal Ganglia, 2022)

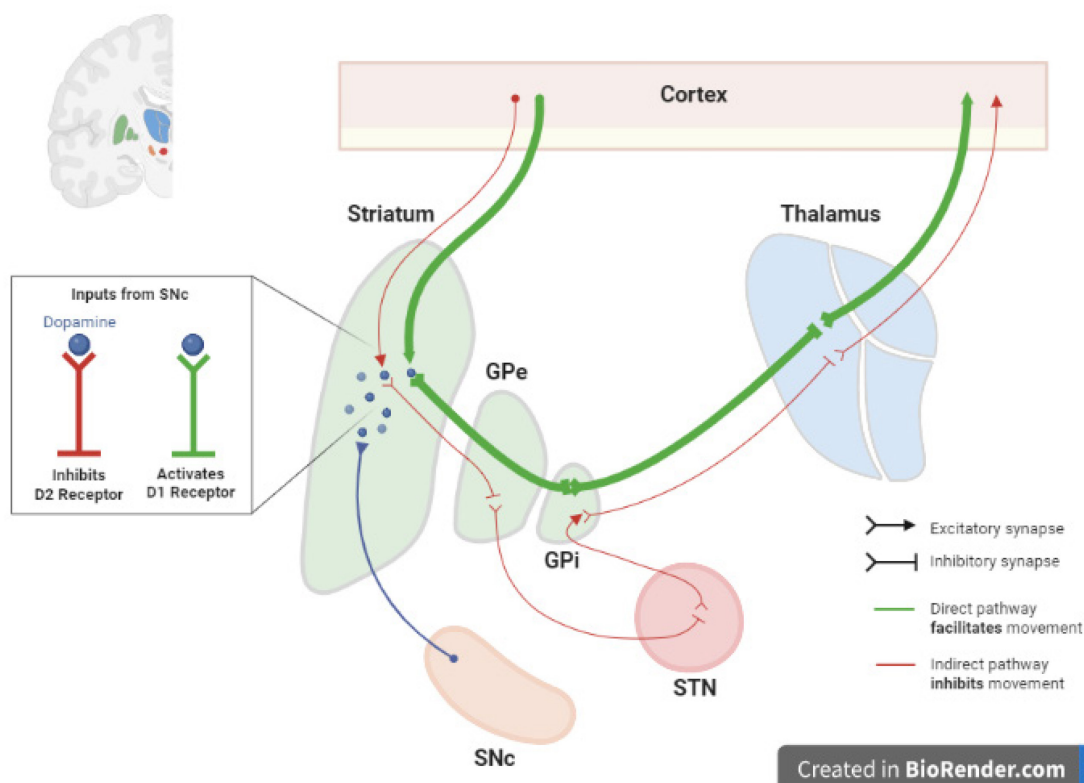


Image 4 Direct pathway of the basal ganglia

The indirect pathway likewise begins with glutamate-based excitatory impulses from the motor cortex to the striatum. When the latter is stimulated, it begins to inhibit the globus pallidus externa (GPext) via GABAergic neurons. The natural action of GPext is to inhibit the subthalamic nucleus. However, because the GPext has been inhibited by the striatum, the inhibition of the subthalamic nucleus will be reduced. By not being inhibited, the latter will be able to stimulate the GPint via glutamate neurons. Its activation will inhibit the thalamus and cause the movement to halt. (khanacademymedicine, 2015a; Knierim, 2020a.) (Image 5) (Direct and Indirect Pathways of the Basal Ganglia, 2022)

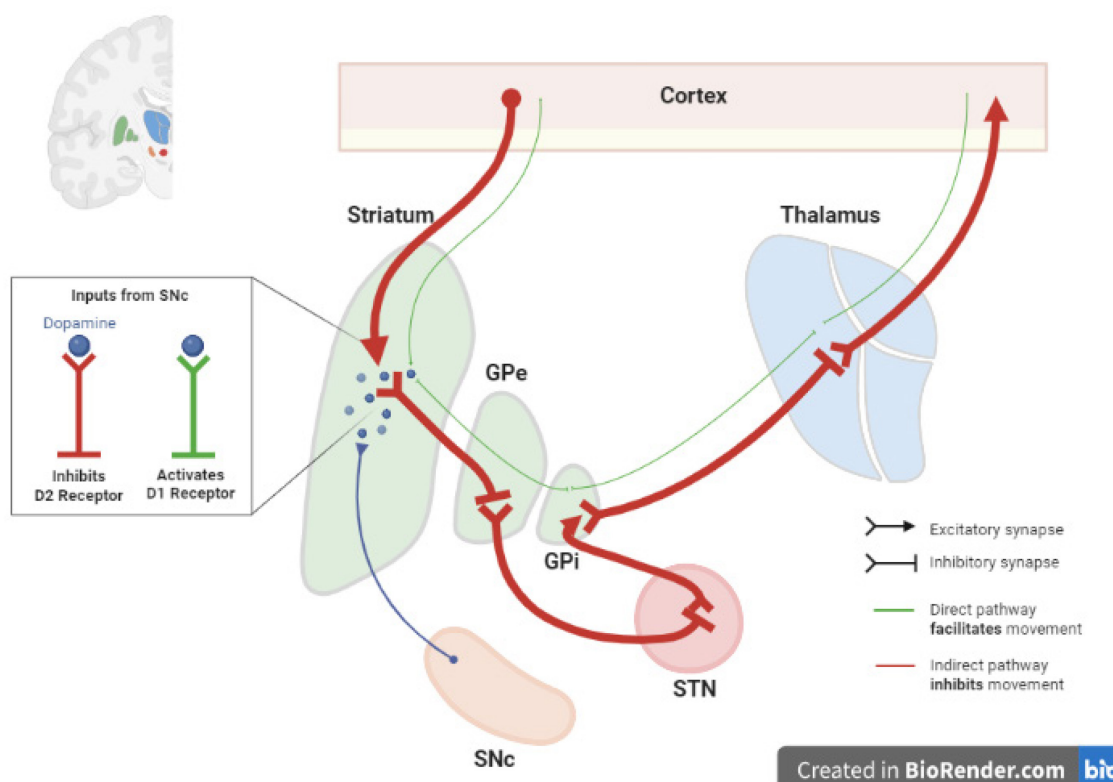


Image 5 Indirect pathway of the basal ganglia

The basal ganglia need to keep a good balance between the direct and indirect pathways to create an appropriate movement. The dopaminergic pathway, also called nigrostriatal project, is there to ensure this balance. Dopamine is a neurotransmitter that enables cells to communicate with one another (Cristol, 2019). It can bind to either the D1 or D2 type of receptor. It has an excitatory effect on the neuron when it binds to D1 receptors, but an inhibitory effect on the neuron when it binds to D2 receptors. Direct pathway neurons in the striatum have D1 receptors and indirect pathway

neurons in the striatum have D2 receptors. In this nigrostriatal project we can distinguish three different structures. The first two are contained in the term; nigro-refers to the substance nigra, and striatal refers to the striatum. The subthalamic nucleus is the final structure. The subthalamic nucleus will send excitatory signals to the substantia nigra pars compacta. This excitatory signal will allow the substantia nigra to produce dopamine. The neurotransmitters when used in the direct pathways, will bind to the D1 receptors via the dopamine neurons and excite the inhibitory neurons in the striatum. The result of this excitation is an increase in the action of the inhibitory neurons so a bigger inhibition of the GPint. This will allow the thalamus to be more active and so have a bigger signal to the motor cortex and then to the muscles. (khanacademymedicine, 2015b; Knierim, 2020a.) In the indirect pathways the neurotransmitters will bind to D2 receptors. These receptors will inhibit the striatum's activity, setting off a series of events in the indirect pathway. The GPext will not be as inhibited, the subthalamic nucleus will not be as excitatory, and the GPint will not be able to completely inhibit the thalamus so that it can send a signal to the motor cortex to cause a movement. (khanacademymedicine, 2015a; Knierim, 2020a.)

Parkinson's disease is caused by the death of dopamine neurons in the substantia nigra pars compacta. The onset of motor symptoms typically coincides with striatal dopamine levels below 20% and neuronal loss of 50% or more. Although the exact causes of this loss are still unknown, current research points to several potential factors that may have contributed. The nigrostriatal system is unable to operate correctly after the dopamine neurons are lost. It will not be able to stimulate the direct pathway and inhibit the indirect pathway. The nigrostriatal pathway plays a crucial function in fine-tuning both pathways to maintain balance and produce controlled fluid movements. Dopamine will not be present in sufficient quantities to bind to either the D1 or D2 receptors. The indirect pathway will become overstimulated due to the nigrostriatal pathway's inability to control it, which will block the activity of the thalamus and prevent movement. This is due to the dopamine inability to bind to the D2 receptors. The nigrostriatal pathways cannot stimulate the direct routes because dopamine will not bind with the D1 receptors. Dopamine will cause the direct pathway to be stimulated, which will result in faster movement; however, low dopamine levels will block this ability. This process will result in decrease signal from the motor cortex to the muscles via the corticospinal tract and produce motor symptoms such as tremors,

rigidity, or bradykinesia. (Knierim, 2020; Parkinson's Disease | Armando Hasudungan, n.d. .)

2.2 Epidemiology, incidence, and prevalence

Because it can take years to get a thorough diagnosis and then record those cases in the incidence and prevalence, Parkinson's disease is a difficult disease to study. Researching on a global scale is incredibly challenging because it is dependent on several factors that are unique to each country. Age, sex, ethnicity, and environmental pollution are only a few of these factors. (Ou et al., 2021.)

More than 9 million people in the world are estimated to have Parkinson's disease; when compared to the 2016 estimate of 6 million, we can see the rapid growth of the disease. (Maserejian et al., 2020.) This number is also expected to rise to 12-17 million by 2040 (Dorsey, 2018.)

In terms of gender, studies have shown that men have a 1.5 to 2 times higher incidence than women. The reasons are unknown, but one avenue of investigation is the neuroprotection provided by estrogen, a female hormone. (Wooten, 2004.)

Parkinson's disease is an illness that primarily affects the elderly. Only a few cases are discovered before the age of 50. The average age of arrival of symptoms is between 62 and 70 years old. The incidence increases between the ages of 70 and 79 but declines after the age of 80. (Muangpaisan et al., 2011.) The category of those above the age of 80 is also the most undiagnosed. The prevalence of Parkinson's disease is 0.3 percent in the general population, 1 percent in those aged 60 and up, and 3 percent in those aged 80 and above. (Lee & Gilbert, 2016.) This information can help us understand why the frequency of PD cases is higher in areas where life expectancy is higher (Driver et al., 2009.)

Ethnicity has a significant role in the current understanding of Parkinson's disease. Numerous research has been conducted to assess its impact on illness distribution in the population. According to current research, Hispanics, followed by Whites, have a

greater PD incidence than Asians, and finally Blacks. It is also worth noting that, when compared to women of the same age and ethnicity, the incidence for Hispanic, white, and black men is nearly doubled. It corresponds to the previous statement. Women, on the other hand, have a slightly greater incidence rate in Asian populations. For the time being, those results have no explanation. (Eeden et al., 2003.) Even though the incidence of ethnicity has been extensively examined, fresh research tends to cast doubt on its validity. The absence of thorough research with Hispanic and Black populations is one of the main points of conflict. Disparities in access to healthcare for those populations are posing a challenge to research based just on hospitalization or only obtaining their data from the healthcare system. (Bailey et al., 2020.) It has also been revealed that Black population in Africa have a lower incidence of Parkinson's disease than Black population in the United States, leading to the hypothesis that ethnicity may not be the most crucial factor, but rather the global environment in which those groups live. (Ben-Joseph et al., 2020; Sauerbier et al., 2018.)

The etiology being still unknown, the hypothesis of an environmental factor has grown, and studies have been conducted to investigate the risk factor of living in urban or rural settings. The outcomes of these studies differ from one another. Some studies find that urban areas have a higher incidence (Chen et al., 2009; Wright Willis et al., 2010), whereas others find no conclusive proof for any difference (Ferraz et al., 1996.) Another aspect that several studies looked at was the quality of life for people with Parkinson's disease in those areas. The Parkinson disease quality of life questionnaire (PDQ-39) yielded a worse score in rural locations. These scores are heavily influenced by stigma, awareness of the pathology, and cognition in those areas. (Klepac, 2007.) In a 2018 study, the average income, rather than the region, was discovered to be an important epidemiological factor. Parkinson's disease was more common in lower-income areas, whether rural or urban. (Marras, 2018.)

2.3 Etiology

Parkinson's disease has an etiology that is currently unknown. Much research has been conducted and continues to be conducted in order to better understand the etiology of this condition. At this time, genetical and environmental factors have been identified as factors that increase the likelihood of developing the condition. (*Causes*, n.d. .)

2.3.1 Genetics

Only a few years ago, genetics was being investigated as a cause of Parkinson's disease. There is a small percentage of cases when the condition is handed along from parents to children due to genetic changes. In the last two decades, key discoveries have been made, including the identification of 28 loci, or genes that are in a specific location on a chromosome and can cause Parkinson's disease if they are mutated. (*Podcast: Six New Genetic Risk Factors for Parkinson's Identified*, 2014.) Unfortunately, scientists are still learning about the full scope of those changes, and even if the mutation is present in someone, they may not get the disease (*Genetics and Parkinson's*, n.d. .) These findings led the researchers to believe that the etiology of Parkinson's disease was multifactorial, that a mix of genetics and environment, together with population aging, was responsible for the disease's significant evolution (Ball, 2019.)

2.3.2 Environmental factors

Many studies have been conducted to assess the impact of various environmental factors on the progression of Parkinson's disease. This research's findings are occasionally inconsistent, and their validity must be judged in retrospect. Some of the environmental factors studied have been demonstrated to protect against illness development, while others have been shown to increase the likelihood of disease development. (*Environmental Factors*, n.d. .)

The results of studies looking at the role of pesticides in the development of Parkinson's disease were mixed and lacked a clear conclusion. Many of the studies were biased by external factors, making it impossible to draw conclusions about the pesticides' effect. However, roughly ten years ago, studies were conducted, and the importance of specific pesticides could be determined with a good degree of certainty. (de Miranda, 2017.)

In a study by Costello et al. (2009), hypotheses that had previously been based on animal research were able to be confirmed on human beings. The first theory was that by combining multiple pesticides, their effects would be amplified. Humans are

exposed to a wide range of chemicals in modern civilization. The second idea was that the younger and longer a person was exposed to the combination of toxic chemicals, the more likely they were to acquire Parkinson's disease. This is a significant step forward in determining the disease's etiology. Researchers can now take their research in a different direction thanks to this discovery. (Costello et al., 2009.)

Metals, particularly heavy metals, are thought to influence Parkinson's disease. Because dietary intake of metals like iron, for example, is tightly regulated, the presence in the body would be attributable to inhalation. (Agim & Cannon, 2015.) Knowing this, doing a non-biased study using consistent metrics is extremely challenging. Ullah et al. established in a study published in 2021 that combining iron, copper, and lead increases their toxicity. Mercury is another metal that has been shown to be extremely hazardous to neurons. When all these metals are combined, the risk of Parkinson's disease rises. (Ullah et al., 2021.)

Some research has investigated the effects of infections like H5N1 on dopaminergic neurons, which can lead to central nervous system disorders like Parkinson's (Jang et al., 2009.) It is simply speculation because H5N1 is not a present epidemic. However, research looked at the incidence of parkinsonism after the Spanish and H1N1 influenzas and found that it had increased (de Miranda, 2017.) Parkinsonism is a broad term that refers to a variety of neurological issues. It is different from Parkinson's disease. Parkinson's disease is merely a minor fraction of the overall condition known as parkinsonism. (Dizon, 2021.) However, this study continues to raise awareness of the role of pathogens in Parkinson's disease etiology.

