THE EFFECTS OF DYNAMIC CYCLING
ON MOTOR FUNCTION, GAIT, MOBILITY, AND BALANCE
IN INDIVIDUALS WITH PARKINSON’S DISEASE

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BACKGROUND: Parkinson’s disease (PD) affects more than 1 million people in the United States, and leads to difficulties in performing activities of daily living. Dynamic cycling can improve motor function; however it is not known if multiple bouts lead to improvements in gait and balance in individuals with PD. PURPOSE: To assess if six bouts of dynamic cycling improves motor function, gait, mobility, and balance in individuals with PD. METHODS: Dynamic, motorized cycling, consisted of a 5 minute warm-up and cool down at 50 rpm and 30 minutes of high cadence cycling between 75–85 rpm. Motor function, gait, mobility, and balance were assessed after every cycling bout using the UPDRS Motor III scale, Kinesia ONE, Timed up and Go (TUG), and the Modified Clinical Test of Sensory Interaction in Balance (mCTSIB). The control group performed a 5-minute warm-up and 30 minutes of body stretches before completing the assessment tests. RESULTS: Six bouts of dynamic cycling significantly improved UPDRS scores ($F = 5.814, p = .030$), kinetic tremor ($F = 15.58, p = .001$), hand movement amplitude ($F = 10.32, p = .006$), rapid alternating hand movement speed ($F = 16.58, p = .001$), gait ($F = 11.504, p = .004$), and TUG time ($F = 8.313, p = .012$). CONCLUSION: Six bouts of dynamic cycling improve motor function, gait, and mobility individuals with PD.
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CHAPTER I
INTRODUCTION

Background

The incidence and prevalence of Parkinson’s disease (PD) continues to increase (Kowal, Dall, Chakrabarti, Storm, & Jain, 2013), affecting more than 1 million people in the United States (Hackney & Earhart, 2009). These impairments lead to a decline in functional status such that people with PD have difficulty with activities of daily living or tasks including but not limited to walking, rising from a chair, and moving in bed (Ellis et al., 2005). This condition leads to a decrease in Quality of Life (QOL) and independence for individuals who are affected by this incurable, neurodegenerative disorder (Hackney & Earhart, 2009). The development of this disease occurs due to selective neuronal loss in the substantia nigra and resultant degeneration of dopaminergic pathways in the basal ganglia (Alberts, Linder, Penko, Lowe & Phillips, 2011). The loss of dopamine alters both inhibitory and excitatory pathways, resulting in motor and sensory deficits (Calne & Langston, 1983). Given the large number of people affected by this disease, the long life span after diagnosis, the progressive nature of PD, and the short duration of medication effectiveness, it is critical to identify additional interventions to maximize QOL and functional status (Ellis et al., 2005). The treatments to this disease vary depending on the disease stage and the patients’ response to drug therapy treatment (levodopa). As the disease progresses, higher medication doses are often required and this can result in negative side effects, such as the drug losing its effectiveness and increased motor symptoms in the individuals (Samii, Nutt, & Ransom, 2004). Several studies have shown...
that the optimal management of Parkinson’s disease involves both pharmacologic treatment and an exercise regimen since exercise can improve motor, cognitive, and sensory function in individuals with Parkinson’s disease (Cakit, Saracoglu, Genc, & Erdem, 2007; Cutson, Laub, & Schenkman, 1995; David et al., 2012). Therefore, exercise is an attractive adjunct treatment intervention in addition to current PD treatment approaches.

**Rationale**

Exercise, in conjunction with drug therapy, has been proven to be an effective method of treatment for PD (Cakit et al., 2007; David et al., 2012; Lees, Hardy, & Revesz, 2009; Ridgel, Phillips, Walter, Discenzo, & Loparo, 2015). Over the years, many different types of exercise programs have been studied, such as high-intensity (Dibble, Hale, Marcus, Droge, et al., 2006), weight-supported (Cakit et al., 2007), and self-selected intensities (Ebersbach et al., 2010). Current research has demonstrated that high-intensity exercise may produce more favorable results than low-intensity or self-selected exercise intensities. Most recently, high-cadence cycling (Ridgel, Peacock, Fickes, & Kim, 2012; Ridgel et al., 2015; Ridgel, Vitek, & Alberts, 2009) exercise has been shown to decrease PD symptoms. Due to the progressive, debilitating nature of the disease and prevalent balance problems, high cadence stationary cycling is an attractive exercise method to examine the effectiveness of high-intensity exercise programs.

Several years ago, Ridgel and colleagues (2009) demonstrated that eight weeks of forced, high intensity exercise on a tandem stationary bike led to improvements in motor function and upper extremity dexterity in Parkinson’s disease individuals (Ridgel et al.,
2009). This study consisted of having Parkinson’s disease individuals complete three 1-hour exercise sessions weekly for eight weeks on a tandem with an able-bodied trainer (Ridgel et al., 2009). Another study found that a single-bout of active-assisted cycling improved tremor and bradykinesia in the upper extremity in individuals with Parkinson’s disease (Ridgel et al., 2012). Specifically, individuals were instructed to pedal a cycle ergometer between 80–85 revolutions per minute (rpm) for 30 minutes but if cadence fell below 75 rpm then the motor on the ergometer would move the participant’s legs to achieve 75 rpm (Ridgel et al., 2012). Most recently, Ridgel and colleagues showed that motorized, high-cadence dynamic cycling, for three sessions improved motor function in individuals with Parkinson’s disease (Ridgel et al., 2015). This study utilized a motorized cycle that had two different cycling settings: dynamic and static. In the dynamic setting, the motor of the cycle was maintained between 75–85 rpm, and in the static setting the rider determined the pedaling cadence (Ridgel et al., 2015). Participants were randomized into either the dynamic or static setting and at the end of the three sessions participants completed different assessments, which consisted of the Unified Parkinson’s Disease Rating Scale (UPDRS) Part III Motor Exam and the timed up-and-go (TUG) test (Ridgel et al., 2015). This study found 30 minutes of dynamic cycling improved tremor UPDRS Motor III score (Ridgel et al., 2015). However, no studies have examined immediate benefits of additional sessions (more than three) of dynamic cycling on motor function, gait and balance in individuals with idiopathic Parkinson’s disease.
**Objective**

The objective of this study is to examine the effectiveness of repeated bouts of dynamic cycling by assessing motor function, gait, mobility, and balance after each session. The primary purpose of this study is to evaluate if dynamic cycling improves PD symptoms (measured by UPDRS and Kinesia ONE) and mobility/balance (measured by TUG and mCTSIB) outcome measures. A secondary purpose of this study is to assess if participants continue to show improvements in motor function, gait, mobility, and balance after 3 sessions of dynamic cycling. A tertiary purpose of this study is to examine if different exercise exertion (HR, RPE, power/torque) levels affect the outcome variables (UPDRS, Kinesia ONE [Chapter 4], TUG, and mCTSIB [Chapter 5]). This work will build on previous studies (Ridgel et al., 2015) by providing data on both immediate and longer term (after 6 sessions) benefits of dynamic cycling. It is hypothesized that repeated bouts of dynamic cycling will promote progressive improvement motor function and balance in individuals with PD. The data from this study will also provide an important dataset that will be used to optimize the dynamic controller. This optimization is an important step in the development of an adaptive dynamic controller for PD exercise therapy.
CHAPTER II

REVIEW OF LITERATURE

What is Parkinson’s Disease?

In 1817 the condition “shaking palsy” was introduced by James Parkinson, which is now formerly known as Parkinson’s disease (PD). PD is a progressive, neurodegenerative disorder characterized by resting tremor, rigidity, bradykinesia, and loss of postural reflexes (Garcia-Borreguere, Larrosa, & Bravo, 2003). Behind Alzheimer’s disease, PD is the second most common neurodegenerative disorder (de Lau & Breteler, 2006), and affects 4–5% of the population by the age of 85 (Kim, Seok Ko, Dawson, & Dawson, 2006). The mean age of onset for PD is 55 years of age (Dauer & Przedborski, 2003). The prevalence is 1% after the age of 65 years (Samii, Nutt, & Ransom, 2004). Aging is one of the major risk factors for PD and the risk for developing the disease increases from ~1% at 65 years of age to ~5% at 85 years of age (Wood-Kaczmar, Gandhi, & Wood, 2006). There are three different forms of this disease: young-onset, sporadic (idiopathic), and heredity PD.

Although it is rare for younger individuals to develop PD, 10% of the people who have been diagnosed with this condition are younger than 45 years of age, which is called young-onset of PD (Lees et al., 2009). Young-onset of PD is thought to occur largely due to the accumulation of Lewy bodies, which are abnormal collections of protein that develop inside nerve cells (Schrag, Shlomo, Brown, Marsden, & Quinn, 1998). There are several differences between young-onset and older-onset PD in terms of clinical features, progression of disease, latency to time of first appearance of drug therapy motor
complications, and prognosis (Schrag et al., 1998). These differences among the two conditions of PD have drawn the assumption that there may be two types of this disease, one a predominant motor disorder with an earlier age of onset and the other with greater mental deterioration and a later age on onset (Schrag et al., 1998). However, due to the rarity of young-onset of PD making firm conclusions about this specific condition is difficult.

Even though most cases of PD have no genetic link, there is a described genetic link, which has increased the interest on hereditary susceptibility factors (Dauer & Przedborski, 2003). About 15–20% of individuals who suffer from PD have a positive family history of this disease in first-degree relatives, suggesting that genes may have a role (Di Fonzo et al., 2005). The heredity category has been divided into two subtypes: an autosomal recessive trait and a subtype with prominent tremor, dominant inheritance, and a high prevalence of family members with essential tremor (Calne & Langston, 1983).