2.4 Diagnosis

Parkinson's disease diagnosis is a lengthy and tough process. The first symptoms appear around the age of 64, but diagnosis takes an average of two years, and it takes longer the younger the person being checked (Wong et al., 2014). There is no one-size-fits-all test, so some people are misdiagnosed and are only recognized with Parkinson's disease when their symptoms worsen (Schrag, 2002).

In 2013, the European Federation of Neurological Societies (ENFS) and the Movement Disorder Society's European Section (MDS-ES) published guidelines on Parkinson's disease diagnosis. They graded the various tests in three levels in their report: A, B, and C. A indicates that it is effective in the diagnosis of Parkinson's disease, B indicates that it is probably effective, and C indicates that it is possibly effective. Patients with parkinsonism are usually subject to nine distinct categories of tests. In those categories, olfactory testing, neuropsychological tests, and neuroimaging, particularly transcranial sonography, and DaTscan-SPECT, were all rated as level A in terms of diagnosing Parkinson's disease. The clinical diagnostic criteria used with the Queen Square Brain Bank (QSBB) and genetic testing were both graded as B, indicating that they were both relevant to the diagnosis. (Berardelli et al., 2012.)

Another common technique for confirming a PD diagnosis is to have a specialist prescribe medicine to treat the disease. If the symptoms improve after a few weeks or months of treatment, the diagnosis of Parkinson's disease may be established. (*Parkinsonin tauti*, 2022; Suchowersky et al., 2006.)

Recent studies in the past years discovered that Parkinson's could have two variants. The "known" one that starts in the brain and then travels to the intestines and other organs. The new variant is that Parkinson's for some patients is actually starting in the intestines and spreading to the brain through the nervous system. It has also been observed that patients with intestines first had REM sleep disorders. This could mean a new way of diagnosing PD patients and because this variant starts with the intestines it could be possible to discover the disease earlier. (Borghammer & van den Berge, 2019; Cassella, n.d.; Horsager et al., 2020.) It is important to keep in mind that this variant is not present in every patient and is usually in younger patients (Rietdijk et al., 2017.)

2.5 Symptoms

Parkinson's disease is a highly individual disorder about which we continue to learn new aspects because of extensive research. The symptoms are diverse and can be divided into two groups: motor and non-motor symptoms. The majority of the time, the symptoms begin asymmetrically before spreading over the entire body. Although scales and phases have been developed to assist specialists in assessing the disease,

symptoms will never be identical in terms of intensity, variety, or duration between patients, making it extremely difficult. (*Stages of Parkinson's*, n.d. .) This thesis will review the most common and present ones, but it is good to remember that the patients might most likely not experience all or many of these symptoms (NHS website, 2021.) Similarly, to how the disease affects more males than women, there is a difference in the symptom presentations based on gender (Scott et al., 2000.)

2.5.1 Motor

Bradykinesia is a key motor sign for establishing the diagnosis. For your clinician to consider Parkinson's disease, you need to have bradykinesia coupled with tremor or stiffness. (Berardelli et al., 2012.) The word bradykinesia comes from the Greek word “brady,” which means slow, and “kinesia,” which means movement. It naturally translates to a slowness of movement. (*Medical Definition of Bradykinetic*, 2021.) It is incredibly challenging for the patient because it is a very unpredictable symptom; they could be functioning fine one minute and then need assistance with simple chores like getting dressed the next (*Parkinson's Disease: Causes, Symptoms, Stages, Treatment, Support*, 2020.) Bradykinesia makes it harder to initiate movements and carry out automatic movements. The changes in daily life are commonly seen by the family; walking may be slower, and people with bradykinesia tend to move less since their muscles react more slowly than before. (*Bradykinesia*, 2020; *Bradykinesia (Slowness of Movement)*, n.d. .)

Parkinson's disease is also characterized by tremor: an involuntary and rhythmic movement. It is asymmetrical in definition, similar to bradykinesia, and can spread throughout the entire body. It has been estimated that around 75 percent of the patients have tremor at rest and 60 percent suffer from action tremor. It is one of the most distressing symptoms for sufferers, both physically and psychologically. It is regarded as a source of embarrassment, and patients attempt to conceal it, particularly in public or with their families. It has a significant impact on the patients' quality of life and is often reported to be the cause of anxiety, stress, or depression. (Heusinkveld et al., 2018.) Rest tremor is a type of tremor that originates in the hands or upper extremities when the patient is at rest. It can also affect the legs, tongue, or lips. This resting tremor

in Parkinson's disease occurs between 4 and 6 Hz and is known as a pill-rolling tremor because the patient appears to be rolling a pill between his thumb and index finger. Patients can stop this tremor by activating their muscle and making a movement. (W. Chen et al., 2017.) A tremor during a voluntary movement, against gravity, or during muscle contraction, such as holding a book, is known as action tremor (Gupta et al., 2020.) It is bothersome for the patients in their daily lives since it affects their fine motor abilities, making simple tasks like writing or holding a cup more challenging (*Tremor*, n.d. .)

Rigidity is the third most common sign of Parkinson's disease, alongside bradykinesia and tremor. It can affect any area of the body and is common in most people with Parkinson's disease. It is preceded by a feeling of muscle weakness or an unfamiliar ache. Rigidity is defined as a tightness or stiffness in the limb that makes correct movement impossible and reduces range of motion. (*Rigidity*, 2016; *Rigidity (Stiffness)*, n.d.) Parkinson's illness causes two types of rigidity: lead-pipe and cogwheel rigidity. The lead-pipe is a constant stiffness caused by the co-contraction of the agonist and antagonist muscles engaged during joint movement. The cogwheel is characterized by abrupt stops and jerkiness during movement. (*Rigidity*, n.d.) The rigidity in the muscle is characterized by the inability of the muscle to relax or stretch. This permanent rigidity of the muscle then leads to numerous problems. Cramps and muscle fatigue might develop because of muscle stiffness that persists. When the facial muscles are compromised, the patient may have a mask-like appearance and be unable to make facial expressions. It is especially harmful to the patient's socialization because they are unable to express their feelings using their face and body. Reduced range of motion in one or both arms might result in an uneven gait pattern, making it more difficult for the patient to walk. The final issue we will look at is sleep disruption. Rigidity by itself has an impact on sleep. Patients who have muscle stiffness during the night find it difficult to fall asleep or sleep for extended periods of time. Their ability to move in the bed is limited, and their position quickly becomes unpleasant. (*Learn the Impact and Treatment of Rigidity in Parkinson's Disease*, 2022.)

We began to observe the impact of PD on the gait in the early sections, but because it is such a crucial movement that is affected by a variety of issues, we needed to expand on it in a separate section. This section will be divided into two parts: the change in

walking pattern and the postural instability and risk of falls that accompany the patients during their movements.

Parkinsonian gait is characterized by slower steps, decreased range of motion in the arms and legs, and a lack of trunk rotation due to rigidity in these muscles, resulting in a shorter stride. The freezing and festination are two main aspects of this gait. When a patient freezes, he or she is unable to begin or continue walking. Before or during the movement, the patient may begin to hesitate. (*Gait*, 2020; *Trouble Moving or Walking*, n.d.) Festination is common at the beginning of a movement. The patient will walk on their toes and the foreparts of their feet, with their upper bodies leaned forward. Because their center of gravity will be displaced forward with their upper body, the patient will take many little, rapid steps to restore their center of gravity before continuing to larger steps. (Nonnekes, 2018.)

Postural instability and the risk of falling are inextricably related. Falls are prevalent in people with Parkinson's disease, and they can be caused by a variety of circumstances. The failure to maintain balance during dynamic or static motions is known as postural instability. (Appeadu, 2022.) The condition affects both the basal ganglia and the brainstem, which are responsible for movement control and balance. Damage to those two components will worsen postural instability since the patient will be unable to modify their posture quickly enough before falling. When freezing occurs the balance will be challenged, and fall can also happen. (*Falls*, 2020.) Finally, when rigidity affects the trunk, the spine curves and the patient develops a stooped posture (*Learn the Impact and Treatment of Rigidity in Parkinson's Disease*, 2022). The patient will employ a festinating gait with this posture, which increases the danger of falling because the center of gravity will be lost (Gilbert, 2021). The main hurdle involved with raising the danger of falls is that it increases the patient's dread of falling, which is very harmful to the patient. They will limit their activity due to fear, which will have a direct impact on their quality of life. (Rahman et al., 2011.)

2.5.2 Non-motor

PD causes a wide range of motor symptoms that affect not only the patient but also their families. Non-motor symptoms, on the other hand, are frequently overlooked. (*Non-Movement Symptoms*, n.d.) They are common in the disease and can be divided

into four main categories: sleep disorders, neuropsychiatric symptoms, autonomic symptoms, and sensory/other symptoms (Hou & Lai, 2007). There are many distinct examples of symptoms under each of those categories and few of these will be presented but it is important to realize that there are many more, and not every patient will experience them or all of them. (Hou & Lai, 2007; Staff, 2022.)

REM sleep behavior disorder and insomnia are two types of sleep disorders. When a person falls asleep, they will go through several phases before reaching REM sleep, which is a profound form of sleep (*What Are REM and Non-REM Sleep?*, 2005). The body is in muscle atonia throughout that time, which means the muscles are inhibited and unable to produce any movement (Hou & Lai, 2007). It is also during this stage of sleep that the person has the most vivid dreams and dreams the most in general. Muscle atonia is absent during REM sleep in Parkinson's patients, causing them to act in accordance with their dreams. (Diaconu et al., 2021; *REM Sleep Behavior Disorder - Symptoms and Causes*, 2018.) Unfortunately, patients with PD are prone to nightmares or dreams with a lot of actions (Hou & Lai, 2007). The patient enacting their dream will put them and/or their bed partner in danger of injuries. The patient will not be able to realize that they are hurting themselves or their partner since they are in a deep sleep. The injuries vary in severity. They range from hair pulling, tooth chipping to fractures, lacerations, and even subdural hematoma. (Schenck, 2019.)

Insomnia is a sleep condition characterized by difficulties falling or staying asleep (*Insomnia*, 2000). It is the most frequent sleep disturbance, as well as one of the most common nonmotor symptoms of Parkinson's disease. Its prevalence can reach as high as 80 percent. Insomnia can manifest itself in a variety of ways, but frequent awakenings, sleep fragmentation, and both initial and terminal insomnia are looked at as a whole in this thesis. Insomnia can be influenced by a variety of variables. Females with PD are more likely to experience sleeplessness; different drugs can also cause insomnia, as can a variety of other factors. These factors can be motor in nature, such as rigidity, , nonmotor in nature, such as nighttime pain, or psychiatric in nature, such as anxiety or depression. Insomnia can be caused by vivid dreams. The last point is on restless leg syndrome. It is described as a strong need to move your leg, which leads to patients getting out of bed to walk. Insomnia throughout the night causes patients to have an extremely poor sleep pattern, causing them to be sleepy during the day and

take naps, further disrupting their sleep routine. (Loddo et al., 2017; *Restless Legs*, 2019; Wallace et al., 2020.)

Depression, like many other nonmotor symptoms, might manifest years before motor symptoms do. According to the literature, depressive disorder affects between 30 and 50 percent of Parkinson's patients, making it one of the most reported neuropsychiatric symptoms. (Ossowska & Lorenc-Koci, 2013.) Depression is divided into three categories: mild, moderate, or severe (Cherney, 2018). Patients with Parkinson's disease can develop any level at any stage of the disease. It is a challenging symptom to identify because it shares many similarities with other Parkinson's disease symptoms. Clinicians use the DSM-5 diagnostic criteria for major depressive disorder to diagnose depression. (Frenklach, 2016.) This tool has been appraised as conclusive for severe types of depression but less effective for milder types (Starkstein et al., 2008). According to the DSM-5, the patient must have at least five of the following symptoms for two weeks and one of the first two symptoms must be experienced. The symptoms are depressed mood, loss of interest in activities, decreased appetite and/or weight loss, decreased thought processing and movement, exhaustion, feelings of worthlessness, reduced concentration capacity, and persistent thoughts of death or suicide. (Truschel, 2020.) It is difficult to diagnose PD patients with depression. A sizable portion of those symptoms may overlap with motor or nonmotor symptoms, skewing the test results. The developing inability to control movements can lead to a loss of interest in activities. Weight loss, slowed movements, difficulty processing thoughts, and poor attention are all indications of Parkinson's disease. Fatigue can be induced by a sleep disorder. A variety of tests, such as blood tests, medical and psychiatric histories, and medication, can be incorporated to get the best possible diagnosis for depression. (Frenklach, 2016.) Anxiety is another element to consider while looking for depression in people with Parkinson's disease. It can be linked to depression since it shares some symptoms, and it can even be a part of depression. (Marsh, 2013; Wen et al., 2016.)

Anxiety can manifest itself in a variety of ways in patients. Panic episodes, generalized anxiety, and even social avoidance are all possibilities. (*Anxiety*, n.d.) Panic attacks are an abrupt, intense feeling of anxiety that might be emotional or physical in nature. It usually lasts anywhere from a few minutes to an hour. Patients may experience a variety of symptoms during this time, including chest tightness, difficulty breathing,

heart racing, and difficulty concentrating. It is a very tumultuous phase in which the sufferer feels grave danger and panic. (*Anxiety Disorders - Symptoms and Causes*, 2018.) The continuance of generalized anxiety is what distinguishes it from the previous one. It is typically a more persistent feeling, accompanied by recurrent thoughts and concern about everything, even ordinary life. Generalized anxiety, like panic attacks, includes bodily manifestations such as difficulty breathing, excessive sweating, nausea, and an increase in tremors. The last type of anxiety, social avoidance, is even more intricately linked to the disease than the others. It is defined as the avoidance of social events due to a fear of being judged, feeling ashamed, or being anxious about others' negative perceptions of the individual. The sensation normally fades once the patient is no longer in a social environment, which is why they tend to avoid such in the first place. (*Anxiety*, n.d.; *Anxiety Disorders - Symptoms and Causes*, 2018.) Anxiety, like depression, can be difficult to diagnose if the patient does not meet the DSM-4 or DSM-5 criteria for anxiety. According to research, around 13 percent of PD patients with anxiety do not fit the criteria. They are classified as having an anxiety disorder that is not otherwise described, or NOS. (Forbes et al., 2021.) Anxiety is common in people with Parkinson's disease, with rates ranging from 20 to 46 percent in some studies, and as high as 68.42 percent in others. Anxiety and depression can occur together. When a patient has anxiety disorder, there is an extraordinarily strong probability (over 90 percent) that they will also have depressive disorder. If they have been diagnosed with depressive illness, they have an almost 70 percent probability of simultaneously having anxiety condition. In average, the percentage of people who have both disorders ranges from 32 to 76 percent. (Chen & Marsh, 2013; Chuquilín-Arista et al., 2019; Hanna & Cronin-Golomb, 2012.) The on-and-off phase of motor fluctuations is one significant hypothesis for why anxiety is so difficult to identify. The medicine, particularly levodopa, causes motor fluctuation, which has an on-and-off phase. The on phase is the time when the medication is working, the symptoms are under control, and the patient can function normally. The off phase occurs when the drug begins to wear off and the symptoms return, sometimes even more severe than before. With the motor symptoms constantly changing so are the non-motors. When anxiety is related to those stages, patients see an increase in anxiety symptoms as the drug wears off. It might be beneficial to know the patient's treatment plan and when they will receive it while providing therapy so that they can

have the session in the most ideal circumstances. Forbes et al., 2021; *Motor Fluctuations*, n.d.)

The prevalence of dementia ranges between 25 and 30 percent (Safarpour & Willis, 2016). It is usually discovered in more severe Parkinson's disease stages (Barbosa, 2013). It is critical to realize that the progression of dementia is greatly influenced by the duration of the condition (Aarsland et al., 2007). Numerous studies have indicated that the likelihood of developing dementia or other cognitive problems increases with the length of time since the disease's diagnosis. Dementia may start to manifest as soon as six years after the condition is identified. (Safarpour & Willis, 2016.) Dementia is described as a collection of symptoms brought on by a decline in brain function. These symptoms can include difficulty thinking, understanding, speaking coherently, and/or speaking, as well as memory loss and/or movement impairment. Dementia shares many of its components with the disease itself, just like anxiety and depression do. It is a very difficult situation for the patient and its relatives because the more the dementia will progress, the less autonomy the patient will have. They can start losing interest in their hobbies, social activities, their behavior can change drastically, and they can even hallucinate. (*Dementia*, n.d.; NHS website, 2021.)

Autonomic symptoms are so named because they are caused by the disease's effect on the autonomic nervous system. The autonomic nervous system regulates the body's automatic functions like breathing, heart rate, and digestion (*Autonomic Dysfunction*, 2020.) We already noted that Parkinson's disease often develops later in life. Time will begin to have some physical effects on a person even without PD. Among these are constipation or urinary incontinence. Urinary incontinence, which occurs in 15% of PD patients, is regarded as the third most troublesome bladder symptom, behind nocturia and urinary urgency. The three most often reported symptoms, including urine frequency and the latter two, can indicate an overactive bladder. (*Urinary Problems in Parkinson's Disease*, n.d.; Winge et al., 2006.) Parkinson is prone to overactive bladder, or OAB, which has been investigated through urodynamic research. (McDonald et al., 2017).

Sickness is affecting many of the body's involuntary functions. In PD patients, constipation is common and typically develops before the motor symptoms. The first explanation is that it originates from the autonomic nervous system. The digestive tract can slow down because of the disease's disruption of the system, which can also affect how quickly the gut's smooth muscles work. The second reason is that some of the

medications used to treat the disease's various symptoms have several side effects, one of which is constipation. (*Constipation*, n.d.; *Parkinson's Disease and Constipation*, 2002.) Levodopa, which will make up for dopamine deficiencies, and artane, which will help with Parkinson's disease (PD) neural disorders, are two examples of medications (<https://www.vidal.fr/medicaments/laboratoires/sanofi-aventis-france-2172.html>, 2022; <https://www.vidal.fr/medicaments/laboratoires/teva-sante-2871.html>, 2022). The enteric nervous system in the digestive tract may be affected by the disease, which brings us to our decisive point. We are aware that patients with Parkinson's disease (PD) have Lewy bodies in their brains. They discovered that the patients' gut neurons and the dorsal motor nucleus of the vagus, a lower region of the brainstem that regulates gut activity, both contained the same protein clumps. The damage of all those cells who oversee the gut activity will provoke constipation. Many research and hypothesis, known as the Braak theory, have been conducted about the possibility of the disease to start either from the brain or from the gut. (*Constipation & Nausea*, n.d.; Gilbert, 2019.) Patients may also have a variety of symptoms that are directly related to constipation, such as bloating, nausea, or vomiting. Additionally, it makes it more difficult for the body to absorb the medications. Constipation can be relieved by drinking lots of water, eating fiber, and exercising, however PD patients may find it difficult due to additional symptoms like incontinence, trouble chewing, and tremors or bradykinesia. (*Bowel Problems*, 2020.)

Although pain can be categorized in a variety of ways, we will describe Ford's classification because it is the most popular. Pain is classified into four or five types: musculoskeletal, neuropathic, dystonic, central, and akathitic. As with other PD symptoms, it is crucial to keep in mind that not all patients will suffer this particular symptom, and some people may even experience multiple types of pain. There is a higher prevalence of the four types of pain in patients with more advanced PD. (Valkovic et al., 2015.) Musculoskeletal discomfort, which affects the joints and everything that makes them up, including the bones, muscles, ligaments, and tendons, is particularly prevalent. It tends to worsen with age and as the condition progresses. It is a very localized sort of pain that lasts for a very long time. The term "neuropathic pain" refers to a sharp sort of pain that is related to a pinched nerve. It is widespread in the population overall, but the tendency toward poor posture that typically goes along with PD makes it more likely to manifest. Dystonic pain and the medications

have a direct link. Dystonia begins to reappear or intensify when the medication wears off. Although it can affect the entire body, it is more frequent in the extremities. It is an uncontrollable and involuntary muscular contraction similar to a spasm. Because central pain is a sensation brought on by brain dysfunction, it is exceedingly complex. The illness interferes with the body's pain sensitivity and enabling the brain to produce pain even in the absence of injuries. Every region of the body can experience it as stabbing or burning feelings. The sensation can get worse with touch or cold. The management of central pain is quite challenging. The final of the five types of pain is akathisia pain. It is described as a strong sense of restlessness. The patient cannot remain still and is always moving. Although it may not necessarily hurt, the body may nonetheless experience pinching or burning feelings. (Downward, 2017; Friedman, 2017; Gilbert, 2019b; *Pain*, n.d.; *Pain*, 2020.)

2.5.3 Stages and scales

There are many different scales available to evaluate the various Parkinson's symptoms, or even the disease's own progression. The Hoehn and Yahr scale and the Unified Parkinson's Disease Rating Scale are two scales that are frequently utilized. It is crucial to remember that an unknown percentage of neurons have already been destroyed by the time the first motor symptoms show. Although each person is unique and has a unique prognosis for the condition, the stages are meant to establish a general pattern. (Cheng et al., 2010; *Diagnosis - Rating Scales*, 2017.) The Hoehn and Yahr scale, which had five stages when it was first published in 1967 by Margaret Hoehn and Melvin Yahr, now contains two more stages: 1.5 and 2.5. It was developed to evaluate the progression of the illness and the various degrees of disability that result from it. The author made the decision to refrain from discussing the typical symptoms at various phases of the disease because they are highly personal and inaccurate to generalize. In stage one, symptoms will begin to manifest, but they are typically quite mild and only affect one side of the body. Patients and medical professionals frequently overlook the PD diagnosis at this stage. The patient is unaffected by it in his day-to-day activities. The symptoms start to worsen, or new ones may arise during the second stage. Since the disease is still in an early stage, a missed diagnosis or an incorrect one could still occur. During this stage, the symptoms appear on both sides

of the body. There is no balance impairment, and the patient is still capable of carrying out most tasks with minor difficulty. The third stage of the illness is considered the mid-stage. Falls are increasingly more frequent, and balance is beginning to deteriorate. Additionally, the movements of the patients are becoming slower. Stage three is when the patient is still able to function independently, but daily activities are becoming significantly impaired. It is usually quite easy to diagnose the disease at this stage. The fourth stage occurs when the patient's severe symptoms make it impossible for them to live alone. The patient is still able to stand up and walk on their own, but many will require a walker or other assistive device to feel more secure and for assistance. In the fifth and last stage, the patient is unable to stand or walk and must rely on a wheelchair or be bedridden. The patient is no longer capable of managing the everyday responsibilities, so a full-time caretaker is required. (Allarakha, 2021; *Diagnosis - Rating Scales*, 2017; *Rating Scales*, 2017; *Stages of Parkinson's*, n.d. .)

3 PHYSIOTHERAPY INVOLVEMENT

Parkinson's disease is a complex condition; thus, it is normally required for the patient to be cared for by a team of professionals in their respective fields, including a neurologist, geriatrician, specialized nurse, but also a physiotherapy or a speech therapist. The patient will require various professionals depending on their stage and needs. Each member of this team will have a specific responsibility to assist the patient in managing their condition as effectively as possible. The physical therapist will be on hand to preserve and work to enhance the patient's independence and function. The physiotherapist will assist with balance, overall body strength, and body control while also reducing the risk of falling. The physiotherapist's target will solely depend on the patient's condition and its own objectives. (Pedersen et al., 2017; Skelly et al., 2012.) There are many diverse types of treatment options in physiotherapy. Considering the available research and their individual experiences, the physiotherapist will evaluate which therapy approach would be most appropriate. The effectiveness of physical activity in those with Parkinson's disease has long been understood. Exercise is one of the primary methods that a physiotherapist will employ in his or her practice. In

addition to giving exercises during the training session, he or she will also recommend suitable workouts for the patient to do at home. The therapist will also be able to inform the patient of the value of engaging in some physical exercise outside of the physiotherapy sessions. Numerous sports, such as tai chi, dance, or treadmill training, might be highly beneficial for the patient. The physiotherapist can assist the patient in finding beneficial activities for them based on their interests and what is available in the city. Numerous studies have shown that physiotherapy is beneficial for the patient especially with gait, freezing gait, endurance, and speed but also in the general mobility and balance. (Bouça-Machado et al., 2019 ; *Parkinson's - Physiotherapy Management and Interventions*, n.d.; Radder et al., 2020 ; Tomlinson et al., 2013.) The physiotherapist will play a significant role in the initial stages of the disease when the symptoms are just beginning. The physiotherapist's major objectives at this time will be to educate the patient and their family about the condition and its progression. Additionally, the significance of staying physically active will be emphasized. If the patient is not currently participating in various physical activities, the physiotherapist will encourage them to do so. This will allow the patient to stay active in their community. The focus of the training will also be on building endurance, muscle strength, and joint mobility. Depending on the symptoms displayed by the patient, the therapist will be able to assist with their management. The physical therapist will produce and teach various techniques to aid the patient in maintaining as much independence as possible when the symptoms worsen. Adaptations can be developed for everyday tasks like getting out of bed or standing from a chair, but they can also be made with assistive equipment that will help the patient or even the caregiver as the disease progresses. When the condition advances to more advanced stages, the physiotherapist's role will be to assist the patient in maintaining their strength, mobility, balance, and endurance. If issues with the gait begin to emerge, the therapist will teach some visual or auditory cues to help, for example with freezing. It will also be necessary to teach the patient how to fall correctly without injuring himself/herself, as well as how to rise from the ground. It is essential to assist the patient in overcoming their fear of falling in order for them to maintain their independence. The transfers can also be divided into a few simpler steps to prevent the patient from becoming stuck. (Bennett, 2019; *Physiotherapy*, n.d.-b; *Physiotherapy*, n.d.-a; *Physiotherapy Works: Parkinson's*, 2017; Sanderson, 2018.)

The ICF, or international classification of functioning, disability, and health, is a classification system designed to identify and assess a person's functional capacity. Disability and functioning are the two key notions on which the classification is founded. These concepts refer to bodily functions, structures, activities, and participation. It indicates the positive or negative effects of the interplay between a person's health condition(s) and contextual circumstances specific to that person. The six components of the ICF model are: health condition, body functions and structures, activities, participation, environmental factors, and personal factors. Each of the elements is interacting with the others. It enables the patient to be placed at the center and establishes their unique needs and functioning profile, rather than just describing them based on their health. It emphasizes putting greater attention on what the patient can perform at their level and on the positive rather than how their limitations prevent them from acting in a "normal" setting. A health condition includes a short-term or long-term illness, a disorder, a trauma, or an injury. Body functions include the physiological and psychological functions of the human organism. The anatomical components of the body, including organs or limbs, are referred to as body structures. Activities are the different actions and tasks done by an individual. Participation refers to a person's role in life, specifically in society. The term "environment factors" refers to any elements of the outside world that affect a person's functioning, either favorably or unfavorably. Although personal factors are not categorized in the ICF, the user can nevertheless integrate them. It includes everything about the individual, namely their age, gender, and social standing. The patient is the focus of attention, with the many professionals as well as the patient's family, friends, and caretaker revolving around him or her. All those individuals required a means of efficient communication using a common vocabulary. That is what the ICF offers, a common language framework that facilitates communication not just among the many professions but also between the patient and the doctors or other healthcare workers who are around him or her. To the greatest extent feasible, all the terms used are neutral. (*ICF E-Learning Tool_English_20220501*, n.d.; *International Classification of Functioning, Disability and Health (ICF)*, n.d.; *What Is ICF?*, n.d. .) Since the 2003 motion endorsing the ICF model's integration in physiotherapy, its application is becoming increasingly widespread. The physiotherapist and multidisciplinary teams more broadly have benefited from the ICF model and tools when evaluating and setting goals for and with

patients. (Finger et al., 2014; Heerkens et al., 2006; *International Classification of Functioning, Disability and Health (ICF)*, n.d. .)

4 THERAPEUTIC EXERCISE

One of the key competencies in physiotherapy is therapeutic competence, which includes therapeutic exercise. The client's engagement should be supported by the physiotherapist in a way that promotes health. In line with the patient's environment, the professional can assess the patient, develop, and carry out a physiotherapy treatment plan based on evidence. Therapeutic exercise aims to improve, maintain, or prevent the decline in the patient's functioning following a health condition. These therapeutic exercises do not exactly fit the concept of physical activity or exercise, even though they are active and functional. It combines the two but does so within the context of function and rehabilitation. (Glynn & Fiddler, 2009; Hynynen et al., 2018.) Physical activity, according to the World Health Organization, is any movement involving the contraction of skeletal muscles that requires the use of energy (*Physical Activity*, 2020). Exercise is defined as repetitive physical activity that is planned, structured, and done with the goal of conditioning any area of the body (*Exercise*, n.d.). It is crucial as a tool for physical rehabilitation and is used to maintain fitness and promote health. The current guidelines for physical activity apply to all individuals, including those 65 and older as well as those with impairments or long-term illnesses. They should exercise for 150 to 300 minutes at a moderate intensity or 75 to 150 minutes at a high intensity. The patient may also choose to mix the two. It is typically advised to engage in continuous or intermittent 30-minute workouts like jogging, swimming, or brisk walking at least three times a week. It is recommended to perform strength training using weights, a resistance band, or your own body weight at least twice a week for at least 30 minutes on separate days. Strength training should concentrate on major muscle groups and should consist of 10 to 15 repetitions. It is recommended to practice balance, agility, and multitasking at least twice to three times a week; however, it would be advantageous to do so every day. Dynamic balance exercises, dance, and tai chi are some good examples. Stretching should be done daily

for best outcomes, but more than three times a week is generally advised. It can be done before, after, or even without exercising, and it can be dynamic or static. (Parkinson's foundation & American college of sports medicine, n.d.; *Physical Activity*, 2020.) Numerous options are available for therapeutic exercises, such as those for coordination, range of motion, or strength. They will be divided into four groups: flexibility, balance, strength, and endurance. These exercises can also be combined to produce something that is completely tailored to the needs of the patient. The purpose of strength training is to enhance muscle strength. There are three types of it: isotonic, which is a dynamic movement with constant load; isometric, which is a static muscle contraction with no change in the length of the muscle; and isokinetic, which is a movement with varying load but constant velocity. (Bielecki, 2022; Gross Saunders, 2007; *Therapeutic Exercise*, n.d. .) Endurance is described as a method of increasing cardiovascular and musculoskeletal endurance by exercising large muscle groups and sustaining 50 to 60% of the patient's VO₂max for an extended period (Bielecki, 2022; Saag, 2015; *What Is Endurance? Definition, Training and Fitness*, 2022). The capacity of a joint to move through its complete range of motion without pain is referred to as flexibility. The physiotherapist can employ three different types of stretching to increase this flexibility: static stretching, in which the patient holds the position for 30 to 60 seconds; dynamic stretching, in which the patient repeats a slow stretching movement to widen the range of motion; and proprioceptive neuromuscular facilitation, or PNF, which involves alternately contracting and relaxing the muscles surrounding the joint. (Bielecki, 2022; Bushman, 2016; The Stretching InstituteTM, 2021.) Balance refers to a person's ability to keep their center of gravity within their base of support. Balance may be static or dynamic. The capacity to keep the body in a stationary position within the base of support is known as static balance. Dynamic balance is the ability to adjust the center of gravity within the base of support while the body is moving. The proprioceptive system, the vestibular system, and the visual system all contribute to maintaining balance. The physiotherapist can challenge those systems by adding an unstable platform or ask the patient to close their eyes. (*Balance*, n.d.; Maharaj, 2022.)