In about 95% of PD cases, there is no apparent genetic linkage, which is referred to as sporadic or idiopathic PD (Dauer & Przedborski, 2003). Idiopathic PD may be the result of environmental and genetic factors (de Lau & Breteler, 2006). Further investigation of the potential causes of idiopathic PD is needed to understand the pathogenesis of this condition and to develop effective therapeutic strategies (de Lau & Breteler, 2006). The symptoms of idiopathic PD may occur due to the loss of dopamine, a neurotransmitter, within the nigrostriatal dopamine pathway, a circuit in the basal ganglia (Hirsch, Toole, Maitland, & Rider, 2003).
The primary symptom of PD is decreased motor movement due to interruptions in both reflexive and voluntary pathways (Glendinning & Enoka, 1994) and the inability for individuals to initiate and produce movement (Cutson et al., 1995). Proper execution of voluntary movements results from the correct processing of sensory-motor information in the brain (Glendinning & Enoka, 1994), but with PD, these neural networks become disrupted due to interruptions in the pathways or the presence of Lewy bodies (Blandini, Nappi, Tassorelli, & Martignori, 2000). PD is a destructive disease within the central, peripheral, and autonomic nervous systems that results in muscle weakness and stiffness, bradykinesia, and decreased mobility (Dibble, Hale, Marcus, Droge, Gerber, & LaStayo, 2006). This is a complex condition, in that, the cause of this disease remains unclear and it affects different systems within the brain including the motor, limbic, and autonomic regions (Braak & Braak, 2000). The complexity of the destruction, primarily in the basal ganglia, makes understanding the pathogenesis of PD difficult.

**Basal Ganglia**

In the 1950s Carlson observed that 80% of the dopamine in the brain is localized in the basal ganglia (Bartels & Leenders, 2009). The basal ganglia (See Figure 1) consist of five interconnected nuclei: the caudate nucleus, putamen, globus pallidus, substantia nigra, and subthalamic nucleus (Blandini et al., 2000). The neurodegenerative process of PD causes different pathways within the basal ganglia to be used (Blandini et al., 2000). The main regions in the basal ganglia for producing movement are the cortex and thalamus (Blandini et al., 2000). There are different levels of the cortex, and one level that may be impacted by PD is the substantia nigra pars compacts (Glendinning & Enoka,
1994). With PD, specific regions of the basal ganglia become hyperactive (Blandini et al., 2000) and result in motor movement deficits such as initiating voluntary movement and suppressing involuntary muscle movement (Mozley, Gur, Mozley, & Gur, 2001).

Figure 1. The basal ganglia are divided into several functionally distinct groups.
The substantia nigra pars compacts projects to the striatum, subthalamic nucleus and globus pallidus (Blandini et al., 2000). The striatum sends and receives signals sent by the cortex, substantia nigra pars reticulata, and medial globus pallidus through a direct and an indirect pathway (Blandini et al., 2000). A variation in PD symptomology can thus result from deficits in selective regions in the striatum and its connections with specific cortical pathways (Bartels & Leenders, 2009).

Abnormalities that occur due to disruptions in the basal ganglia might originate in the cortex or in other regions that receive input from the basal ganglia (Glendinning & Enoka, 1994). In PD, the pathways that originate in the basal ganglia are disrupted which affects how the signals are sent from region to region (Glendinning & Enoka, 1994). The complexity of the basal ganglia includes various brain structures, and in order to send neural signals the information from the basal ganglia travels through a direct and an indirect pathway. Each pathway is specifically designed to create different input that affects how the signals react to the motor neurons.

**Direct and Indirect Pathway**

The two pathways originate from different subsets of striatal neurons and remain segregated (Blandini et al., 2000). Through nigrostriatal pathways (connecting the substantia nigra and the striatum), dopamine influences both the direct and the indirect pathways creating different signals (excitatory and inhibitory; Cutson et al., 1995). Depending on the pathway, direct or indirect, the effect of dopamine on the striatum is different. In the direct pathway, dopamine appears to produce excitatory signals and in the indirect pathway dopamine produces inhibitory signals (Cutson et al., 1995).
**Direct Pathway**

In the direct pathway, signals are sent to the striatum, specifically the putamen (Bartels & Leenders, 2009). From the putamen, signals are sent to output nuclei (Globus Pallidus pars interna and the Substantia Nigra reticulate), which reduce the inhibitory response of these nuclei and as a result movement is produced (Bartels & Leenders, 2009). In the direct pathway, various cortical areas send input to the striatum and then the thalamus produces excitatory input to the cortex (Cutson et al., 1995). Figure 2 displays the loops within the direct pathway of the basal ganglia.

![Diagram of the direct pathway of the basal ganglia](image)

*Figure 2. The loops within the direct pathway of the Basal Ganglia are short, quick projections producing movement.*

**Indirect Pathway**

In the indirect pathway, the output nuclei are signaled in a more complex course then when compared to the direct pathway (Blandini et al., 2000). The putamen send signals to the output nuclei (Globus Pallidus pars external [GPe] and the Subthalamic Nucleus [STN]), which indirectly decreases the inhibition of the subthalamic nucleus
(Bartels & Leenders, 2009; Blandini et al., 2000). The output nuclei send signals to the thalamus which then sends the information to the cortex, closing the circuit (Blandini et al., 2000). This pathway uses the neurotransmitter glutamate that produces excitatory signals on the striatum, which increases the firing rate of the signals that are sent to the output nuclei, Globus Pallidus pars interna and the Substantia Nigra reticulate (Blandini et al., 2000). Figure 3 displays the indirect pathway loops of the basal ganglia.

Figure 3. The indirect pathway of the basal ganglia. In the indirect pathway, quick active decrease movement.

Pathophysiology of Parkinson’s Disease

Complications, specifically motor function, of PD occur due to neural impairments within different areas of the brain, specifically in the basal ganglia circuitry. The production of movement involves neurons receiving information from different regions within the brain including the descending brainstem and cortical pathways, and
from different sensory afferents (Glendinning & Enoka, 1994). Any disruptions within these areas lead to impaired movement since the pathways leading to the motor units have become altered (Glendinning & Enoka, 1994). The disruptions in motor units are thought to be caused by inconsistent discharge rates, activation of more motor units at low forces of contraction, a failure to recruit large motor units, and increased coactivation of antagonist muscles (Glendinning & Enoka, 1994). Large motor units are important because they may be responsible for fast movements; however, individuals with PD appear not to have these large motor units (Glendinning & Enoka, 1994). Thus, individuals with PD may have to recruit more motor units but as the number of motor units increase the action potential signals become less clear and may result in uncoordinated motor movements (Glendinning & Enoka, 1994). Additionally, antagonist muscles are abnormally coactivated, which creates disturbances in muscle movement and activation (Glendinning & Enoka, 1994).

**Dopamine**

Dopamine is a neurotransmitter that assists cells within the neural circuit in communicating to one another. It is produced in the substantia nigra compacta of the brain stem (Cutson et al., 1995), and regulates the substantia nigra and striatum (Baatile, Langbein, Weaver, Maloney, & Jost, 2000). Through different pathways, dopamine has a role in controlling movement, learning and memory, and motivation and personal reward (Vallone, Picetti, & Borrelli, 2000).

In addition to the different dopamine pathways, there are different dopamine receptors (D1, D2, D3, D4, and D5) located in the basal ganglia and are important in
cognitive and motor functioning (Mozley et al., 2001). These dopamine receptors are important because specific receptors are required for the binding of dopamine onto neurons (Vallone et al., 2000). The primary dopamine receptors are D1 and D2, which are postsynaptic on the substantia nigra (SN) and presynaptic on the substantia nigra pars compacta, respectively (Vallone et al., 2000).

Parkinson’s disease is the result of the loss of dopamine neurons in the substantia nigra pars compacta (Dauer & Przedborski, 2003). Dopamine depletion alters the basal ganglia circuit, which results in movement impairment (Bartels & Leenders, 2009). The progressive loss of dopamine producing cells in the basal ganglia may cause movements to become slow, and reduced in amplitude (M. Morris, Iansek, & Kirkwood, 2009). The presence of dopamine in the basal ganglia allows for proper communication between cells, but when dopamine levels decrease it results in a slow progression of the disease.

**Dopamine System**

The dopamine system is the pathway that is used by dopamine axons to connect to different areas of the brain so that a particular function can be performed. The dopamine system, much of which arises from the midbrain, consists of three main groups of neurons designated as areas A8, A9, and A10 (Smith & Kieval, 2000). The A8 group corresponds to an area posteriorly to the midbrain, called the retrorubral area, and the A9 and A10 groups are in the substantia nigra pars compacta and an area near the midbrain called the ventral tegmental (Smith & Kieval, 2000). Midbrain dopaminergic neurons are commonly divided into a dorsal and ventral tier that separate into many different parts of the brain (Smith & Kieval, 2000).
Many areas of the basal ganglia are the major targets for dopaminergic neurons, including the striatum, globus pallidus, and subthalamic nucleus (Smith & Kieval, 2000). Dopamine may increase its response by stimulating both pre- and postsynaptic receptors in various areas of the basal ganglia (Smith & Kieval, 2000). Striatum dopamine deficiency contributes to the bulk of parkinsonian abnormalities (Agid, 1991). The rate of loss of dopaminergic neurons in the substantia nigra is about 1% per year in individuals who develop PD, in contrast to 0.5% per year in normal individuals (Agid, 1991).

**Lewy Bodies**

Besides the effect that dopamine and the basal ganglia pathways have on the neurodegenerative aspects of PD, parkinsonian motor symptoms can occur due to the formation of Lewy bodies. Lewy bodies are a collection of protein consisting of α-synuclein, parkin, ubiquitin, and neurofilaments (Dauer & Przedborski, 2003). The formation of Lewy bodies is a result of altered “building blocks” of the protein filaments within a cell’s cytoplasm (Braak & Braak, 2000). The proteins that accumulate may have been flagged for removal but were never broken down (Samii et al., 2004). As a result, Lewy bodies begin to form in the cell body of neurons. Within the central nervous system, only a select few of the neurons develop Lewy bodies and this development appears to occur bilaterally symmetrical (Braak & Braak, 2000). Lewy bodies do not degenerate surrounding neurons; instead, PD appears to be a multifactorial disease that is linked to several factors working in unison (Kim et al., 2006). The presence of Lewy bodies is one marker used to confirm the diagnosis of PD. It seems that Lewy bodies
interrupt the flow of signals within the neural pathway and interferes with communication (Braak & Braak, 2000).

**Etiology of Parkinson’s Disease**

Neuropathology of PD arises from dopamine depletion and the formation of Lewy bodies. However, the exact trigger (or triggers) for the events that lead to dopamine depletion and Lewy bodies formation is not known. Proposed mechanisms are protein accumulation and phosphorylation, oxidative stress, exposure to environmental neurotoxins, and oxidative stress (de Lau & Breteler, 2006; Samii et al., 2004).

**Protein Accumulation**

The misfolding and collection of proteins (alpha synuclein, parkin, leucine-rich repeat kinase 2, and pink1) are primarily responsible for the death of dopaminergic neurons (Dauer & Przedborski, 2003). Protein accumulation could indirectly cause damage to surrounding neurons by deforming the cell or interfering with cellular communication (Dauer & Przedborski, 2003). Cells respond to misfolded proteins by inducing chaperones, which are proteins assisting in the protein folding when the cell is undergoing physiological stress, and if the protein is not properly refolded then these cells are targeted for degradation (Dauer & Przedborski, 2003). The exact mechanism by which abnormal protein accumulation leads to neuronal death is unknown (Samii et al., 2004). In idiopathic PD, altered protein formation or malfunctioning chaperones may lead to the accumulation of misfolded proteins (Dauer & Przedborski, 2003). A mutation in α-synuclein, parkin, pink1, DJ-1, and LRRK2 typically leads to PD (Kim et al., 2006).
**Alpha Synuclein**

The protein, α-synuclein, is normally expressed in all brain regions, including the substantia nigra pars compacta (Blandini et al., 2000). The exact function of α-synuclein protein is unknown, but it may be linked to the formation of Lewy bodies (Samii et al., 2004). There is strong evidence to suggest that α-synuclein accumulation might be an early step in the pathogenesis of both idiopathic and inherited PD (Wood-Kaczmar, Gandhi, & Wood, 2006). High levels of α-synuclein cause abnormal protein aggregation and neurotoxicity in dopamine neurons (Wood-Kaczmar et al., 2006). The overexpression α-synuclein protein depletes the dopamine neuronal cell line and causes apoptosis of dopamine neurons (Wood-Kaczmar et al., 2006). There is much evidence that α-synuclein cause oxidative stress which this may lead to dopamine neuron death (Kim et al., 2006).

**Parkin Gene**

Parkin plays a role in degrading defective proteins (Samii et al., 2004) and mutations in this protein may be the cause of young onset recessive parkinsonism (Wood-Kaczmar et al., 2006). Decrease in parkin appears to cause dopamine cell death (Wood-Kaczmar et al., 2006), but it remains unclear how the loss of parkin leads to dopaminergic neuron death (Dauer & Przedborski, 2003). In addition to dopamine depletion, reduced levels of parkin may lead to muscle degeneration and increased oxidative stress (Wood-Kaczmar et al., 2006). Parkin mutations are present in ~50% of all individuals with recessive early onset parkinsonism and in 77% of sporadic cases with disease onset before the age of 20 (Wood-Kaczmar et al., 2006).
**Leucine-Rich Repeat Kinase 2 (LRRK2)**

Mutations in LRRK2 may give rise to the symptoms of PD (Wood-Kaczmar et al., 2006). Indirectly LRRK2 helps with cell to cell communicate, cell replication, and cell growth (Wood-Kaczmar et al., 2006). Alterations in the LRRK2 gene may lead to apoptosis (Wood-Kaczmar et al., 2006). A single mutation in the LRRK2 gene has been identified as the most commonly known genetic cause in PD, accounting for 1% of sporadic forms and 5% of hereditary PD (Kim et al., 2006).

**PINK1**

Behind Parkin, PINK1 mutation are the second most-common cause of PD (Wood-Kaczmar et al., 2006). PINK1 is an amino acid that protects cells against apoptosis (Samii et al., 2004) but deformities in this protein may lead to the presence of Lewy bodies (Wood-Kaczmar et al., 2006). This protein may have a role in maintaining cell’s mitochondria function (Wood-Kaczmar et al., 2006). PINK1 seems to have a neuroprotective function that helps maintain mitochondria function but the role of mitochondrial function in PD remains unclear (Wood-Kaczmar et al., 2006).

**Oxidative Stress**

One trigger of protein accumulation may be oxidative stress, specifically reactive oxygen species (ROS; Dauer & Przedborski, 2003). Oxidative stress is a result of increased production or decreased elimination of extremely reactive free radicals including ROS. The presence of ROS may be linked to misfolded proteins (Dauer & Przedborski, 2003). Oxidative stress may occur because a part, complex 1 of the electron transport chain, of the mitochondria is malfunctioning which causes electrons to leak out
of the mitochondria and kill the neuron (Shimohama, Sawada, Kitamura, & Taniguchi, 2003). ROS may cause further damage in the mitochondria by targeting these malfunctioning areas, which leads to further neuron damage and death (Dauer & Przedborski, 2003). The relationship between oxidative stress and mitochondrial deficiency is unknown, that is, does a mutation in one cause a mutation in the other (Blandini et al., 2000).

**Apoptosis**

Apoptosis is programmed cell death, and although cell death is normal, it is accelerated in PD and may lead to neurodegeneration (Dauer & Przedborski, 2003). Apoptosis activity is regulated by glutamate, which can affect different receptors on a cell’s membrane (Blandini et al., 2000). Apoptosis can occur due to a mutation in Guanine-nucleotide proteins (G proteins), which is found inside neurons and monitors cell to cell communication (Blandini et al., 2000). A mutation in G protein leads to disruption in communication and protein formation (Blandini et al., 2000).

**Environmental Neurotoxicity**

The pathogenesis of PD is not completely understood but environmental and genetic factors are believed to play important role (Shimohama et al., 2003). In a rural environment there may be increased exposure to herbicides and pesticides, which increases the risk for developing PD (Dauer & Przedborski, 2003). Pesticide exposure has been linked to the development of idiopathic PD (Shimohama et al., 2003).

A dopamine neurotoxin called 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) freely crosses the blood-brain barrier and is converted to 1-methyl-4-
phenylpyruvdonium (MPP+) which binds to dopamine receptors and accumulates in the mitochondria (Shimohama et al., 2003). Once inside the mitochondria, MPP+ impairs oxidative processes in the electron transport chain (Dauer & Przedborski, 2003). This inhibition reduces ATP, energy, generation and causes the production of ROS leading to apoptosis of dopamine neurons (Shimohama et al., 2003). MPTP ultimately leads to neurodegeneration (Dauer & Przedborski, 2003).

Like MPP+, rotenone also affects the mitochondrial of cells by inhibiting specific complexes within this structure and eventually leading to dopamine neuron death (Dauer & Przedborski, 2003). Dopaminergic neurons are preferentially sensitive to mitochondrial complex inhibition (Dauer & Przedborski, 2003). Rotenone is a naturally occurring pesticide derived from the roots of particular plant species (Shimohama et al., 2003).

**Diagnosis of Parkinson’s Disease**

In order to confirm the diagnosis of PD, an autopsy needs to be performed (Samii et al., 2004) in which the formation of Lewy bodies and evidence of dopaminergic neuron loss of the substantia nigra pars compacta both have to be identified (Dauer & Przedborski, 2003). Clinically, PD is diagnosed by having three or more of the following symptoms: unilateral symptom onset, excellent response to levodopa (drug therapy), resting tremor, severe levodopa-induced chorea, progressive disorder, continued levodopa response for 5 years or more, persistent asymmetric symptoms, and clinical course of over 10 years. Sustained improvement of motor symptoms with levodopa is generally a feature of PD (Samii et al., 2004), along with weak and clumsy limbs,
postural abnormalities, stiff and aching limb, immobile and rigid facial expression, slow expression of emotions, slow or quiet speech that is irregular in rhythm and melody, and gait dysfunctions (Nutt & Wooten, 2005).

When diagnosing PD, a clinical must be careful not to mistake parkinsonism for PD. Parkinsonism is a common movement disorder and PD is the most common cause of parkinsonism (Nutt & Wooten, 2005), which accounts for ~80% of cases (Dauer & Przedborski, 2003). Current diagnosis of parkinsonism requires tremor, bradykinesia, rigidity, or postural instability, which are considered the cardinal symptoms of PD (de Lau & Breteler, 2006).