The word "forced" in forced exercise refers to a faster pace of pedaling than during voluntary activity. The term "forced exercise" can also be seen in more recent studies as "high cadence cycling" or "cycling training." Tandem bikes or motorized bikes can

be used for forced exercise, pushing the patient to maintain a faster pedaling pace like what the other person would do on the tandem bike. Special bikes have been developed to monitor each participant's power output or the patient's output on the motorized bicycle.

Participants in studies are typically trained three times for an hour each. Including a 10-minute warm-up, a 40-minute main workout, and a 10-minute cool-down. Rest is permitted during the designated 40 minutes. The pedaling speed must be maintained between 80 and 90 RPMs during the main set. It is possible to follow the recommendations for aerobic exercise by engaging in this type of activity three times per week. (Alberts et al., 2011; Ridgel et al., 2009; Theracycle, 2010, 2019.)

5 HEALTH PROMOTION

Although it is not typically seen as a full component of rehabilitation, it is nonetheless one of a physiotherapist's fundamental competencies. Successful physical therapy practice requires education of the patients and their families. However, in addition to providing knowledge, physiotherapists have a significant role to play in the promotion of health. (Hynynen et al., 2018) The objectives of health promotion are to preserve and support physical and mental health, work, and functional capacity, prevent different diseases and health issues, lessen health disparities in the population, and promote improved public health. This is directed at both people and more general entities like the community, the population, and the living environment. (Ministry of Social Affairs and Health, Finland, 2010.) There are many different activities that fall under the category of health promotion. Prevention is a crucial one for physiotherapists. Prevention is classified into three levels: primary, secondary, and tertiary. The goal of primary prevention is to stop an illness or injury before it starts. This can be achieved by outlawing dangerous products, establishing healthy practices, educating people about healthy lifestyle choices like regular exercise and a balanced diet, or by encouraging the immunization of the general public against infectious diseases. The goal of secondary prevention is to lessen the consequences of an illness or injury that has already taken place. It is done by conducting routine tests to identify

diseases as soon as feasible and treating them to stop, slow down, or at least temporarily halt their progression. It will also put a strong emphasis on preventing recurrence or reinjury by developing programs to assist individuals in enhancing their health. The goal of tertiary prevention is to mitigate the consequences of a chronic illness or injury. By implementing management, rehabilitation, or vocational programs, it seeks to increase the patient's life quality, expectancy, and functional ability, if possible. For some diseases, a combination of the three levels may be required to develop an efficient protection and prevention strategy. (Primary, Secondary and Tertiary Prevention, 2015.) Most of the Parkinson's disease prevention is done at the tertiary level. When the symptoms are identified early and the treatment is started right away, it can occasionally be done on the secondary level, but primary and secondary preventions have not yet grown as much. (Earhart et al., 2012.)

6 AIM, PURPOSE, AND RESEARCH QUESTION

The aim of this thesis is to provide a deeper understanding and knowledge of that pathology and of the integration of forced exercise in the treatment of Parkinson's symptoms. Its objective is to conduct a narrative literature review about the effectiveness of forced exercise on Parkinson's disease symptoms.

The research question is as follows:

- What is the evidence regarding the effectiveness of forced exercise on Parkinson's symptoms?

7 METHODS

7.1 Narrative literature review

This thesis is structured as a narrative literature review. One of the most prevalent types of literature reviews is a narrative or traditional literature review. It provides a summary of the body of knowledge based on a broad question. The typical structure for this kind of review will be to summarize and evaluate the research, draw conclusions about the subject from the literature, and then point out any gaps or inconsistencies in the material. The methodology process is far less defined in a narrative literature review than it is in a systematic literature review. A literature review will often involve a procedure in which the material is assessed and selected depending on criteria. It is challenging for the reader to determine the risk of bias in a narrative literature review because a transparent data collection process is not required. The incorporation of a systematic method is, nevertheless, highly advised at the academic degree level. There are four major categories of narrative literature. The standard type of literature, the general literature review, summarizes the most essential elements of the current knowledge on a certain subject. Theoretical reviews of the literature look at how theories are influencing the research. In the methodological literature the approach utilized in each of the included studies is reviewed, along with each method's advantages and disadvantages. Historical literature examines literature by placing it in a historical perspective. (Aveyard, 2010; Baker, 2016; Grant & Booth, 2009; Onwuegbuzie & Frels, 2016.)

7.2 Data collection process

Numerous criteria were used to gather the data for this thesis in order to address the research question. To include data from the most recent research, the publications gathered must be published or revised between 2012 and 2022. The papers had to be peer-reviewed, written in English, and have access to the entire free text. Only human subjects should be used in the testing. The research was to include information about Parkinson's disease, forced exercise, and the impact of the aforementioned on the

disease. Forced exercise is sometimes referred to by other names, such as high cadence cycling or cycle training. Therefore, it was critical that they adhered to the concept of forced exercise provided previously in this thesis. The inclusion and exclusions criteria can be found in TABLE 1.

TABLE 1. Criteria of inclusion and exclusion

Criteria of inclusion	Criteria of exclusion
Articles published between 2012 and 2022	Articles published before 2012
Written in English	Written in other languages
Full free text available	Full free text not available
Peer reviewed	Not peer reviewed
The articles include information about Parkinson's disease, forced exercise and its effects on the disease	The articles were not relevant to the research question
	Tests on animals

Finding a research question is an usual next step after the subject has been selected and background research has been completed. A well-defined research question is essential for the next phases and will make the remainder of the process go more smoothly. Key concepts will be determined based on the research topic and entered as keywords in the databases. The keywords must be thoroughly considered to provide a more effective study. In this study, the search terms "Parkinson's disease," "forced exercise," and "cycli*" were utilized. (Ferrari, 2015.)

To maximize the relevance of the many articles that may be retrieved, two separate databases: Finna and PubMed (Medline) have been used for this narrative literature review. These databases were chosen because they provide relevant material for medical research. The initial keyword search on both databases produced hundreds of hits. Applying the following criteria resulted in the first part of the exclusion: written in English, published between 2012 and 2022, complete free text accessible, peer-reviewed, and without animal testing. Following this stage, the total on Finna and PubMed was 35 and 10, respectively. The duplicate articles were eliminated, bringing the total down to 43. The second screening involved reading each article's abstract. Similar to the first screening stage, publications that contained material from the

abstract that did not directly address the issue were eliminated. A total of 16 articles have been chosen based on the abstract. The 16 papers were carefully reviewed and evaluated to determine their applicability in the last phase, and five articles were selected to be included in this narrative literature review. Since none of the publications found in PubMed met the requirements or were pertinent to this thesis, they were all disregarded throughout the process. However, one more article from PubMed has been added to this thesis by manual research. The entire inclusion process is reviewed in FIGURE 1. The main information of the six final articles included in this narrative literature review can be found in TABLE 2.

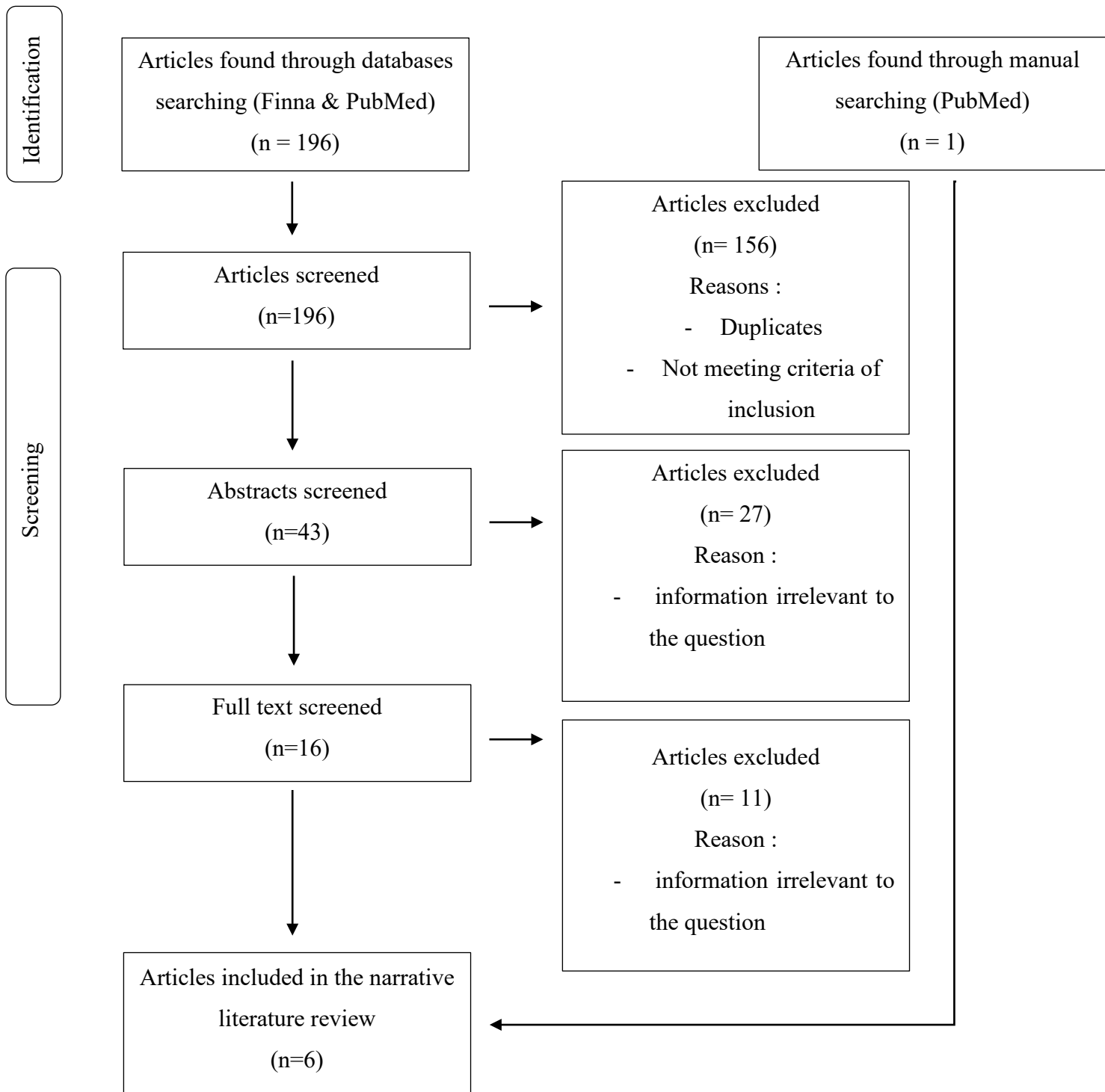


FIGURE 1. Inclusion process based on the PRISMA 2020 flow diagram

TABLE 2. Summary of the articles

Authors and year of publication	Title of the article	Study objectives	Main results
Angela L. Ridgel, Robert S. Phillips, Benjamin L. Walter, Fred M. Discenzo and Kenneth A. Loparo (2015)	Dynamic high-cadence cycling improves motor symptoms in Parkinson's disease	To examine if high cadence dynamic cycling promotes improvements in motor function	Significant improvement of the motor function following three sessions of forced exercise
Angela L. Ridgel and Dana L. Ault (2019)	High-Cadence Cycling Promotes Sustained Improvement in Bradykinesia, Rigidity, and Mobility in Individuals with Mild-Moderate Parkinson's Disease	To assess if six bouts of high-cadence cycling improves motor function and mobility in individuals with PD	Improvement of motor functions and mobility following six sessions of forced exercise
Abu Qutubuddin, Timothy Reis, Raed Alramadhani, David X. Cifu, Alan Towne, and William Carne (2013)	Parkinson's Disease and Forced Exercise: A Preliminary Study	To ascertain any significant effect of forced exercise using a motorized stationary bicycle when compared to controls on Parkinson's disease symptoms	No difference was noted between the control group and the FE group, but improvements of the motor functions were seen within the FE group following 16 sessions of forced exercise

<p>Sara A. Harper, Bryan T. Dowdell, Jin Hyun Kim, Brandon S. Pollock and Angela L. Ridgel (2019)</p>	<p>Non-Motor Symptoms after One Week of High Cadence Cycling in Parkinson's Disease</p>	<p>To investigate if high cadence cycling altered non- motor cognition and depression symptoms in individuals with Parkinson's disease</p>	<p>No improvements of cognition or depression, but improvement of the emotional recognition following 3 sessions of forced exercise</p>
<p>Alexandra Nadeau, Ovidiu Lungu, Arnaud Boré, Réjean Plamondon, Catherine Duchesne, Marie- Ève Robillard, Florian Bobeuf, Anne-Louise Lafontaine, Freja Gheysen, Louis Bherer and Julien Doyon (2018)</p>	<p>A 12-Week Cycling Training Regimen Improves Upper Limb Functions in People With Parkinson's Disease</p>	<p>To assess the effects of aerobic exercise training (AET) on general upper limb functions in sedentary people with PD and healthy adults</p>	<p>Significant improvement of the upper limb motor functions following 12 weeks (3 times per week) of forced exercise</p>
<p>Ellen L McGough, Cynthia A Robinson, Mark D Nelson, Raymond Houle, Gabriell Fraser, Leslie Handley, Emilie R Jones, Dagmar Amtmann, Valerie E Kelly (2016)</p>	<p>A Tandem Cycling Program: Feasibility and Physical Performance Outcomes in People With Parkinson Disease</p>	<p>To examine the feasibility and physical performance outcomes of a community-based indoor tandem cycling program</p>	<p>Significant improvement of the motor functions especially gait, balance and mobility following 10 weeks (3 times per week) of forced exercise</p>

7.3 Thematic analysis

One sort of analysis that is frequently used with qualitative research is thematic analysis or synthesis. There are three steps to it. The first one entails line-by-line coding of the crucial data from each study. This enables an assessment of the key findings free from the influence of the research topic. The second phase entails organizing the previously completed codes into more comprehensive categories, which produce the overall meaning of all the codes contained. It is crucial to return to the research topic for the last phase and establish final primary categories based on the previous step's categories. Given that it is mostly focused on the author's point of view, this section is far more likely to have biases. In order to make the results of the thematic analysis more understandable for the reader, they are typically presented as tabulations. (Paré & Kitsiou, 2017; Thomas & Harden, 2008; Systematic Reviews, 2009.) The method previously outlined was used for this thesis, and the outcomes are shown in TABLE 3.