The diagnosis of PD appears to be higher in men than women, which could be due to the neuroprotective effects of estrogen (Samii et al., 2004). Estrogen is found in the cortical and subcortical areas, including the striatum (Mozley et al., 2001). The lack of estrogen in males has been suggested as a possible explanation for a higher incidence of PD in men (de Lau & Breteler, 2006).

**Symptoms of Parkinson’s Disease**

The classical clinical features of PD are progressive tremor, rigidity, and bradykinesia (Michell, Lewis, Foltynie, & Barker, 2004). Of the cardinal symptoms, resting tremor is typically seen first in individuals (Samii et al., 2004). These cardinal symptoms cause difficulty in initiating movement, slowness and difficulty in maintaining movement, stiffness in arms, legs, and trunk, postural instability and tremor (Kwakkel, Goede, & Wegen, 2007). Commonly, PD symptoms appear asymmetric (Samii et al., 2004). Other side effects of PD are diminished expression, kyphotic posture, seborrhea
(excess oil secreted from an exocrine gland), sialorrhea (drooling or excessive salivation), muscle aches or cramps, depression, dementia, dysarthria, dysphagia, orthostatic hypotension, bladder problems, and sexual problems (Baatile et al., 2000; Cutson et al., 1995).

Movement appears to be most affected in individuals with PD because recruitment patterns of motor units change which causes abnormalities in their firing commands (Glendinning & Enoka, 1994). As a result, secondary musculoskeletal symptoms occur such as stooped posture, kyphosis, head flexion, shoulder protraction, and knee or elbow contractures (Cutson et al., 1995). Despite the efficacy of levodopa and related drug therapy, patients experience increasing difficulties with time (Agid, 1991). Over time, medications and drug therapy lose their effectiveness on controlling fluctuations in motor movement and not all symptoms of PD respond to medications, such as gait and postural instability (Agid, 1991). As these complications begin, individuals with PD gradually reduce their movement and physical activity (Canning, Alison, Allen, & Groeller, 1997).

**Tremor**

Tremor may be the result of coactivation of both the agonist and antagonist muscles, which occur due to the output nuclei in the basal ganglia receiving abnormal signals (Glendinning & Enoka, 1994). It is often the most visible symptom of PD (Bartels & Leenders, 2009). Tremor can be classified into different types, such as resting, kinetic, or postural. The most common tremor seen in PD is the resting tremor, which occurs in a resting limb but usually dampens with the onset of voluntary
movement (Nutt & Wooten, 2005). Resting tremor has a frequency of 3-5 Hz and worsens as the disease progresses (Samii et al., 2004). Tremor worsens with anxiety, contralateral motor activity, and during ambulation (Samii et al., 2004). Tremor is often more difficult to treat, and in some patients it only disappears after several years of treatment, which might indicate a delayed pharmacological effect or evolution of the disease (Lees et al., 2009).

**Rigidity**

Rigidity is the stiffness in joints and is noticed throughout the entire range of movement (Samii et al., 2004). The stiffness that accompanies rigidity may cause aching and discomfort in the affected limbs (Nutt & Wooten, 2005), which could lead to conditions such as the frozen shoulder and masked face expression (Cutson et al., 1995; Nutt & Wooten, 2005). Muscular rigidity is a disabling symptom of PD and results in decreased range of movement and slowness, as well as fatigue (Cutson et al., 1995). The development of rigidity is not fully known, but it may occur due to individuals with PD having an altered stretch reflex response or there is an increase in the excitability of motor neurons causing altered firing patterns (Glendinning & Enoka, 1994). It seems that PD patients have decreased activity in their Golgi tendon organs, which could affect how sensory information is sent to the central nervous system PD (Glendinning & Enoka, 1994). Additionally, PD alters how the reciprocal inhibition, a circuit that allows a group of muscles to contract while another group of muscles relax, functions which could increase the muscle stiffness (Glendinning & Enoka, 1994).
Bradykinesia

Bradykinesia, or the slowness of movement, is a common symptom and usually develops along with rigidity (Cutson et al., 1995). The slowness and reduction in movement increases the amount of time it takes individuals to complete tasks and activities of daily living, and ultimately decreases their independency (Cutson et al., 1995). Of the cardinal symptoms of PD, bradykinesia is the most disabling symptom (Samii et al., 2004) and requires extensive concentration from patients when completing simple tasks (Glendinning & Enoka, 1994). Bradykinesia begins asymmetrically in about 75% of patients, and often results in muscle weakness, difficulty in walking, speaking, or getting into and out of chairs, and eventually leading to the inability to move (Glendinning & Enoka, 1994; Nutt & Wooten, 2005).

It is believed that bradykinesia is the result of inability to excite the cortex within the basal ganglia (Glendinning & Enoka, 1994). As a result, motor neurons are not stimulated fully and produce small and weak movements (Glendinning & Enoka, 1994). Bradykinesia may significantly impair the quality of life of patients due to the prolonged amount of time it takes to complete very simple tasks, such as dressing and eating (Dauer & Przedborski, 2003). Decreased muscle speed also leads to multiple secondary symptoms of PD, such as masked face, excessive salvia, altered speech, and small handwriting (Bartels & Leenders, 2009).

Akinesia

Akinesia is the inability to remain still due to the manifestation of restlessness and the need to change positions (Ford, 2010). Individuals have extreme difficulty with
voluntary movement and often have the inability to initiate movement (Bartels & Leenders, 2009). Akinesia may occur due to deficits in motor planning which may be the result of dopamine depletion within the basal ganglia (Ford, 2010). Parkinsonian akinesia can be severe; patients may be unable to sit, drive a car, eat at a table, or attend social gatherings (Ford, 2010).

**Postural Instability**

Postural instability usually begins in the late stages of the disease and is often the most challenging symptom to overcome (Lees et al., 2009). The inability to gain/regain balance is likely related to bradykinesia, which is the result of dopamine depletion (Cutson et al., 1995). Side effects of postural instability include patients having a fear of falling, increased immobilization, and stooped posture (Dauer & Przedborski, 2003; Lees et al., 2009). The incidence of falls and reoccurrence of falls increases in individuals with PD, which typically occur when patients are in a forward or sideways direction and are attempting to complete a turn (Lees et al., 2009). As postural instability beings to manifest, individuals alter their gait by taking quicker and shorter strides, which is termed shuffling gait (Cutson et al., 1995).

**Gait Abnormalities**

PD gait is characterized by shuffling, small slow steps, decreased arm swing, and a forward bended posture (Bartels & Leenders, 2009). Mobility becomes slower, with shuffling, and turning done as one motion (Samii et al., 2004). Some patients experience sudden cessation of movement called freezing episodes, which may be the result of bradykinesia (Cutson et al., 1995). Freezing of gait (FOG) is a sudden disturbance of
gait, where patients feel stuck with their feet being “glued to the floor,” and occurs in 30–60% of PD patients (Bartels & Leenders, 2009). FOG frequently happens in challenging situations with increased “mental stress,” and can often be overcome by applying external tricks such as visual cues (Bartels & Leenders, 2009). FOG is a common, yet poorly understood symptom of PD and can be manifested as start hesitation, turn hesitation, target hesitation, and sudden transient hesitation (Bhidayasiri & Truong, 2008).

**Non-Motor Deficits**

Typically, non-motor features are considered secondary complications of PD, and result from the motor deficits. Non-motor features include autonomic dysfunction, cognitive and psychiatric changes, sensory difficulties, and sleep disturbances (Samii et al., 2004).

**Cognitive Deficits**

Individuals with PD typically have difficulty with attention control, working memory, reasoning, problem solving, and planning, which collectively is known as deficits in executive function (Bartels & Leenders, 2009). Along with cognitive deficits, individuals may develop psychological problems, such as depression and emotional instability (Cutson et al., 1995). About 25–40% of the patients with PD eventually develop dementia due to the spread of neural degeneration and Lewy bodies development in the brain (de Lau & Breteler, 2006). The combination of dementia and the drugs used to treat parkinsonism can lead to hallucinations and psychotic behavior in some individuals (Samii et al., 2004).
Sleep Disorder

There is a ‘sleep-related hypothesis’ that states during sleep there is an accumulation of dopamine within the brain (Garcia-Borreguero et al., 2003). However, about 74–81% of PD individuals have interrupted sleep or a decreased amount of total sleep time than healthy individuals (Garcia-Borreguero et al., 2003). Thus, according to the sleep-related hypothesis, PD individuals do not effectively accumulate dopamine during this time. The combination of the reduced sleep efficiency and an increased number of awakenings contributes to the sleep disorder experienced by PD patients (Garcia-Borreguero et al., 2003). PD often results in frequent awakenings (~2–5 per night) during the night and a difficulty falling back to sleep after being awake (Garcia-Borreguero et al., 2003). Additional motor abnormalities during sleep are increased muscle tone (repetitive muscle contractions), restless leg syndrome, and rapid eye movements (REM) during non-rapid eye movement (NREM) sleep (Garcia-Borreguero et al., 2003). As a result of the disturbed sleeping, PD patients show an increase in excessive daytime sleepiness (Garcia-Borreguero et al., 2003).

The cause for sleep disorders in PD is multifactorial, including disease progression and symptoms, age and related comorbidities, and treatments (Garcia-Borreguero et al., 2003). One explanation for sleep disturbances is that the circadian rhythm, located in the basal ganglia, is altered (Garcia-Borreguero et al., 2003). The loss of neurotransmitters within the basal ganglia circuit affects the function of the circadian rhythm (Garcia-Borreguero et al., 2003). Therefore, PD places individuals at a higher risk for sleep disorders due to the basal ganglia not functioning properly.
**Apathy**

Apathy is a multifactorial condition that leads to reduced interest in things, decreased motivation, lack of concern, and a flattening effect (Pluck & Brown, 2002). Approximately 16.5–42% of people with PD will experience apathy (Pluck & Brown, 2002). Apathy has a direct impact on the overall level of handicap, as it reduces participation in age appropriate activities above and beyond that due to other aspects of the disease (Pluck & Brown, 2002).