TABLE 3. Categories based on thematic analysis

Subcategories	Secondary categories	Primary categories
Rigidity	United PD Rating Scale -III (motor control part)	Motor symptoms
Tremor at rest		
Postural tremor		
Finger taps		
Hand movement		
Rapid alternating movement of hand		
Bradykinesia		
Gait		
Dyskinesia		
Time up and go	Mobility	
Cognitive inhibition		
Gait		

Motor sequence learning	Procedural learning	
Kinematic properties	Fast simple reaction time task (FSRTT)	
Balance	Berg balance test	
Lower extremity functions	Five-times-sit-to-stand test (FTSTS)	
Risk of falls		
BDI-II	Depression	Non motor symptoms
MoCA	Cognition	
Attention/concentration		
Executive functions		
Emotional recognition		

8 RESULTS

The author's initial query focused on whether forced exercise was effective, and if so, which symptoms were alleviated. Following the thematic analysis, it was determined that the studies presented in this thesis covered motor symptoms and non-motor symptoms. All the publications used specific tests to track changes in either motor or non-motor functions. These tests served as the foundation for our discussion regarding the effectiveness of forced exercise on Parkinson's disease symptoms.

8.1 Motor symptoms

Five of the six publications evaluated the impact of forced exercise on motor symptoms. The United PD Rating Scale was the most often utilized test. Different tests were conducted to evaluate various motor symptoms, and they will all be discussed in a subsequent section.

8.1.1 UPDRS-III

The united Parkinson disease rating scale was utilized in four articles, and only the third part of the test corresponding to the motor assessment was used in all of them. This section asks a variety of questions regarding the symptoms of the motor system, such as tremor, rigidity, or hand movements. In a study by Ridgel & Ault (2019), it was discovered that while there was no improvement in the control group's UPDRS-III score, there was in the forced exercise group. Each session's progress was noticeable, as well as 48 hours after the final cycling session, which was the post-testing period. According to Qutubuddin et al. (2013), improvements in the forced exercise group were observed only between the baseline and four months post-testing. It is the only study in that thesis that records changes not immediately following testing but several months later. In the study by Ridgel et al. (2015), improvements were shown throughout both the dynamic and static cycling sessions, but they were noticeably greater for the dynamic ones (forced exercise). Only three sessions were conducted for this investigation. The study by Nadeau et al. (2018) does not show progress. After three months of forced exercise, their study found no improvement between the pretesting and the post-testing. (Nadeau et al., 2018.)

Some of the research looked at which elements of the UPDRS-III have improved. Improvements were noted for rigidity, finger tapping, hand movements, and pronation/supination in the study by Ridgel & Ault (2019). The UPDRS-III already includes bradykinesia, but this study focused further on it, particularly for the upper limb by employing a device to quantify movement quality. They demonstrated a 23% increase in the quick alternating movement speed and a 36% increase in movement amplitude. The study by Ridgel et al. (2015) produced similar findings; it demonstrated improvements in rigidity in the lower as well as in the upper extremities. Finger tapping was a separate test in the Qutubuddin et al. (2013) study, but it is also a component of the UPDRS-III motor test. An improvement in this test is visible within the group according to the results, which are presented in the research in a table.

8.1.2 Mobility and gait

In three research, the mobility and bradykinesia while walking were evaluated using the time up and go test. Similar findings about the impact of forced exercise on the time up and go test and so on the mobility and bradykinesia are shown in all the articles. In the forced exercise group known as the dynamic group, the timing of the test improved by 16.5% according to the study by Ridgel et al. (2015), but only by 8% in the static group. In the study by Ridgel & Ault (2019), the forced exercise group showed an improvement of 13% between the pretesting and the post-testing, while interestingly the control group showed a 3% decline in performance. Finally, only one group—the exercising group—constituted the research in the study by McGough et al. (2016). The mean pre-testing and mean post-testing showed improvement, which is similar to what was discovered in the two previous studies that was mentioned.

These three studies help us comprehend the effects of a total of three, six and 30 (3 times per week for 10 weeks) sessions of forced exercise on mobility and on bradykinesia during walking.

Kinesia ONE was utilized in the study by Ridgel and Ault (2019) to measure participants' bradykinesia as well as their gait. The device was attached to the shoe and used to measure the rotation time, angular velocity, and coefficient of variation of time during leg swing while walking. According to this study, gait has improved by 60%. In the research by McGough et al. (2016), a new apparatus was employed, but comparable findings were made. Gait speed, cadence, and stride were measured using the GAITRite Walkway System at both a normal and rapid pace. The cadence and speed of the standard pace both showed improvements, while the fast tempo exhibited no noticeable effects. (McGough et al., 2016.)

8.1.3 Risk of falls

The Berg balance scale (BBS) and the five-time sit-to-stand (FTSTS) tests were employed in the research to evaluate the risk of falls. Two studies that exhibit different results both use the Berg Balance test. In the study by Qutubuddin et al. (2013), the results for the BBS between the control group and the forced exercise group as well as

within the exercising group at the 8-week checkpoint and at the end of the training program were nonsignificant. In the study by McGough et al. (2016), a mean increase of 1.5 points in the BBS performance was observed between the pretesting (one week prior to the start of the trial) and the post testing after 10 weeks. In addition to the BBS, the FTSTS test was employed in this study to evaluate the risk of falls and the functioning of the lower limbs. This test revealed a notable reduction in the performance time. The short physical performance battery was an additional element that was carried out in this investigation. It comprises of three distinct tasks: a timed 5-times-sit-to-stand test, a static standing balance test, and a four-meter comfortable walking speed test. This exam is used to evaluate the lower extremities' functionality. The first two tasks were previously covered. Although there are not specific results for each test task, the study indicates that the results for the test have improved. (McGough et al., 2016.)

8.2 Non motor symptoms

In the studies that were included in this thesis two were reviewing non-motor symptoms. The symptoms reviewed were cognition and depression. (Harper et al., 2019; Nadeau et al., 2018.)

8.2.1 Cognition

Harper et al.'s (2019) study separated cognition into three smaller categories: executive functions, emotional recognition, and attention and concentration. The individuals' overall cognitive skills were also assessed using the Montreal Cognitive Assessment (MoCA). Executive functions, the MoCA, and the category of attention and concentration all yielded no results. Over time, significant results were observed for the emotional recognition, pointing to the improvement of this form of cognition with forced exercise. The Stroop test and the trail-making test were used in research by Nadeau et al. (2018) to measure the flexibility and inhibition of cognition. The trail making test revealed no progress. Stroop test results revealed an improvement in cognitive inhibition.

8.2.2 Depression

Both the study by Nadeau et al. and the one by Harper et al. (2019) included assessments of depression. The Beck depression inventory (BDI) was utilized in the study by Nadeau et al. (2018), whereas the Beck depression inventory II (BDI-II) was employed in the study by Harper et al. Because there was a significant difference in the levels of depression between the groups, Nadeau et al. (2018) used this as a covariable in their statistical analysis. In the study by Harper et al. (2019), depression was tested before and after exercise training, and neither the group as a whole nor when comparing the exercising group to the control group showed any signs of improvement.

8.3 Engagement

Even though participation was not one of the articles' goals or objectives, there is still some significant information about patient involvement in the process. One article specifically evaluated the feasibility and patient participation. The reasons why some patients were excluded from the final analysis in the studies by Nadeau et al. (2018), Ridgel et al. (2015), and Ridgel & Ault (2019) varied, but they were all related to personal or medical issues, injuries, or the patients' failure to disclose certain medical factors that were influencing the results during the interview. Depending on the aforementioned factors, patients from both the control or non-forced exercise and the forced exercise groups were being removed. Harper et al. (2019) state that two participants were excluded because they did not participate in the exercise program, but no mention is made of whether they were from the control or cycling groups. Three participants were initially withdrawn from the study by Qutubuddin et al. (2013) because they were unable to obtain a medical clearance for the test, and six other participants were removed due to illness or missing exercise sessions. Which group these participants belonged to is unknown. Finally, four participants were dropped because they did not attend the four-month follow-up. One of those four participants was in the cycling group, while the other three were in the control group.

McGough et al. (2016) analyzed participant involvement as a research goal in their investigations, which went beyond just looking at the data. Three participants in their

program were left out of the final calculations. One was absent due to medical reasons, another due to an injury, and the third did not engage in follow-up. The program was completed by all participants from start to finish. The ten-week program has a 96% attendance rate indicating a high level of involvement with this program. Additionally, throughout the 10 weeks of the program, 95% of participants attained their intended cadence and 87% reached and maintained their target heart rate range. In this research, tandem bikes with a healthy pedaling partner were utilized. In addition to encouraging the PD patient throughout the session, the partner was giving assistance by pedaling. Before and after the session, the teammates had to get together to assess their blood pressure and heart rates, complete a readiness to exercise checklist, and set weekly team goals. The ongoing support of the partner is a key aspect in PD patients' engagement and attainment of adequate exercise intensities.

9 DISCUSSION

All the studies (Harper et al., 2019; McGough et al., 2016; Nadeau et al., 2018; Qutubuddin et al., 2013; Ridgel et al., 2015; Ridgel & Ault, 2019) came to the same conclusion: the motor symptoms were improved. The author chose to group the symptoms with a test in consideration of the outcomes and thematic analysis. These tests are ones that physiotherapists utilize since they are relevant to evaluating the symptoms and offering a trustworthy reference for future reevaluation. Finding tools that are accurate but can also be trusted to analyze changes over time is essential for physiotherapists. The author observed that using those tests made the discussion of the results more meaningful since they were all based on the same tool and the possible risk of bias was decreased.

The research made clear the procedure for choosing participants, the protocol, and the aims and objectives. The results were obtained through the use of valid and reliable tests. When doing the research and conducting the follow-up, the same amount of time was given to each group. The number of participants who did not complete the entire program was disclosed, along with the explanations for their absence. These details

provide further protection against bias risk and ensure that the research's findings, and obviously this thesis, are reliable.

Finding conclusive answers to the study topic was made simpler because the same test was used in all the experiments. With the use of this thesis, it has been demonstrated that using forced exercise benefited mobility, gait, fall risk, and the motor systems of both the upper and lower limbs. Depending on the individual, the severity of the condition, their age, their gender, and several other unique factors, the outcomes may vary slightly. It is crucial to keep in mind that those techniques are not universal. Depending on the participants' physical condition and perceived level of exertion, some research adjusted for them. Although there is a chance that the results may be biased as a result, the author of this thesis saw the adjustments as a great approach to demonstrate that results could still be obtained even when the protocol was not strictly followed. By tailoring the exercise for them, it would be possible to make forced exercise accessible to a larger range of Parkinson patients and encourage them to engage in regular forced exercise in the future.

In this thesis, the findings on the non-motor symptoms appear to be inconclusive. The different articles that were evaluating those symptoms failed to show any improvement with forced exercise. However, discussion can be brought to the relevance of those results. Only two studies evaluated the non-motor symptoms and the symptoms that were chosen were cognition and depression. It is quite restricted and might not represent the full impact of forced exercise on non-motor symptoms. In addition, the study by Nadeau et al. (2018) opted to add depression as a covariable because there was too much disparity between the two groups. This difference was easily expected since PD patients are at higher risk of depression. As a result, there will be one less study analyzing this symptom, leading to this thesis's conclusion being dependent solely on Harper et al.'s (2019) research.

All the studies had extremely high levels of engagement, and most of the patients showed up for every session and achieved their cadence and heart rate objectives. Attendance and successful outcomes are linked in a virtuous circle. Participants who frequently attend the sessions may experience positive outcomes, which motivates them to attend more classes. Almost all of the studies' sessions took place in a very

research-oriented setting. The study by McGough et al., however, was one that was very instructive on the participants' participation and, consequently, the possible implementation in the physiotherapist's practice. Since therapeutic exercise is a crucial part of a physiotherapist's job, the author first considered the advantages of implementing it with patients in a private office or a more established setting. The patient could benefit from it, as evidenced by the prior results. But the promotion of health was something that only started to emerge later and with the help of this research. It is one of a physiotherapist's responsibilities both to the community at large and to their workplace. Physiotherapists implementing this type of program for their patient or in the community in general could help Parkinson's disease patients to alleviate some of their symptoms and by creating a program with healthy people, raise awareness to the disease, include the patients more in the community and promote health for the patients but also for the healthy partners.

The entire thesis-writing process was challenging, and there were numerous difficulties. However, the author gained some crucial knowledge for her career as a physiotherapist and as a person in general. One of the important ideas was standing up for the topic chosen and believing in it because the author was genuinely passionate about it. Sometimes people will question our choices, but it is crucial to be able to defend them by stating why we believed they were the proper course to take. It was challenging for the author to understand how to find reliable, pertinent scientific documentation, but it will be crucial to stay updated on old and new knowledge because it will form the foundation of her work.

The first factor that contributes to this thesis' limitations is the inclusion of exclusively free full publications. Using this criterion did result in the removal of some papers that would have otherwise satisfied the research standards and the research question. The articles that were eliminated based on this criterion might have provided additional knowledge to this thesis. The second restriction that this thesis encounters is that, because it was not a systematic assessment of the literature, the risk of bias is less addressed. Despite the author's best efforts to pay close attention to it, a precise evaluation of the risk of bias has not been undertaken, which consequently places a restriction on the reliability of this thesis.

10 CONCLUSION

The majority of research discovered a beneficial effect of forced exercise on Parkinson's disease motor symptoms. The findings for the non-motor symptoms were inconclusive, and no discernible improvement was observed. Improvements in the motor symptoms can be observed, and the patients appear eager to engage in forced exercise sessions.