**Pain**

Pain is a frequently overlooked clinical feature of PD that may be severe enough to overshadow the motor symptoms of the disorder (Ford, 2010). Approximately 40% of patients with PD experience pain, and in severe cases pain becomes the most distressing symptom (Ford, 2010). Often, the source of pain is caused by muscle cramps and back pain (Ford, 2010). However, pain can affect many different areas on the body including the face, head, pharynx, epigastrium, abdomen, pelvis, rectum, and genitalia (Ford, 2010).

The pain pathway in individuals with PD appears to be altered, specifically in the nociceptive (pain) receptors (Ford, 2010). Other reasons for pain may be related to the Neuropathic central pain (NCP), which is difficult to treat (Ford, 2010). NCP may arise due to lesions affecting the somatosensory system (Ford, 2010).

**Quality of Life (QOL)**

QOL is affected by the symptoms of the disease, progression of the disease, and treatment (Bhidayasiri & Truong, 2008). As the disease progresses, individuals begin to
lose their functional status and their independency (Burini et al., 2006). As a result of the combined central nervous system (CNS) impairments and peripheral muscular impairments, many individuals with PD enter into a downward spiral of immobility (Dibble, Hale, Marcus, Droge, et al., 2006). The last stages of the disease result in progressively increased deficits in muscle strength, mobility, and quality of life (Dibble, Hale, Marcus, Droge, et al., 2006).

**Disease Progression**

There are different stages of PD and with the progression of each stage the severity of the disease progresses in motor and secondary complications. The stages of PD are typically divided into three stages, which are newly diagnosed (Hoehn-Yahr stage I), moderately severe disease (stages II and III), and advanced disease (stages IV and V; Calne, 1993). The frequency of motor complications progresses as the years of the disease increase, such that after one year of being diagnosed 3% of individuals have motor deficits, 41% after six years, and 70% after nine years (Bhidayasiri & Truong, 2008).

**Early Phase of PD**

In the very early stages, patients may complain of specific symptoms (shaking in one hand, weakness in a leg) but they remain independent and still have a good QOL (Cutson et al., 1995). Early signs of PD including deficits with coordination and fine motor skills and decreased ability to produce repetitive movements (Nutt & Wooten, 2005). Postural and gait abnormalities are rarely seen in the early stages of PD (Samii et al., 2004). In this stage, patients typically respond well to drug therapy specifically
levodopa (Bhidayasiri & Truong, 2008). Oftentimes, individuals will be encouraged and instructed to engage in an exercise program, consisting of stretching, muscle strengthening, cardiovascular fitness, and balance training (Nutt & Wooten, 2005). This early stage of PD, often called the presymptomatic phase, lasts ~5 years (Michell et al., 2004).

**Moderately Severe Phase of PD**

At the beginning of the moderate severe phase, individuals have increasing symptoms, yet they remain functional, with some limitations, but can still complete activities of daily living (Cutson et al., 1995). In most patients the first sign of motor complications is that the effects of levodopa are lasting shorter and shorter (Bhidayasiri & Truong, 2008). This causes symptoms of PD to reappear after 4 hours or less of taking levodopa (Bhidayasiri & Truong, 2008). Toward the end of the moderate severe stage, patients’ symptoms become more severe and they begin experiencing difficulty and slowness in movement and may require assistance with functional activities (Cutson et al., 1995). The symptoms that are often seen in this stage are gait disturbances, difficulties with balance control, and falls (Cutson et al., 1995). Clinical fluctuations may be emerging faster requiring further adjustment of medications (Cutson et al., 1995). Managing medications at this point is important to help control the cardinal symptoms of PD (Cutson et al., 1995).

For this stage of PD, the goals of physical intervention are to correct musculoskeletal impairment where possible and to try and slow the progression of the disease (Cutson et al., 1995). Individuals are still encouraged to engage in an exercise
program that includes range of motion, posture, and function exercises (Cutson et al., 1995). With the progression of this disease, patients frequently will have motor planning problems, which further limit their freedom of movement (Cutson et al., 1995). In addition, patients may be referred to speech therapy to assist in their verbal communication and help with any swallowing deficits (Cutson et al., 1995).

**Advanced Phase of PD**

During the advanced stage of PD, the progression of the disease has led to multiple symptoms including rigidity and bradykinesia, which result in immobility (Cutson et al., 1995). The individual movements are slow and are typically done as one piece, which is accompanied by falls and uncomfortable movements (Lees et al., 2009). In this stage, individuals lose their independency and need assistance with dressing, feeding, bathing, and functional movements (Lees et al., 2009). Patients experience extreme fatigue due to the energy that is expended during pulmonary and swallowing functions (Cutson et al., 1995). PD patients display an unstable medication response, which leads to further motor complications such as dyskinesia (Bhidayasiri & Truong, 2008). This unpredictability in medication response decreases patients QOL because they cannot count on having their motor fluctuations controlled at any particular time and the transition between symptoms being controlled and not controlled occurs abruptly (Bhidayasiri & Truong, 2008). The term “complex fluctuations” previously known as “on/off” phenomenon or “yo-yo-ing,” was recently introduced to characterize patients with advanced disease who develop the most unpredictable of fluctuating states (Bhidayasiri & Truong, 2008). Drug therapy is directed toward decreasing the dose of
whichever drug is causing the most troublesome side effects (Calne, 1993). The most common problems that occur during long-term therapy are dyskinesia, fluctuations in mobility, increasing confusion, and psychosis (Calne, 1993).

**Treatment of Parkinson’s Disease**

The traditional treatment of PD is through the administration of drugs to help ease the symptoms (Calne, 1993). Often, the drug treatment will consist of a form of dopamine to increase the concentration within the basal ganglia (Calne, 1993). With time (5–10 years), drug therapy begins to lose effectiveness in treating PD (Scandalis, Bosak, Berliner, Helman, & Wells, 2001). Drug therapy is warranted when the patient is sufficiently bothered by symptoms or when the disease is producing disability (Nutt & Wooten, 2005). Optimal management of PD involves both pharmacologic treatment and encouragement of physical activity (Hirsch et al., 2003) because some symptoms (postural instability, falling, and gait abnormalities) of PD are restraint to pharmacological treatment (Kwakkel et al., 2007). The treatment of PD is a multi-dimensional process that may involve pharmacological and rehabilitation management, in addition to other mechanisms such as stimulation and surgery.

**Agonist**

The use of dopamine agonists is associated with a reduced occurrence of motor complications (Blandini et al., 2000). These agonists act directly on D2 dopamine receptors and effectively ease rigidity and bradykinesia (Calne, 1993; Cutson et al., 1995). Common agonist medications are levodopa, anticholinergic, and seliginline.
Levodopa

Levodopa offers the best symptom management and is a commonly used drug in treating PD (Bhidayasiri & Truong, 2008). Levodopa helps dopamine across the blood-brain barrier and enter into specific receptors on neurons (Cutson et al., 1995). Clinical data suggest that levodopa either slows the progression of PD or has a prolonged effect on the symptoms of the disease (Bhidayasiri & Truong, 2008; Crosby, Deane, & Clarke, 2003). With time, levodopa loses its effectiveness on symptoms, and complications such as dyskinesia, clinical fluctuations, akinesia, and psychiatric disturbances occur (Cutson et al., 1995). With each year of levodopa treatment, about 10% of patients will develop motor complications (Bhidayasiri & Truong, 2008). The dyskinesia and clinical fluctuations may be managed by lowering the dosage of levodopa and increasing the frequency of administration (Cutson et al., 1995). Toxicity of levodopa can occur from prolonged use and can contribute to the degenerative process of PD (Blandini et al., 2000).

Anticholinergic Drugs

Anticholinergic drugs have a slight effect on the clinical manifestations of PD (Calne, 1993). They act by correcting the imbalance between dopamine and acetylcholine in the striatum of patients with PD (Calne, 1993; Cutson et al., 1995). However, adverse side effects of anticholinergics include memory impairment, hallucinations, dry mouth, constipation, urinary retention, and blurred vision (Cutson et al., 1995).
**Seligiline**

Seligiline delays the need for levodopa in PD patients through decreasing the number of free radicals and protecting damaged neurons (Cutson et al., 1995). Seligiline has also been shown to prevent the development of parkinsonian symptoms induced by the neurotoxin MPTP (Cutson et al., 1995).

**Deep Brain Stimulation (DBS)**

Deep brain stimulation is a surgical treatment option that involves implanting electrodes in certain areas of the brain so that electrical impulses can interact with cells and chemicals (Benabid, 2003). Typically, surgery is reserved for when the disease and the side effects of drug therapy are severely disabling (David et al., 2012). Drug therapy and deep brain stimulation in conjunction can help relieve symptoms and improve muscle strength (David et al., 2012). However, there are risks associated with DBS such as urinary tract infection, aspiration pneumonia, and bacterial infections, which occur in 50% of individuals (David et al., 2012).