REFERENCES

- Aarsland, D., Kvaløy, J., Andersen, K., Larsen, J., Tang, M., Lolk, A., Kragh-Sørensen, P., & Marder, K. (2007). The effect of age of onset of PD on risk of dementia. *Journal of Neurology*, 254(1), 38–45. <https://doi.org/10.1007/s00415-006-0234-8>
- Agim, Z. S., & Cannon, J. R. (2015). Dietary Factors in the Etiology of Parkinson's Disease. *BioMed Research International*, 2015, 1–16. <https://doi.org/10.1155/2015/672838>
- Alberts, J. L., Linder, S. M., Penko, A. L., Lowe, M. J., & Phillips, M. (2011). It Is Not About the Bike, It Is About the Pedalling. *Exercise and Sport Sciences Reviews*, 39(4), 177–186. <https://doi.org/10.1097/jes.0b013e31822cc71a>
- Allarakha, S. (2021, September 30). *What Are the 5 Stages of Parkinson's Disease? Symptoms*. MedicineNet. Retrieved August 3, 2022, from https://www.medicinenet.com/what_are_the_5_stages_of_parkinsons_disease/article.htm
- Anxiety disorders - Symptoms and causes*. (2018, May 4). Mayo Clinic. Retrieved June 6, 2022, from <https://www.mayoclinic.org/diseases-conditions/anxiety/symptoms-causes/syc-20350961>
- Anxiety*. (n.d.). Parkinson's Foundation. Retrieved June 6, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Symptoms/Non-Movement-Symptoms/Anxiety>
- Appeadu, M. (2022, February 10). Postural Instability. Statpearls. Retrieved April 30, 2022, from <https://www.statpearls.com/ArticleLibrary/viewarticle/27572>
- ArmandoHasudungan. (2016, March 18). *Parkinson's Disease (Shaking Palsy) - Clinical Presentation and Pathophysiology* [Video]. YouTube. https://www.youtube.com/watch?v=Hu5KVfFnrh0&ab_channel=ArmandoHasudungan
- Autonomic dysfunction*. (2020, January). European Parkinson's Disease Association. Retrieved July 9, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/non-motor-symptoms/autonomic-dysfunction/>
- Aveyard, H. (2010). *Doing A Literature Review In Health And Social Care : A Practical Guide* (2nd ed.). McGraw-Hill Education.
- Bailey, M., Anderson, S., & Hall, D. A. (2020). Parkinson's Disease in African Americans: A Review of the Current Literature. *Journal of Parkinson's Disease*, 10(3), 831–841. <https://doi.org/10.3233/jpd-191823>
- Baker, J. D. (2016). The Purpose, Process, and Methods of Writing a Literature Review. *AORN Journal*, 103(3), 265–269. <https://doi.org/10.1016/j.aorn.2016.01.016>

Balance. (n.d.). Physiopedia. Retrieved August 15, 2022, from <https://www.physio-pedia.com/Balance>

Balestrino, R., & Schapira, A. (2019). Parkinson disease. *European Journal of Neurology*, 27(1). <https://doi.org/10.1111/ene.14108>

Ball, N. (2019). *Parkinson's Disease and the Environment*. Frontiers. Retrieved February 5, 2022, from <https://www.frontiersin.org/articles/10.3389/fneur.2019.00218/full>

Barbosa, E. R. (2013). Non-motor symptoms in Parkinson's disease. *Arquivos de Neuro-Psiquiatria*, 71(4), 203–204. <https://doi.org/10.1590/0004-282x20130001>

Ben-Joseph, A., Marshall, C. R., Lees, A. J., & Noyce, A. J. (2020). Ethnic Variation in the Manifestation of Parkinson's Disease: A Narrative Review. *Journal of Parkinson's Disease*, 10(1), 31–45. <https://doi.org/10.3233/jpd-191763>

Bennett, C. B. (2019, February 27). *Physiotherapy for Parkinson's Disease*. News-Medical.Net. Retrieved August 11, 2022, from <https://www.news-medical.net/health/Physiotherapy-for-Parkinsons-Disease.aspx>

Berardelli, A., Wenning, G. K., Antonini, A., Berg, D., Bloem, B. R., Bonifati, V., Brooks, D., Burn, D. J., Colosimo, C., Fanciulli, A., Ferreira, J., Gasser, T., Grandas, F., Kanovsky, P., Kostic, V., Kulisevsky, J., Oertel, W., Poewe, W., Reese, J. P., . . . Vidailhet, M. (2012). EFNS/MDS-ES recommendations for the diagnosis of Parkinson's disease. *European Journal of Neurology*, 20(1), 16–34. <https://doi.org/10.1111/ene.12022>

Bielecki, J. E. (2022, July 4). *Therapeutic Exercise*. Statpearls. Retrieved August 15, 2022, from <https://www.statpearls.com/ArticleLibrary/viewarticle/30043>

Borghammer, P., & van den Berge, N. (2019). Brain-First versus Gut-First Parkinson's Disease: A Hypothesis. *Journal of Parkinson's Disease*, 9(s2), S281–S295. <https://doi.org/10.3233/jpd-191721>

Bowel problems. (2020, January). European Parkinson's Disease Association. Retrieved July 9, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/non-motor-symptoms/bowel-problems/>

Bradykinesia (Slowness of Movement). (n.d.). Parkinson's Foundation. Retrieved February 27, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Symptoms/Movement-Symptoms/Bradykinesia-Slowness-of-Movement>

Bradykinesia. (2020, January). European Parkinson's Disease Association. Retrieved February 27, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/motor-symptoms/bradykinesia/>

Bushman, B. A. (2016). Flexibility Exercises and Performance. *ACSM'S Health & Fitness Journal*, 20(5), 5–9. <https://doi.org/10.1249/fit.0000000000000226>

Caddick, A. (2020, July 14). *The role of physiotherapy for Parkinson's*. Open Access Government. Retrieved October 25, 2021, from <https://www.openaccessgovernment.org/role-physiotherapy-parkinsons/33261/>

Cassella, C. (n.d.). *Brain Imaging Study Suggests Parkinson's Might Actually Be Two Diseases in One*. ScienceAlert. Retrieved February 25, 2022, from https://www.sciencealert.com/brain-imaging-study-suggests-parkinson-s-might-actually-be-two-diseases-in-one?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+sciencealert-latestnews+%28ScienceAlert-Latest%29

Causes. (n.d.). Parkinson's Foundation. Retrieved February 4, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Causes>

Chen, C. C., Chen, T. F., Hwang, Y. C., Wen, Y. R., Chiu, Y. H., Wu, C. Y., Chen, R. C., Tai, J. J., Chen, T. H. H., & Liou, H. H. (2009). Different Prevalence Rates of Parkinson's Disease in Urban and Rural Areas: A Population-Based Study in Taiwan. *Neuroepidemiology*, 33(4), 350–357. <https://doi.org/10.1159/000254572>

Chen, J. J., & Marsh, L. (2013). Anxiety in Parkinson's disease: identification and management. *Therapeutic Advances in Neurological Disorders*, 7(1), 52–59. <https://doi.org/10.1177/1756285613495723>

Chen, W., Hopfner, F., Becktepe, J. S., & Deuschl, G. (2017). Rest tremor revisited: Parkinson's disease and other disorders. *Translational Neurodegeneration*, 6(1). <https://doi.org/10.1186/s40035-017-0086-4>

Cheng, H. C., Ulane, C. M., & Burke, R. E. (2010). Clinical progression in Parkinson disease and the neurobiology of axons. *Annals of Neurology*, 67(6), 715–725. <https://doi.org/10.1002/ana.21995>

Cherney, K. (2018, August 22). *Signs and Symptoms of Mild, Moderate, and Severe Depression*. Healthline. Retrieved June 5, 2022, from <https://www.healthline.com/health/depression/mild-depression>

Chuquilín-Arista, F., Álvarez-Avellón, T., & Menéndez-González, M. (2019). Prevalence of Depression and Anxiety in Parkinson Disease and Impact on Quality of Life: A Community-Based Study in Spain. *Journal of Geriatric Psychiatry and Neurology*, 33(4), 207–213. <https://doi.org/10.1177/0891988719874130>

Constipation. (n.d.). The Michael J. Fox Foundation for Parkinson's Research | Parkinson's Disease. Retrieved July 9, 2022, from <https://www.michaeljfox.org/news/constipation>

Costello, S., Cockburn, M., Bronstein, J., Zhang, X., & Ritz, B. (2009). Parkinson's Disease and Residential Exposure to Maneb and Paraquat From Agricultural Applications in the Central Valley of California. *American Journal of Epidemiology*, 169(8), 919–926. <https://doi.org/10.1093/aje/kwp006>

Cristol, H. (2019, June 19). *What Is Dopamine?* WebMD. Retrieved September 3, 2022, from <https://www.webmd.com/mental-health/what-is-dopamine>

de Miranda, B. R. (2017). *CHAPTER 1 Etiology and Pathogenesis of Parkinson's Disease (RSC Publishing)* DOI:10.1039/9781782622888-00001. Pubs.Rsc.Org. Retrieved February 4, 2022, from <https://pubs.rsc.org/en/content/chapterhtml/2017/bk9781782621881-00001?isbn=978-1-78262-188-1&sercode=bk>

Dementia. (n.d.). Parkinson's Foundation. Retrieved June 22, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Symptoms/Non-Movement-Symptoms/Dementia>

Diaconu, T., Falup-Pecurariu, O., Țînt, D., & Falup-Pecurariu, C. (2021). REM sleep behaviour disorder in Parkinson's disease (Review). *Experimental and Therapeutic Medicine*, 22(2). <https://doi.org/10.3892/etm.2021.10244>

Diagnosis - Rating Scales. (2017, March 8). Parkinsonsdisease.Net. Retrieved August 3, 2022, from <https://parkinsonsdisease.net/diagnosis/rating-scales-staging>

Direct and Indirect Pathways of the Basal Ganglia. (2022). BioRender. <https://app.biorender.com/biorender-templates/t-5f7f90a71892ae00ac869473-direct-and-indirect-pathways-of-the-basal-ganglia>

Direct pathway. (2020, October 20). <https://nba.uth.tmc.edu/>. <https://nba.uth.tmc.edu/neuroscience/s3/chapter04.html>

Dizon, M. (2021, October 27). *Parkinson's vs. Parkinsonism.* Davis Phinney Foundation. Retrieved February 13, 2022, from <https://davisphinneyfoundation.org/parkinsons-vs-parkinsonism/>

Dorsey, R. E. (2018, January 1). *The Emerging Evidence of the Parkinson Pandemic - IOS Press.* IOS Press. Retrieved February 4, 2022, from <https://content.iospress.com/articles/journal-of-parkinsons-disease/jpd181474>

Downward, E. (2017, March). Symptoms - Pain. Parkinsonsdisease.Net. Retrieved July 23, 2022, from <https://parkinsonsdisease.net/symptoms/pain>

Driver, J. A., Logroschino, G., Gaziano, J. M., & Kurth, T. (2009). Incidence and remaining lifetime risk of Parkinson disease in advanced age. *Neurology*, 72(5), 432–438. <https://doi.org/10.1212/01.wnl.0000341769.50075.bb>

Earhart, G. M., Ellis, T., Nieuwboer, A., & Dibble, L. E. (2012). Rehabilitation and Parkinson's Disease. *Parkinson's Disease*, 2012, 1–3. <https://doi.org/10.1155/2012/371406>

Eeden, D. S. V. K., Tanner, C. M., Bernstein, A. L., Fross, R. D., Leimpeter, A., Bloch, D. A., & Nelson, L. M. (2003, June 1). *Incidence of Parkinson's Disease: Variation by Age, Gender, and Race/Ethnicity.* OUP Academic. Retrieved January 19, 2022, from <https://academic.oup.com/aje/article/157/11/1015/151509#1251156>

Environmental Factors. (n.d.). Parkinson's Foundation. Retrieved February 13, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Causes/Environmental-Factors>

exercise. (n.d.). TheFreeDictionary.Com. Retrieved August 15, 2022, from <https://medical-dictionary.thefreedictionary.com/exercise>

Falls. (2020, June). European Parkinson's Disease Association. Retrieved April 30, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/motor-symptoms/falls/>

Ferrari, R. (2015). Writing narrative style literature reviews. *Medical Writing*, 24(4), 230–235. <https://doi.org/10.1179/2047480615z.000000000329>

Ferraz, H. B., Andrade, L. A. F., Tumas, V., Calia, L. C., & Borges, V. (1996). Rural or urban living and Parkinson's disease. *Arquivos de Neuro-Psiquiatria*, 54(1), 37–41. <https://doi.org/10.1590/s0004-282x1996000100006>

Finger, M. E., Selb, M., de Bie, R., & Escorpizo, R. (2014). Using the International Classification of Functioning, Disability and Health in Physiotherapy in Multidisciplinary Vocational Rehabilitation: A Case Study of Low Back Pain. *Physiotherapy Research International*, 20(4), 231–241. <https://doi.org/10.1002/pri.1587>

Forbes, E. J., Byrne, G. J., O'Sullivan, J. D., Yang, J., Marsh, R., & Dissanayaka, N. N. (2021). Defining Atypical Anxiety in Parkinson's Disease. *Movement Disorders Clinical Practice*, 8(4), 571–581. <https://doi.org/10.1002/mdc3.13193>

Frenklach, A. (2016). Management of Depression in Parkinson's Disease. *American Journal of Psychiatry Residents' Journal*, 11(4), 8–11. <https://doi.org/10.1176/appi.ajp-rj.2016.110405>

Friedman, J., MD. (2017, February 22). Pain in Parkinson's Disease. American Parkinson Disease Association. Retrieved July 23, 2022, from <https://www.apdaparkinson.org/article/pain-parkinsons-disease/#:%7E:text=Radicular%20pain%20is%20generally%20a,abnormal%20spine%20curvature%20in%20PD.>

Gait. (2020, January). European Parkinson's Disease Association. Retrieved April 30, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/motor-symptoms/gait/>

Genetics and Parkinson's. (n.d.). Parkinson's Foundation. Retrieved February 4, 2022, from <https://www.parkinson.org/understanding-parkinsons/causes/genetics>

Gilbert, R. (2019, August 19). Listen to your gut – what is the gastrointestinal tract telling us about Parkinson's disease? American Parkinson Disease Association. Retrieved July 9, 2022, from <https://www.apdaparkinson.org/article/the-gut-and-parkinsons/#:%7E:text=The%20gut%20has%20its%20own%20nervous%20system&text=First%20of%20all%20C%20alpha%20Dsynuclein,motor%20nucleus%20of%20the%20vagus.>

Gilbert, R. (2019b, August 27). Is Pain a Symptom of Parkinson's Disease? American Parkinson Disease Association. Retrieved July 23, 2022, from <https://www.apdaparkinson.org/article/is-pain-a-symptom-of-parkinsons-disease/>

- Gilbert, R. (2021, April 6). Posture problems in Parkinson's Disease. APDA. Retrieved April 30, 2022, from <https://www.apdaparkinson.org/article/posture-problems-in-parkinsons-disease/>
- Glynn, A., & Fiddler, H. (2009). Principles of Therapeutic Exercise Design. *The Physiotherapist's Pocket Guide to Exercise*, 13. <https://doi.org/10.1016/b978-0-443-10269-1.00002-1>
- Goetz, C. G. (2011). The History of Parkinson's Disease: Early Clinical Descriptions and Neurological Therapies. *Cold Spring Harbor Perspectives in Medicine*, 1(1), a008862. <https://doi.org/10.1101/cshperspect.a008862>
- Grant, M. J., & Booth, A. (2009). A typology of reviews: an analysis of 14 review types and associated methodologies. *Health Information & Libraries Journal*, 26(2), 91–108. <https://doi.org/10.1111/j.1471-1842.2009.00848.x>
- Gross Saunders, D. (2007). Therapeutic Exercise. *Clinical Techniques in Small Animal Practice*, 22(4), 155–159. <https://doi.org/10.1053/j.ctsap.2007.09.003>
- Gupta, D. K., Marano, M., Zweber, C., Boyd, J. T., & Kuo, S. H. (2020). Prevalence and Relationship of Rest Tremor and Action Tremor in Parkinson's Disease. *Tremor and Other Hyperkinetic Movements*, 10(0), 58. <https://doi.org/10.5334/tohm.552>
- Hanna, K. K., & Cronin-Golomb, A. (2012). Impact of Anxiety on Quality of Life in Parkinson's Disease. *Parkinson's Disease*, 2012, 1–8. <https://doi.org/10.1155/2012/640707>
- Harper, S. A., Dowdell, B. T., Kim, J. H., Pollock, B. S., & Ridgel, A. L. (2019, June 14). Non-Motor Symptoms after One Week of High Cadence Cycling in Parkinson's Disease. *International Journal of Environmental Research and Public Health*, 16(12), 2104. <https://doi.org/10.3390/ijerph16122104>
- Heerkens, Y., Hendriks, E., & Oostendorp, R. (2006). Assessment instruments and the ICF in rehabilitation and physiotherapy. *Medical Rehabilitation*, 1–14. https://www.researchgate.net/publication/242109246_Assessment_instruments_and_the_ICF_in_rehabilitation_and_physiotherapy
- Heusinkveld, L. E., Hacker, M. L., Turchan, M., Davis, T. L., & Charles, D. (2018). Impact of Tremor on Patients With Early Stage Parkinson's Disease. *Frontiers in Neurology*, 9. <https://doi.org/10.3389/fneur.2018.00628>
- Horsager, J., Andersen, K. B., Knudsen, K., Skjærbæk, C., Fedorova, T. D., Okkels, N., Schaeffer, E., Bonkat, S. K., Geday, J., Otto, M., Sommerauer, M., Danielsen, E. H., Bech, E., Kraft, J., Munk, O. L., Hansen, S. D., Pavese, N., Göder, R., Brooks, D. J., . . . Borghammer, P. (2020). Brain-first versus body-first Parkinson's disease: a multimodal imaging case-control study. *Brain*, 143(10), 3077–3088. <https://doi.org/10.1093/brain/awaa238>
- Hou, J. G. G., & Lai, E. C. (2007). Non-motor Symptoms of Parkinson's Disease. *International Journal of Gerontology*, 1(2), 53–64. [https://doi.org/10.1016/s1873-9598\(08\)70024-3](https://doi.org/10.1016/s1873-9598(08)70024-3)

Hou, J. G. G., & Lai, E. C. (2007b). Non-motor Symptoms of Parkinson's Disease. *International Journal of Gerontology*, 1(2), 53–64. [https://doi.org/10.1016/s1873-9598\(08\)70024-3](https://doi.org/10.1016/s1873-9598(08)70024-3)

<https://www.vidal.fr/medicaments/laboratoires/sanofi-aventis-france-2172.html>. (2022, April 15). ARTANE. VIDAL. Retrieved July 9, 2022, from <https://www.vidal.fr/medicaments/gammes/artane-665.html#:~:text=Dans%20quel%20cas%20le%20m%C3%A9dicament,parkinsoniens%20induits%20par%20les%20neuroleptiques>.