**Exercise**

The combination of pharmacological and nonpharmacological appears to be one of the most commonly used methods in managing PD (Rubinstein, Giladi, & Hausdorff, 2002). Individuals can gain a lot of benefit from exercise such as maximizing functional ability, improving mobility, decreasing the risk for falls, improving sleep habits, and minimizing secondary complications (Kwakkel et al., 2007; M. Morris et al., 2009). Drug therapy in conjunction with exercise helps individuals manage their symptoms that may be eased with medication (tremor) and symptoms that are restraint to medication.
(postural instability; Li et al., 2012). People with PD are three times more likely to sustain a hip fracture as a result of a fall when compared to a healthy individual (Goodwin, Richards, Taylor, Taylor, & Campbell, 2008). Regular physical and mental exercise should be encouraged at all stages of PD (Lees et al., 2009).

The purpose of any PD exercise intervention should be to maximize a patient’s ability to function independently by improving walking ability, balance, muscle strength, and cardiovascular endurance (Allen et al., 2012). Exercise appears to decrease extra muscle activity, helping with tremor, while improving range of motion throughout joints and delaying dyskinesia (Cakit et al., 2007). In fact, exercise may be the best at treating musculoskeletal changes that occur as a result of rigidity, bradykinesia, loss of mobility, and inactivity (Allen et al., 2012). Repetitive exercises for range of motion, endurance, balance and gait, and fine motor dexterity demonstrated benefit in areas of rigidity and bradykinesia (Dibble, Hale, Marcus, Droge, et al., 2006). Individuals with PD also gain improvements in psychological well-being, including increase self-efficacy, memory, and confidence when engaging in an exercise program (Baatile et al., 2000). Although exercise has shown to be beneficial for PD, individuals with this disease tend to decrease their physical activity levels (Goodwin et al., 2008).

**Exercise Regimens for PD**

Some forms of exercise may increase dopamine levels, by increasing production in remaining neurons, within the central nervous system and ease the symptoms of PD (Baatile et al., 2000; Goodwin et al., 2008). The best type of exercise to increase dopamine production is still unclear, but it appears that frequency, intensity, and duration
of the exercise is important (Baatile et al., 2000). Exercise may decrease striatum hyperexcitability, which could allow processing signals within that area to become clearer and more precise (Ahlskog, 2011). Although the release of dopamine receives much attention, the question remains whether other mechanisms (such as activity-dependent neuroplasticity and brain derived neurotrophic factor [BDNF]) occur in response to exercise (Petzinger et al., 2010).

One benefit of exercise may be activity-dependent neuroplasticity, or the ability of the brain to create and utilize new neural pathways in response to physical activity (Petzinger et al., 2010). Activity-dependent neuroplasticity may lead to other processes such as neurogenesis, synaptogenesis, and molecular adaptations (Fisher et al., 2008). Activity-dependent neuroplasticity can occur due to neurotrophic factors or a greater concentration of oxygen (Goodwin et al., 2008). What remains unclear about activity-dependent neuroplasticity are the impact that exercise parameters such as intensity, specificity, difficulty, and complexity have on promoting this mechanism (Petzinger et al., 2010).

The potential for exercise intensity to drive activity-dependent neuroplasticity needs further investigation; however, it does appear that exercise intensity impacts the cortical silent period (CSP; Fisher et al., 2008). CSP is a reflection of corticomotor excitability, where a higher excitability is represented with a shortened CSP period (Fisher et al., 2008). Interestingly, abnormal CSP durations, short durations, are often reported in individuals with PD (Fisher et al., 2008). High intensity exercise has been reported to lengthen the CSP to maximum duration in individuals with PD (Fisher et al.,
Thus, these findings may link the importance of exercise intensity on releasing dopamine (Petzinger et al., 2010).

Another benefit of exercise may be an increase in BDNF (Fisher et al., 2008). BDNF may help protect dopamine neurons within the substantia nigra and striatum in individuals with PD (Ahlskog, 2011). A relationship may exist between BDNF concentrations and exercise intensity, which is as exercise intensity increases so does the BDNF concentration levels (Ahlskog, 2011). There are many benefits of BDNF, such as the neurotrophic and neuroprotective properties, which can enhance brain plasticity (Fisher et al., 2008). These properties may assist in neuronal growth, synaptogenesis, and neuromotor recovery (Hirsch et al., 2003).

Although there are many benefits of exercise, currently there are no guidelines for individuals with PD (Keus, Bloem, Hendriks, Bredero-Cohen, & Munneke, 2007). An obstacle that may prevent exercise guidelines is the various symptoms and progression of the disease (Scandalis et al., 2001). Exercise has been proven to be beneficial for PD patients but it remains unclear as to what type of exercise is best for these individuals and what is the optimal exercise intensity for PD.

**Balance Training and Tai Chi**

Tai chi, a balance-based exercise, has been shown to improve balance and postural stability in PD (Hackney & Earhart, 2009; Li et al., 2012). Li and colleagues demonstrated that a 24-week tai chi program, performed twice-weekly, improved postural stability and functional outcomes in patients with mild-to-moderate PD (Li et al., 2012). Hackney and Earhart demonstrated that after 20 one-hour sessions of tai chi individuals
with PD improved their scores on the Berg Balance Scale and Timed Up and Go (Hackney & Earhart, 2009).

**Dance-Tango**

The tango is a partner dance that consists of rhythmic and metered movements (Hackney & Earhart, 2009). Hackney and Earhart demonstrated that after 20 one-hour sessions 2 times per week, of tango individuals with PD improved on the Berg Balance Scale, six minute walk test, and backward stride length (Hackney & Earhart, 2009). Similar, Hackney and colleagues found that 20 one-hour sessions of tango improved scores on the UPDRS and Berg Balance Scale, with a trend towards improvement in the Timed Up and Go test, in individuals with PD (Hackney, Kantorovich, Levin, & Earhart, 2007).

**Body Weight Supported Treadmill Training**

Treadmill training has been used in individuals with PD to improve gait, mobility, and postural stability (Cakit et al., 2007; Herman, Giladi, Gruendlinger, & Hausdorff, 2007; Pohl, Rockstroh, Ruckriem, Mrass, & Mehrholz, 2003). A study done by Cakit and colleagues reported eight weeks of progressive increase in walking speed on the treadmill improved mobility, postural stability, and reduced fear of falling in individuals with PD (Cakit et al., 2007). Pohl and colleagues compared the immediate effects in gait function after 30 minutes of walking on the treadmill in three different conditions: speed-dependent training (STT), limited progressive training (LTT), and conventional gait training (CGT), and found that greater gait improvements were seen in STT and LTT (Pohl et al., 2003).
Another type of treadmill training involves a harness that supports individual’s body weight, called body weight supported treadmill training (BWSTT). Fisher and colleagues found that 45 minutes of BWSTT improved gait parameters and mobility in individuals with PD (Fisher et al., 2008). Similarly, Miyai and colleagues showed that 45 minutes of BWSTT three times a week produced greater improvement in activities of daily living, motor performance and ambulation than voluntary exercise in PD (Miyai et al., 2000). Another study performed by Miyai and colleagues reported 45 minutes of BWSTT three times a week improved gait for 4 months in individuals with PD (Miyai et al., 2002). Herman and colleagues studied the effects of intense BWSTT on gait rhythmicity, and reported improvements in QOL and gait stability in individuals with PD (Herman et al., 2007).

**Cycling (Dynamic)**

Dynamic cycling is performed on a motorized bicycle, and if needed the motor can assist individuals in maintaining a specific cadence, speed. Ridgel and colleagues demonstrated that eight weeks of FE (30% more than individual’s preferred work rate) improved motor function in the upper limbs (Ridgel et al., 2009). Another study by Ridgel and colleagues found that 30 minutes of active-assisted cycling (AAC) improved tremor and bradykinesia in the upper extremity in individuals with PD while in the off medication state (Ridgel et al., 2012). In a separate study, Ridgel and colleagues found that 3 one-hour sessions of dynamic cycling (75–85 rpm) for 30 minutes improved tremor and bradykinesia in individuals with PD (Ridgel et al., 2015).
Research has demonstrated that high intensity exercise improves motor functions of PD; however, there is still a need to determine what aspects of exercise are most important (intensity, complexity, specificity, and duration) and whether the benefits received from exercise occur immediately after exercise. Additionally, there is a need to investigate if increasing the bouts of dynamic cycling will lead to an increase in motor function. Ridgel and colleagues (Ridgel et al., 2015) found that 3 sessions of dynamic cycling improved bradykinesia and tremor; however, this study investigates if extending the number of exercise sessions to 6 produces additional benefit and if these improvements occur immediately after each bout of exercise.
CHAPTER III

METHODOLOGY

Recruitment

Participants were recruited for this study from support groups, from a local Parkinson’s symposium, and from a list of individuals who previously participated in studies at Kent State University. All participants obtained a clearance from their physician prior to baseline testing. When an individual was eligible to participate in the study, they received a phone call from the researcher to set up an initial appointment. At that time the participant visited Kent State University’s Exercise Physiology laboratory to sign an informed consent and HIPPA (Appendix A), and baseline data (UPDRS, Kinesia ONE, TUG, and mCTSIB) were collected along with the participant being familiarized with the protocols.