<https://www.vidal.fr/medicaments/laboratoires/teva-sante-2871.html>. (2022, April 15). LEVODOPA BENSERAZIDE TEVA. VIDAL. Retrieved July 9, 2022, from <https://www.vidal.fr/medicaments/gammes/levodopa-benserazide-teva-37748.html#:~:text=Ce%20m%C3%A9dicament%20est%20un%20antiparkinsonien,de%20la%20maladie%20de%20Parkinson>.

Hynynen, P., Häkkinen, H., Hännikäinen, H., Kangasperko, M., Karihtala, T., Keskinen, M., Leskelä, J., Liikka, S., Lähteenmäki, M.-L., Mämmelä, E., Partia, R., Piirainen, A., Sjögren, T., & Suhonen, L. (2018). *The core competences of a physiotherapist*. Finnish Association of Physiotherapists. <https://www.suomenfysioterapeutit.fi/wp-content/uploads/2018/04/CoreCompetencies.pdf>

ICF e-Learning Tool_English_20220501. (n.d.). Icf-Elearning. Retrieved August 13, 2022, from https://www.icf-elearning.com/wp-content/uploads/articulate_uploads/ICF%20e-Learning%20Tool_English_20220501%20-%20Storyline%20output/story_html5.html

Indirect pathway. (2020, October 20). <https://nba.uth.tmc.edu/>. <https://nba.uth.tmc.edu/neuroscience/s3/chapter04.html>

Insomnia. (2000, January 1). WebMD. Retrieved June 4, 2022, from <https://www.webmd.com/sleep-disorders/insomnia-symptoms-and-causes>

International Classification of Functioning, Disability and Health (ICF). (n.d.). Physiopedia. Retrieved August 13, 2022, from [https://www.physio-pedia.com/International_Classification_of_Functioning_Disability_and_Health_\(ICF\)](https://www.physio-pedia.com/International_Classification_of_Functioning_Disability_and_Health_(ICF))

Jang, H., Boltz, D., Sturm-Ramirez, K., Shepherd, K. R., Jiao, Y., Webster, R., & Smeyne, R. J. (2009). Highly pathogenic H5N1 influenza virus can enter the central nervous system and induce neuroinflammation and neurodegeneration. *Proceedings of the National Academy of Sciences*, 106(33), 14063–14068. <https://doi.org/10.1073/pnas.0900096106>

Keus, S., Munneke, M., Graziano, M. et al. (2014). European physiotherapy guideline for Parkinson's disease. Parkinsonnet.com. Retrieved October 25, 2021 from https://www.parkinsonnet.nl/app/uploads/sites/3/2019/11/eu_guideline_parkinson_guideline_for_pt_sl.pdf

khanacademymedicine. (2015a, May 15). *The basal ganglia - Details of the indirect pathway* | NCLEX-RN | Khan Academy [Video]. YouTube. https://www.youtube.com/watch?v=VZer0w7foLg&ab_channel=khanacademymedicine

khanacademymedicine. (2015b, May 15). *The basal ganglia - The direct pathway* | Nervous system diseases | NCLEX-RN | Khan Academy [Video]. YouTube. https://www.youtube.com/watch?v=Mmev06nabvk&t=306s&ab_channel=khanacademymedicine

Klepac, N. (2007, February 1). *Association of rural life setting and poorer quality of life in Parkinson's disease patients: a cross-sectional study in Croatia*. Wiley Online Library. Retrieved January 20, 2022, from <https://onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2006.01604.x>

Knierim, J. (2020a, October 20). Basal Ganglia (Section 3, Chapter 4) Neuroscience Online: An Electronic Textbook for the Neurosciences | Department of Neurobiology and Anatomy - The University of Texas Medical School at Houston. Neuroscience Online. Retrieved September 3, 2022, from <https://nba.uth.tmc.edu/neuroscience/s3/chapter04.html>

Knierim, J. (2020b, October 20). Motor Cortex (Section 3, Chapter 3) Neuroscience Online: An Electronic Textbook for the Neurosciences | Department of Neurobiology and Anatomy - The University of Texas Medical School at Houston. Neuroscience Online. Retrieved September 2, 2022, from <https://nba.uth.tmc.edu/neuroscience/s3/chapter03.html>

Knierim, J. (2020c, October 20). Motor Cortex (Section 3, Chapter 3) Neuroscience Online: An Electronic Textbook for the Neurosciences | Department of Neurobiology and Anatomy - The University of Texas Medical School at Houston. Neuroscience Online. Retrieved September 2, 2022, from <https://nba.uth.tmc.edu/neuroscience/s3/chapter03.html>

Kurupparachchi, A., & Faigl, A. (n.d.). *Parkinson's Disease* | Armando Hasudungan. Armando Hasudungan. Retrieved September 2, 2022, from <https://armandoh.org/disease/parkinsons-disease/>

Learn the Impact and Treatment of Rigidity in Parkinson's Disease. (2022, February 24). Verywell Health. Retrieved April 30, 2022, from <https://www.verywellhealth.com/what-is-rigidity-in-parkinsons-disease-2612097>

Lee, A., & Gilbert, R. M. (2016, November 1). *Epidemiology of Parkinson Disease*. ScienceDirect. Retrieved January 11, 2022, from <https://www.sciencedirect.com/science/article/abs/pii/S0733861916300342?via%3Dihub>

Lee, A., & Gilbert, R. M. (2016a). Epidemiology of Parkinson Disease. *Neurologic Clinics*, 34(4), 1–8. <https://doi.org/10.1016/j.ncl.2016.06.012>

Lobes of the brain. (2022, May 5). Pixabay. <https://pixabay.com/illustrations/brain-anatomy-lobes-medical-7174144/>

Loddo, G., Calandra-Buonaura, G., Sambati, L., Giannini, G., Cecere, A., Cortelli, P., & Provini, F. (2017). The Treatment of Sleep Disorders in Parkinson's Disease: From Research to Clinical Practice. *Frontiers in Neurology*, 8. <https://doi.org/10.3389/fneur.2017.00042>

Maharaj, S. (2022, July 27). *Static Balance vs. Dynamic Balance Exercises*. Propel Physiotherapy. Retrieved August 15, 2022, from <https://propelphysiotherapy.com/exercise/static-balance-vs-dynamic-balance-exercises/>

Main regions of the motor cortex. (n.d.). The Brain From Top to Bottom. https://thebrain.mcgill.ca/flash/a/a_06/a_06_cr/a_06_cr_mou/a_06_cr_mou.html

Marras, C. (2018, July 10). *Prevalence of Parkinson's disease across North America*. Nature. Retrieved January 20, 2022, from <https://www.nature.com/articles/s41531-018-0058-0#additional-information>

Marsh, L. (2013). Depression and Parkinson's Disease: Current Knowledge. *Current Neurology and Neuroscience Reports*, 13(12). <https://doi.org/10.1007/s11910-013-0409-5>

Maserejian, N., Vinikoor-Imler, L., & Dilley, A. (2020, September 7). *Estimation of the 2020 Global Population of Parkinson's Disease (PD)*. MDS Abstracts. Retrieved January 11, 2022, from <https://www.mdsabstracts.org/abstract/estimation-of-the-2020-global-population-of-parkinsons-disease-pd/>

McCoy, K., & Bass, P. F., III MD. (2016, April 27). *The History of Parkinson's Disease*. EverydayHealth.Com. Retrieved February 27, 2022, from <https://www.everydayhealth.com/parkinsons-disease/history-of-parkinsons-disease.aspx>

McDonald, C., Winge, K., & Burn, D. J. (2017). Lower urinary tract symptoms in Parkinson's disease: Prevalence, aetiology and management. *Parkinsonism & Related Disorders*, 35, 8–16. <https://doi.org/10.1016/j.parkreldis.2016.10.024>

McGough, E. L., Robinson, C. A., Nelson, M. D., Houle, R., Fraser, G., Handley, L., Jones, E. R., Amtmann, D., & Kelly, V. E. (2016, October). A Tandem Cycling Program: Feasibility and Physical Performance Outcomes in People With Parkinson Disease. *Journal of Neurologic Physical Therapy*, 40(4), 223–229. <https://doi.org/10.1097/npt.0000000000000146>

Medical Definition of Bradykinetic. (2021, March 29). RxList. Retrieved February 27, 2022, from <https://www.rxlist.com/bradykinetic/definition.htm>

Meireles, J., & Massano, J. (2012). Cognitive Impairment and Dementia in Parkinson's Disease: Clinical Features, Diagnosis, and Management. *Frontiers in Neurology*, 3. <https://doi.org/10.3389/fneur.2012.00088>

Milsom, I., & Gyhagen, M. (2018). The prevalence of urinary incontinence. *Climacteric*, 22(3), 217–222. <https://doi.org/10.1080/13697137.2018.1543263>

Ministry of Social Affairs and Health, Finland. (2010, December 10). *No. 1326/2010 Health Care Act*. Retrieved September 8, 2022, from https://www.finlex.fi/en/laki/kaannokset/2010/en20101326_20131293.pdf

Motor Fluctuations. (n.d.). Parkinson's Foundation. Retrieved June 6, 2022, from <https://www.parkinson.org/pd-library/fact-sheets/motor-fluctuations>

Muangpaisan, W., Mathews, A., Hori, H., & Seidel, D. (2011). A systematic review of the worldwide prevalence and incidence of Parkinson's disease. *Journal of the Medical Association of Thailand*, 94(6), 749–753. Retrieved January 11, 2022, from <https://www.thaiscience.info/journals/Article/JMAT/10817133.pdf>

Nadeau, A., Lungu, O., Boré, A., Plamondon, R., Duchesne, C., Robillard, M. V., Bobeuf, F., Lafontaine, A. L., Gheysen, F., Bherer, L., & Doyon, J. (2018, September 11). A 12-Week Cycling Training Regimen Improves Upper Limb Functions in People With Parkinson's Disease. *Frontiers in Human Neuroscience*, 12. <https://doi.org/10.3389/fnhum.2018.00351>

NHS website. (2021, November 18). About dementia. Nhs.Uk. Retrieved June 22, 2022, from <https://www.nhs.uk/conditions/dementia/about/>

NHS website. (2021, November 18). Symptoms. Nhs.Uk. Retrieved February 27, 2022, from <https://www.nhs.uk/conditions/parkinsons-disease/symptoms/>

Nitti, V. W. (2001). The prevalence of urinary incontinence. *Reviews in Urology*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1476070/#:~:text=In%20men%2C%20the%20prevalence%20of,%2C%20trauma%2C%20or%20neurological%20injury.>

Non-Movement Symptoms. (n.d.). Parkinson's Foundation. Retrieved May 18, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Non-Movement-Symptoms>

Nonnekes, J. (2018, December 7). Gait festination in parkinsonism: introduction of two phenotypes. SpringerLink. Retrieved April 30, 2022, from https://link.springer.com/article/10.1007/s00415-018-9146-7?error=cookies_not_supported&code=672f1102-1815-4926-bf5a-043c6d19e5b9

Onwuegbuzie, A. J., & Frels, R. (2016). *Seven Steps to a Comprehensive Literature Review: A Multimodal and Cultural Approach* (First ed.). SAGE Publications Ltd.

Ossowska, K., & Lorenc-Koci, E. (2013). Depression in Parkinson's disease. *Pharmacological Reports*, 65(6), 1545–1557. [https://doi.org/10.1016/s1734-1140\(13\)71516-0](https://doi.org/10.1016/s1734-1140(13)71516-0)

Ou, Z. (2021). *Global Trends in the Incidence, Prevalence, and Years Lived With Disability of Parkinson's Disease in 204 Countries/Territories From 1990 to 2019*. Frontiers. Retrieved January 11, 2022, from <https://www.frontiersin.org/articles/10.3389/fpubh.2021.776847/full#B29>

Pain. (2020, July). European Parkinson's Disease Association. Retrieved July 23, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/non-motor-symptoms/pain/>

Pain. (n.d.). Parkinson's Foundation. Retrieved July 23, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Symptoms/Non-Movement-Symptoms/Pain>

Paré, G., & Kitsiou, S. (2017, February 27). Chapter 9: Methods for Literature Reviews. In F. Lau & C. Kuziemsky (Eds.), *Handbook of eHealth Evaluation: An Evidence-based Approach*. University of Victoria.
<https://www.ncbi.nlm.nih.gov/books/NBK481583/>

Parkinson's disease - Diagnosis and treatment - Mayo Clinic. (2022, January 14). Mayoclinic. Retrieved February 25, 2022, from <https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/diagnosis-treatment/drc-20376062#:~:text=Levodopa%2C%20the%20most%20effective%20Parkinson's,to%20dopamine%20outside%20your%20brain.>

Parkinson's Disease | Armando Hasudungan. (n.d.). Retrieved September 5, 2022, from <https://armandoh.org/disease/parkinsons-disease/>

Parkinson's Disease and Constipation. (2002, March 20). WebMD. Retrieved July 9, 2022, from <https://www.webmd.com/parkinsons-disease/guide/parkinsons-constipation>

Parkinson's disease: Causes, Symptoms, Stages, Treatment, Support. (2020). Cleveland Clinic. Retrieved February 27, 2022, from <https://my.clevelandclinic.org/health/diseases/8525-parkinsons-disease-an-overview>

Parkinson's foundation & American college of sports medicine. (n.d.). *Parkinsons Exercise Recommendations*. Parkinson's Foundation. Retrieved August 24, 2022, from <https://www.parkinson.org/library/fact-sheets/exercise-recommendations>

Parkinsonin tauti. (2022, March 28). kaypahoito. Retrieved August 11, 2022, from <https://www.kaypahoito.fi/hoi50042#s6>

Pedersen, S. W., Suedmeyer, M., Liu, L., Domagk, D., Forbes, A., Bergmann, L., Onuk, K., Yegin, A., & van Laar, T. (2017). The role and structure of the multidisciplinary team in the management of advanced Parkinson's disease with a focus on the use of levodopa-carbidopa intestinal gel. *Journal of Multidisciplinary Healthcare*. <https://doi.org/10.2147/JMDH.S111369>

Physical activity. (2020, November 26). World Health Organization. Retrieved August 15, 2022, from <https://www.who.int/news-room/fact-sheets/detail/physical-activity>

Physical Therapy and Parkinson's. (2019). Parkinson's Foundation. Retrieved October 25, 2021, from <https://www.parkinson.org/pd-library/fact-sheets/Physical-Therapy-Parkinsons>