Sample Size Calculation

An apriori sample size calculation was conducted to calculate the number of participants needed to maintain a power of at least 0.80. A matched pairs, one tail, \( t \)-test was performed on the mean difference in Unified Parkinson’s disease rating scale (UPDRS) scores between the pre- and post-test in dynamic cycling after three sessions of dynamic cycling. For this power analysis, the following information was entered into a computer program called GPower: effect size = 0.554, alpha error probability = 0.05, power (1 - \( \beta \) error probability which is the chance of committing a type 2 error) = .8. From the information that was entered, the following information was obtained: critical \( t \) = 1.72, degrees freedom = 21, sample size = 22, and actual power = 0.81.
**Inclusion**

Only individuals who were diagnosed with idiopathic PD, in phases 1, 2, or 3 according to the Hoehn and Yahr scale, were included in this study (Goetz et al., 2004). All individuals were between the ages of 50–79 years old and had no contraindications to exercise including untreated cardiovascular disease or stroke. Participants were ambulatory with the ability to follow simple instructions. Individuals had the ability and willingness to comply with a 3-week dynamic cycling exercise program. Participants remained on stable doses of anti-Parkinson medications, which was consistent through the testing and intervention protocol. Participants were pre-screened with the American Heart Association/American College of Sports Medicine exercise pre-participation questionnaire, and were required to obtain approval from their physician. Upon approval for the study, participants completed an informed consent and a health history questionnaire to fully assess their physical health. Approval was obtained from Kent State University’s Institutional Review Board (IRB).

**Exclusion**

The exclusion criteria disqualifying participants from the study included: not between the ages of 50–79 years old, not diagnosed with PD, or those who were diagnosed with PD but were identified as high risk. Individuals with unpredictable motor fluctuations, with uncontrolled dyskinesia, and with a history of any neurological (stroke, multiple sclerosis), cardiovascular (recent heart surgery, pacemaker), hematological, or orthopedic condition that limits their ability to participant in dynamic cycling were excluded from the study.
**Risk Minimization**

Current research indicates that exercise is safe and beneficial for individuals who have PD, and may slow the progression of this disease through the release of neurotrophins that have a supporting role in neuroplasticity (Alberts et al., 2011). Specifically, cycling is a type of exercise that can be performed when individuals may be declining in postural stability and gait. Cycling is a mode of exercise that can increase the heart rate in individuals, but does not lead to quick fatigue, such as walking on a treadmill (Alberts et al., 2011). This study follows similar protocols to a dynamic cycling PD study that was done by Ridgel and colleagues (2015), who concluded that a dynamic cycling protocol is safe and beneficial for PD individuals.

For any individual there will always be a risk for medical complications, such as heart attack and sudden death, when engaging in exercise. To minimize this risk, a clearance was obtained from a physician prior to any data being collected. When individuals reported to the Exercise Physiology laboratory to exercise, there was always an exercise physiologist present to ensure proper technique was being used throughout the exercises and to provide guidance throughout the program. The exercise physiologist monitored any symptoms and discomfort that the participants may have experienced, and participants were allowed to stop exercising at any time. Participants were instructed to stop exercising if they experienced chest pain, shortness of breath, pallor, fainting, wheezing, light-headiness, confusion, nausea, cold and clammy skin, noticeable change in heart rhythm, severe fatigue, and any other discomfort.
To ensure proper attention and focus was being provided the participant the research ratio (2:1) was low. Participants were instructed on how to stay within their target exercise intensity and how to maintain their prescribed pedaling rate (revolutions per minute [RPM]), which was found on a display screen on the cycle ergometer. The participants’ heart rates were recorded through a heart rate monitor and were obtained every second, and their ratings of perceived exertion (RPE) were recorded every minute throughout the exercise protocol. Individuals were instructed to decrease the resistance or stop cycling if their heart rate exceeded 80% of their heart rate reserve.

**Protocol**

When individuals were telephoned and they responded with interest to participate in the study, the researcher screened the individual for inclusion and exclusion criteria and further explained the study protocol. After an individual was screened, and he or she met the inclusion criteria, the researcher faxed an exercise clearance form to the participant’s primary care physician so that approval to exercise could be obtained. After clearance was obtained, participants were asked to come to Kent State University’s exercise physiology laboratory. The participant’s first session of the study consisted of three different components: (a) familiarization period, (b) baseline testing, and (c) intervention (dynamic cycling or stretching). During the familiarization period, the participants signed an informed consent form and completed a health history questionnaire; then the researcher further explained and demonstrated the assessment tests. Prior to having the participant complete baseline testing, the researcher obtained resting heart rate, RPE, and blood pressure. Baseline testing consisted of having the
participant complete the assessment tests, which included the unified Parkinson’s disease rating scale (UPDRS), Kinesia ONE, modified clinical test of sensory integration of balance (mCTSIB), and Timed Up and Go (TUG). Participants were evaluated in the ‘ON’ medication state. Participants were randomly assigned to an exercise group or a control group. Each participant, regardless of the group to which he or she was assigned, was given a MOV Band to record and track their physical activity throughout the duration of the study. Participants in the control group completed six sessions of functional stretching that was supervised by the exercise physiologist three times a week for 40 minutes. Each visit was separated by a day of rest. The individuals who were assigned to the exercise group completed six sessions of dynamic cycling for 40 minutes three times a week, separated by a day of rest. On the seventh session (last day of the study), participants of both groups completed post-testing which resembled the assessment tests taken at baseline testing.

Control

When randomly assigned to the control group, participants were given a MOV Band and instructions on how to use this device. A MOV Band is a wrist-worn activity monitor that has technology, similar to an accelerometer, which tracks and records all movements done by the participants (http://www.motionfitness.com/Mov-Band-p/mov-b2.html). Participants were instructed to wear the MOV Band at all times so that their activity level and movements could be tracked and recorded. Additionally, participants in the control group reported to the Exercise Laboratory at Kent State University three times a week to perform functional stretching with the guidance of an exercise
The majority of the exercises included a variety of seated and standing stretches involving the upper body (neck, upper back, shoulders, chest, and arms) and lower extremities (quadriceps, hamstrings, calves, and hips; Li et al., 2012). The specific upper and lower body stretches are displayed in Figure 4. Each stretch was held for 20 seconds and upon completion of all the stretches, the regimen was performed again. The stretching session lasted approximately 45 minutes, and consisted of a 5-minute warm-up on the Schwinn airdyne before beginning the stretches. The control group was designed to provide a low-intensity exercise program with social interaction and enjoyment similar to the dynamic cycling sessions. On the seventh session (the last day of the study) participants gave the researcher the MOV Band when post-testing had been completed. The researcher was able to download software that synced the activity data from the participant’s MOV Band to an online account that only the researcher was able to access.

<table>
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<tr>
<th>Upper body stretches</th>
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<tr>
<td>Head tilt sideways</td>
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<tr>
<td>Head rotation left-to-right</td>
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Arm in front shoulder stretch

Upper-arm-up shoulder stretch

Arms behind back reach
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<th>Trunk Rotation</th>
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<th>Arm up upper body sideways stretch</th>
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<th>Push forward calf stretch</th>
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<td>Seated hamstring stretch</td>
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<tr>
<td>Seated quadriceps stretch</td>
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<tr>
<td>Seated hip flexor stretch</td>
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<td>Seated knees to chest</td>
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<tr>
<td>Seated inside ankle stretch</td>
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<td>Seated outside ankle stretch</td>
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*Figure 4.* Stretches that the control group performed.
Dynamic Cycling

Participants in the exercise group were also given a MOV Band and completed six sessions of dynamic cycling, which occurred every other day. Figure 5 lists the cycling protocol. Participants sat upright in an adjustable bike at a distance from the pedals allowing for a 10–20 degree bend in their knees. Their feet were strapped into the pedals to ensure the safety of the participant. Prior to starting the dynamic cycling warm-up, participants had their resting blood pressure recorded.

Prior to Enrollment

Total 16: Screen potential subjects by inclusion and exclusion criteria; obtain health history

Obtain informed consent.
Perform baseline assessments.

Baseline

Visit 1

Primary Outcomes: UPDRS “ON” Meds, Kinesia ONE, mCTSIB, and TUG

Visit 7

Post-test

Primary Outcomes: UPDRS “ON” Meds, Kinesia ONE, mCTSIB, TUG

Figure 5. Exercise protocol.
The dynamic cycling consisted of a 5-minute warm-up on the stationary bicycle at 50 rpm and then 30 minutes of dynamic cycling between 75–85 rpm, and then a 5-minute cool down at 50 rpm. The bike fluctuated between 75–85 rpm to maintain dynamic cycling, but the controller was set for 80 rpm. During the dynamic cycling, the participant’s heart rate, rating of perceived exertion (RPE), cadence, power, and torque were measured. The heart rate was measured through a polar heart rate monitor every minute and the RPE was measured through the Borg’s scale every 5 minutes. Participants’ heart rates were elevated to 60–80% of their age-predicted heart rate maximum and the RPE were between 8–13. Cadence was measured through the total number of revolutions that were completed per minute by the participant while he or she cycled to ensure the exercise protocol was being met. The cadence was recorded through the control box that is connected to the top of the cycle. The power and torque were both measured through the control box and were indicators of the amount of force the participant was producing during each revolution. Participants were told that the motor would assist but that they would have to push on the pedals. If the participant was overpowering than there were positive power and torque numbers displayed on the control box and if there were negative power and torque numbers then the motor was assisting the subject with the cycling movement. Participants were encouraged to display positive motor power and torque numbers on the cycle display screen. Data from the dynamic cycles (heart rate, cadence, power, torque) were collected every second and saved to a computer during each session. Motor assessments were completed at baseline and approximately five minutes after each cycling session was completed. Participants’
blood pressures were obtained 30 minutes after dynamic cycling (near the end of the assessment tests) to ensure they recovered from the exercise before being sent home.

**Outcome Variables**

The outcome variables were overall UPDRS Part III motor scores, Kinesia ONE, Mobility, and balance. Each outcome variable was measured at each session.