Physiotherapy works: Parkinson's. (2017, July 6). The Chartered Society of Physiotherapy. Retrieved August 11, 2022, from <https://www.csp.org.uk/publications/physiotherapy-works-parkinsons>

Physiotherapy. (n.d.-a). European Parkinson's Disease Association. Retrieved August 11, 2022, from <https://www.epda.eu.com/living-well/therapies/therapists-and-multidisciplinary-care/physiotherapy/>

Physiotherapy. (n.d.-b). Parkinson's UK. Retrieved August 11, 2022, from <https://www.parkinsons.org.uk/information-and-support/physiotherapy>

Podcast: Six New Genetic Risk Factors for Parkinson's Identified. (2014, July 30). The Michael J. Fox Foundation for Parkinson's Research | Parkinson's Disease. Retrieved February 4, 2022, from <https://www.michaeljfox.org/podcast/podcast-six-new-genetic-risk-factors-parkinsons-identified>

Primary, secondary and tertiary prevention. (2015, April). Institute for Work and Health. Retrieved September 8, 2022, from <https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention>

PRISMA. (n.d.). Retrieved September 17, 2022, from <https://www.prisma-statement.org/PRISMAStatement/FlowDiagram.aspx>

Qutubuddin, A., Reis, T., Alramadhani, R., Cifu, D. X., Towne, A., & Carne, W. (2013). Parkinson's Disease and Forced Exercise: A Preliminary Study. *Rehabilitation Research and Practice*, 2013, 1–5. <https://doi.org/10.1155/2013/375267>

Radder, D. L. M., Lígia Silva De Lima, A., Domingos, J., Keus, S. H. J., van Nimwegen, M., Bloem, B. R., & de Vries, N. M. (2020). Physiotherapy in Parkinson's Disease: A Meta-Analysis of Present Treatment Modalities. *Neurorehabilitation and Neural Repair*, 34(10), 871–880. <https://doi.org/10.1177/1545968320952799>

Rahman, S., Griffin, H. J., Quinn, N. P., & Jahanshahi, M. (2011). On the Nature of Fear of Falling in Parkinson's Disease. *Behavioural Neurology*, 24(3), 219–228. <https://doi.org/10.1155/2011/274539>

Rating scales. (2017, March). European Parkinson's Disease Association. Retrieved August 3, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/rating-scales/>

Reeve, A., Simcox, E., & Turnbull, D. (2014). Ageing and Parkinson's disease: Why is advancing age the biggest risk factor? *Ageing Research Reviews*, 14, 19–30. <https://doi.org/10.1016/j.arr.2014.01.004>

REM sleep behavior disorder - Symptoms and causes. (2018, January 18). Mayo Clinic. Retrieved May 22, 2022, from [https://www.mayoclinic.org/diseases-conditions/rem-sleep-behavior-disorder/symptoms-causes/syc-20352920#:~:text=Rapid%20eye%20movement%20\(REM\)%20sleep,sometimes%20called%20dream%2Denacting%20behavior.](https://www.mayoclinic.org/diseases-conditions/rem-sleep-behavior-disorder/symptoms-causes/syc-20352920#:~:text=Rapid%20eye%20movement%20(REM)%20sleep,sometimes%20called%20dream%2Denacting%20behavior.)

Restless legs. (2019, February). Parkinson's UK. Retrieved June 4, 2022, from <https://www.parkinsons.org.uk/information-and-support/restless-legs#:~:text=Restless%20legs%20syndrome%20is%20a,that%20is%20unrelated%20to%20Parkinson's>.

Ridgel, A. L., & Ault, D. L. (2019, March 3). High-Cadence Cycling Promotes Sustained Improvement in Bradykinesia, Rigidity, and Mobility in Individuals with Mild-Moderate Parkinson's Disease. *Parkinson's Disease*, 2019, 1–7. <https://doi.org/10.1155/2019/4076862>

Ridgel, A. L., Phillips, R. S., Walter, B. L., Discenzo, F. M., & Loparo, K. A. (2015, September 2). Dynamic High-Cadence Cycling Improves Motor Symptoms in Parkinson's Disease. *Frontiers in Neurology*, 6. <https://doi.org/10.3389/fneur.2015.00194>

Ridgel, A. L., Vitek, J. L., & Alberts, J. L. (2009). Forced, Not Voluntary, Exercise Improves Motor Function in Parkinson's Disease Patients. *Neurorehabilitation and Neural Repair*, 23(6), 600–608. <https://doi.org/10.1177/1545968308328726>

Rietdijk, C. D., Perez-Pardo, P., Garssen, J., van Wezel, R. J., & Kraneveld, A. D. (2017). *Exploring Braak's Hypothesis of Parkinson's Disease*. *Frontiers in neurology*, 8, 37. <https://doi.org/10.3389/fneur.2017.00037>

Rigidity (Stiffness). (n.d.). Parkinson's Foundation. Retrieved April 30, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Symptoms/Movement-Symptoms/Rigidity-Stiffness>

Rigidity. (2016, February). European Parkinson's Disease Association. Retrieved April 30, 2022, from <https://www.epda.eu.com/about-parkinsons/symptoms/motor-symptoms/rigidity/>

Rigidity. (n.d.). Physiopedia. Retrieved April 30, 2022, from <https://www.physio-pedia.com/Rigidity>

Saag, T. (2015, March 4). *Types of Endurance Training Explained*. The Sportlyzer Blog. Retrieved August 15, 2022, from <https://blog.sportlyzer.com/en/types-of-endurance-training-explained/>

Safarpour, D., & Willis, A. W. (2016). Clinical Epidemiology, Evaluation, and Management of Dementia in Parkinson Disease. *American Journal of Alzheimer's Disease & Other Dementias*, 31(7), 585–594. <https://doi.org/10.1177/1533317516653823>

Sanderson, L. (2018, October 16). *How Physiotherapy Can Help If You Have Parkinson's Disease*. Physiotas. Retrieved August 11, 2022, from <http://physiotas.com.au/physiotherapy-help-parkinsons-disease/>

Sauerbier, A., Aris, A., Lim, E. W., Bhattacharya, K., & Ray Chaudhuri, K. (2018). Impact of ethnicity on the natural history of Parkinson disease. *Medical Journal of Australia*, 208(9), 410–414. <https://doi.org/10.5694/mja17.01074>

Schenck, C. H. (2019). The spectrum of disorders causing violence during sleep. *Sleep Science and Practice*, 3(1). <https://doi.org/10.1186/s41606-019-0034-6>

Schrag, A. (2002). How valid is the clinical diagnosis of Parkinson's disease in the community? *Journal of Neurology, Neurosurgery & Psychiatry*, 73(5), 529–534. <https://doi.org/10.1136/jnnp.73.5.529>

Schwerin, S. (2013, March 5). Principal cortical domains of the motor system. The primary motor cortex (M1) lies along the precentral gyrus, and generates the signals that control the execution of movement. Secondary motor areas are involved in motor planning. The plane of section is elaborated in figure 1b. <https://brainconnection.brainhq.com>. <https://brainconnection.brainhq.com/wp-content/uploads/2013/03/1a.gif>

Scott, B., Borgman, A., Engler, H., Johnels, B., & Aquilonius, S. M. (2000). Gender differences in Parkinson's disease symptom profile. *Acta Neurologica Scandinavica*, 102(1), 37–43. <https://doi.org/10.1034/j.1600-0404.2000.102001037.x>

Seven million cases of Parkinson's disease - The fastest growing brain disease in the world. (2021, April 13). Radboudumc. Retrieved October 25, 2021, from <https://www.radboudumc.nl/en/news/2021/seven-million-cases-of-parkinsons-disease>

Skelly, R., Lindop, F., & Johnson, C. (2012). Multidisciplinary care of patients with Parkinson's disease. *Progress in Neurology and Psychiatry*, 10–14. <https://wchh.onlinelibrary.wiley.com/doi/pdf/10.1002/pnp.230>

Stages of Parkinson's. (n.d.). Parkinson's Foundation. Retrieved February 27, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/What-is-Parkinsons/Stages-of-Parkinsons#:~:text=Hoehn%20and%20Yahr%20stages%20follow,and%205%20advanced%2Dstage%20Parkinson's>.

Stages of Parkinson's. (n.d.). Parkinson's Foundation. Retrieved August 3, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/What-is-Parkinsons/Stages-of-Parkinsons#:~:text=Hoehn%20and%20Yahr%20stages%20follow,and%205%20advanced%2Dstage%20Parkinson's>.

Starkstein, S. E., Merello, M., Jorge, R., Brockman, S., Bruce, D., Petracca, G., & Robinson, R. G. (2008). A validation study of depressive syndromes in Parkinson's disease. *Movement Disorders*, 23(4), 538–546. <https://doi.org/10.1002/mds.21866>

Systematic Reviews: CRD's Guidance for Undertaking Reviews in Health Care. (2009). Centre for Reviews and Dissemination. https://www.york.ac.uk/media/crd/Systematic_Reviews.pdf#page=60

The relative homuncular representation of the primary motor cortex reveals the relative sizes of the regions of the primary motor cortex, which represent different parts of the body as determined by electrical stimulation experiments. (n.d.).

<http://what-when-how.com/>. <http://what-when-how.com/neuroscience/the-upper-motor-neurons-motor-systems-part-1/>

The relative homuncular representation of the primary motor cortex. (n.d.). What-when-how. <http://what-when-how.com/neuroscience/the-upper-motor-neurons-motor-systems-part-1/>

The Stretching Institute™. (2021, September 21). *PNF Stretching Explained | Proprioceptive Neuromuscular Facilitation*. StretchCoach.Com | Stretching and Flexibility. Retrieved August 15, 2022, from <https://stretchcoach.com/articles/pnf-stretching/>

Theracycle. (2010, August 12). *Forced Exercise with Theracycle Parkinson's Disease Bikes Study*. Theracycle Physical Therapy Exercise Bike and Rehabilitation Equipment. Retrieved August 24, 2022, from https://www.theracycle.com/research_and_studies/forced-exercise-with-theracycle-parkinsons-disease-bikes-a-cleveland-clinic-research-study/

Theracycle. (2019, August 16). *Stationary exercise bikes for Parkinson's disease | Theracycle*. Theracycle Physical Therapy Exercise Bike and Rehabilitation Equipment. Retrieved August 24, 2022, from <https://www.theracycle.com/why-forced-exercise-is-a-key-parkinsons-disease-treatment-option/>

Therapeutic Exercise. (n.d.). Physiopedia. Retrieved August 15, 2022, from https://www.physio-pedia.com/Therapeutic_Exercise#cite_note-4

Thomas, J., & Harden, A. (2008). Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Medical Research Methodology*, 8(1). <https://doi.org/10.1186/1471-2288-8-45>

Tomlinson, C. L. (2012, August 6). *Physiotherapy intervention in Parkinson's disease: systematic review and meta-analysis*. *The BMJ*. Retrieved November 10, 2021, from <https://www.bmj.com/lookup/doi/10.1136/bmj.e5004>

Tremor. (n.d.). Parkinson's Foundation. Retrieved February 28, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Symptoms/Movement-Symptoms/Tremor>

Trouble Moving or Walking. (n.d.). Parkinson's Foundation. Retrieved April 30, 2022, from <https://www.parkinson.org/Understanding-Parkinsons/Symptoms/Movement-Symptoms/Trouble-Moving-or-Walking>

Truschel, J. (2020, September 25). *Depression Definition and DSM-5 Diagnostic Criteria*. PSYCOM; Remedy Health Media. <https://www.psycom.net/depression-definition-dsm-5-diagnostic-criteria/>

Ullah, I., Zhao, L., Hai, Y., Fahim, M., Alwayli, D., Wang, X., & Li, H. (2021). "Metal elements and pesticides as risk factors for Parkinson's disease - A review." *Toxicology Reports*, 8, 607–616. <https://doi.org/10.1016/j.toxrep.2021.03.009>

Urinary Problems in Parkinson's Disease. (n.d.). Parkinson's Foundation. Retrieved July 2, 2022, from <https://www.parkinson.org/pd-library/fact-sheets/urinary-problems-in-parkinson-s-disease>

Valkovic, P., Minar, M., Singliarova, H., Harsany, J., Hanakova, M., Martinkova, J., & Benetin, J. (2015). Pain in Parkinson's Disease: A Cross-Sectional Study of Its Prevalence, Types, and Relationship to Depression and Quality of Life. *PLOS ONE*, *10*(8), e0136541. <https://doi.org/10.1371/journal.pone.013654>

Wallace, D. M., Wohlgemuth, W. K., Trotti, L. M., Amara, A. W., Malaty, I. A., Factor, S. A., Nallu, S., Wittine, L., & Hauser, R. A. (2020). Practical Evaluation and Management of Insomnia in Parkinson's Disease: A Review. *Movement Disorders Clinical Practice*, *7*(3), 250–266. <https://doi.org/10.1002/mdc3.12899>

Wen, M., Chan, L. L., Tan, L. C. S., & Tan, E. K. (2016). Depression, anxiety, and apathy in Parkinson's disease: insights from neuroimaging studies. *European Journal of Neurology*, *23*(6), 1001–1019. <https://doi.org/10.1111/ene.13002>

What Are REM and Non-REM Sleep? (2005, April 26). WebMD. Retrieved May 22, 2022, from [https://www.webmd.com/sleep-disorders/sleep-101#:~:text=Rapid%20eye%20movement%20\(REM\)%20sleep,important%20for%20learning%20and%20memory](https://www.webmd.com/sleep-disorders/sleep-101#:~:text=Rapid%20eye%20movement%20(REM)%20sleep,important%20for%20learning%20and%20memory).

What is Endurance? Definition, Training and Fitness. (2022, June 2). Training 4 Endurance. Retrieved August 15, 2022, from <https://training4endurance.co.uk/physiology-of-endurance/what-is-endurance/>

What is ICF? (n.d.). ICF Education. Retrieved August 13, 2022, from <http://icfeducation.org/what-is-icf>

What Is Parkinson's? (n.d.). Parkinson's Foundation. Retrieved October 25, 2021, from <https://www.parkinson.org/understanding-parkinsons/what-is-parkinsons>

Winge, K., Skau, A. M., Stimpel, H., Nielsen, K. K., & Werdelin, L. (2006). Prevalence of bladder dysfunction in Parkinsons disease. *Neurology and Urodynamics*, *25*(2), 116–122. <https://doi.org/10.1002/nau.20193>

Wong, S. L., Gilmour, H., & Ramage-Morin, P. L. (2014). Parkinson's disease: Prevalence, diagnosis and impact. *Health Reports*, *25*(11), 10–14. <https://www150.statcan.gc.ca/n1/en/pub/82-003-x/2014011/article/14112-eng.pdf?st=117hLLVD>

Wooten, G. F. (2004, April 1). *Are men at greater risk for Parkinson's disease than women?* *Journal of Neurology, Neurosurgery & Psychiatry*. Retrieved January 11, 2022, from <https://jnnp.bmj.com/content/75/4/637>

World health organization. (2020, November 26). *Physical activity*. Retrieved November 10, 2021, from <https://www.who.int/news-room/fact-sheets/detail/physical-activity>

Wright Willis, A., Evanoff, B. A., Lian, M., Criswell, S. R., & Racette, B. A. (2010). Geographic and Ethnic Variation in Parkinson Disease: A Population-Based Study of US Medicare Beneficiaries. *Neuroepidemiology*, *34*(3), 143–151.
<https://doi.org/10.1159/000275491>