**UPDRS**

UPDRS was originally developed in the 1980s and has become the most widely used clinical rating scale for PD severity (Goetz et al., 2008). The UPDRS is a multidimensional, reliable, and valid scale that measures motor function in individuals with PD. The scale rates a range of motor manifestations on a 0 to 4 integer scale corresponding to normal, slight, mild, moderate, and severe (Heldman et al., 2012). On the first day of testing, and after every session, the researcher had participants complete a series of motor assessments and rated them from 0 to 4 on how well they performed the task. To ensure consistency the same researcher completed the UPDRS with the participants. Part III of the UPDRS, which consists of evaluating tremor, bradykinesia, rigidity, gait/ posture, speech, and facial expression, was utilized to assess motor function. The UPDRS has tested satisfactory for validity and reliability on rating motor manifestations in individuals with PD. Intraclass correlation coefficients indicated good to excellent agreement for speeded repeated movements, resting tremor, and rising from a chair (Richards, Marder, Cote, & Mayeux, 1994). The internal consistency for UPDRS is good, indicated by a Cronbach’s alpha of 0.96 (Martin et al., 1994).
Kinesia ONE

The Kinesia ONE is a program that is performed on an iPad and objectively measures motor symptoms such as tremor, bradykinesia, and dyskinesia. This program consists of a patient-worn motion sensor and a touch-screen, portable, tablet that programmed to a specific clinical protocols (http://glneurotech.com/kinesia/products/kinesia-one/). The motion sensor was worn on the participant’s finger while he or she completed various motor tasks, and information collected through this sensor was transmitted to the tablet through Bluetooth. For this protocol motor function of the upper and lower extremity was assessed through 18 motor tasks, at baseline and after the cycling sessions, with outcome variables including tremor score (rest, postural and kinetic), amplitude, speed and rhythm of movement (finger and toe taps, pronation/supination, hand grasp, leg lifts). The wireless motion sensor was worn by the participant, on his or her dominant pointer-finger, while guided by a video through a series of motor assessments that assessed his or her symptom severity. Once the motor assessment tests were completed, the data were uploaded to the tablet and were correlated to Parkinson’s motor symptoms of tremor, bradykinesia, and dyskinesia. The data were quantified through an algorithm that scores the motor function on a 0 to 4 severity scale, which is highly correlated to clinical ratings (Heldman et al., 2012). All data were managed through secure, HIPPA-compliant Internet-based storage for analysis, reporting, and backup. Kinesia ONE has previously demonstrated that patients with PD have little trouble using this system and has good reliability of assessing tremor and upper extremity
bradykinesia (Heldman et al., 2012). The quantified results from the Kinesia ONE were compared to the results of UPDRS motor assessments.

**TUG**

The Timed Up & Go Test (TUG) is a test of balance that is commonly used to examine functional mobility in older adults (Shumway-Cook, Brauer, & Woollacott, 2000). Participants began in a seated position in the chair and when the researcher said “go” the participant got up from the chair and walked at a preferred speed 3 meters, turned around a cone, walked back to the chair, and sat down. The researcher recorded the amount of time it took the participant to walk 3 meters and sit back down in the chair. Time started when the researcher said, “go,” and time stopped when the participant sat back down in the chair. The participants completed two trials and the average time of those trials was analyzed. Time taken to complete the test is strongly correlated to level of functional mobility (Shumway-Cook et al., 2000). Older adults who are able to complete the task in less than 20 seconds have been shown to be independent in transfer tasks involved in activities of daily living (Shumway-Cook et al., 2000). In contrast, older adults requiring 30 seconds or longer to complete the task tend to be more dependent in activities of daily living, requiring assistive devices for ambulation (Shumway-Cook et al., 2000). TUG results indicate that the time score is reliable, correlates well with log-transformed scores on the Berg Balance Scale ($r = -0.81$), gait speed ($r = -0.61$), and Barthel Index of ADL ($r = -0.78$; Podsiadlo & Richardson, 1991). Outcome variables were time to completion, walking speed, and step length. TUG is useful for the measurement of mobility in people with mild to moderate PD (S. Morris,
Morris, & Lansek, 2001) and is a valid method for screening both level of functional mobility and risk for falls (Shumway-Cook et al., 2000).

**Modified Clinical Test of Sensory Integration of Balance**

The Biodex Balance SD (BBS) is a multi-axial device that objectively measures and records an individual’s ability to stabilize the involved joint under dynamic stress (Parraca et al., 2011). This system is useful for evaluating balance and the risk of falls in participants (Parraca et al., 2011). BBS uses a circular platform that is free to move in the anter-posterior and medial-lateral axes simultaneously, and the stability level of the platform is provided through eight springs that are located underneath the outer edge of the platform (Parraca et al., 2011). Attached to the platform is a display screen that can provide feedback in real time about the position of the participant’s center of pressure during the trials (Parraca et al., 2011). This device is interfaced with dedicated software (Biodex, Version 1.08, Biodex Inc.) that allows the BBS to measure the degree of tilt in each axis, providing an average sway score (Parraca et al., 2011). The larger the sway score the more unstable the participant is and the smaller the sway score the more stable the participant is. Participants stood bipedal on the circular platform (with shoes off) and looked at the display screen during all trials, but the tracking system on the screen was turned off. To reduce the risk of falling during these testing sessions, a safety harness system was used. All trials were done without shoes and participant’s foot position was recorded through coordinates on the platform’s grid to ensure same foot place throughout all trials (Parraca et al., 2011). The participants performed four different conditions (eyes open firm surface, eyes opened soft surface, eyes closed firm surface, eyes closed soft
surface), and each trial was 20 seconds, with a 10-second break between each trial. One trial was performed for each of the different conditions. Four different conditions were performed so that each sensory system (vision, vestibular, and proprioception) could be controlled for during different conditions. During two conditions, vision was removed (by having the participants close their eyes) and proprioception stimuli were decreased (when participants stood on a foam surface) while all four conditions eliminated the vestibular system. Eliminating or inhibiting the sensory systems during different conditions highlighted which sensory systems individuals with Parkinson’s disease rely on the most while maintaining balance. Outcome variables included sway index for each condition, which represents the amount of postural sway during the task. The BBS measures have been found to be reliable and therefore are a good method for evaluating balance (Parraca et al., 2011). Additionally, the mCTSIB has a test-retest reliability, analyzed by intraclass correlation coefficient, of 0.91 when testing individuals with Alzheimer’s disease (Suttanon et al., 2011), and has been used in previous Parkinson’s disease research studies (Colnat-Coulbois et al., 2011; Landers et al., 2008).

**MOV Bands**

All participants were given a MOV Band to record their physical activity levels throughout the duration of the study. The purpose of the MOV Band was to determine if there is a correlation in the amount of physical activity a participant performs and the severity of their symptoms. Exercise has been shown to help individuals with managing their symptoms of PD which may be correlated to increasing their movement to maintain their strength and flexibility, and decreasing their fear of falling (Playford, 2011).
Exercise Variables and Parameters

The exercise variables were values that were measured during and/or after each exercise session. The parameters were values that were predetermined for each participant to ensure that proper exercise intensity was being achieved.

Blood Pressure

In the dynamic cycling group blood pressure was recorded. Blood pressure was recorded prior to starting the warm-up and then 30 minutes after cycling. The reason for obtaining blood pressure was to assess if individuals with PD experience orthostatic hypertension after exercising. Literature is unclear if PD leads to changes in vascular health (Barbic et al., 2006); therefore, this variable was measured to record blood pressure response before and after exercise and compare these responses to that of healthy individuals.

Age-Predicted Heart Rate Maximum

During the baseline testing on day one, participant’s resting heart rate was recorded so that his or her age-predicted heart rate maximum could be calculated using the Karvonen method, which is HRmax = 220-age (Karvonen, Kentala, & Mustala, 1957). The participants exercised at 60–80% of their heart rate max. A polar heart rate monitor was used to record resting and exercising heart rate. Heart rate was monitored prior to beginning the warm-up, after the warm-up was completed, every minute during the 30-minute dynamic cycle, and then after the 5-minute cool down to ensure that their heart rate was at a safe and appropriate range. Participants were instructed on how to maintain, increase, or decrease their heart rate, to ensure proper intensity was being
maintained, by altering the amount of force they contributed into their revolutions. To increase their heart rate they needed to produce more force during the revolutions, and to decrease their heart rate they needed to reduce the amount of forced applied during the revolutions. Individuals that reached a target heart rate greater than 80% of their maximum heart rate were required to slow their cycling until their heart rate was within appropriate range. Once an appropriate heart rate had been reached, the participant was allowed to cycle at his or her desired pace again, as long as it was within 60–80% of his or her heart rate max. Participants were closely monitored to ensure that they did not exercise to exhaustion. Upon completion of the exercise session, HR was required to be below 40% of heart rate max in order for the heart rate monitor to be removed and participants to complete their motor assessments.

**Rating of Perceived Exertion (RPE)**

RPE is a scale that is used to measure the feelings of effort, strain, discomfort, and fatigue experienced during exercise. Using the Borg scale, the participants indicated their intensity level by pointing to the numerical value that was associated with their experience during that time while exercising. RPE was assessed using Borg’s Rate of Perceived Exertion Scale and was recorded every 5 minutes. Participants were instructed to be between 8–13 on the RPE scale (Borg, 1982).

**Statistical Analysis**

Statistical analysis was conducted by using IBM SPSS Statistics 20 computer software program. Three different statistical analysis tests were performed on the data. The first statistical analysis was an independent *t*-test on participants’ demographics (age,
weight, height, body mass index [BMI], duration of PD, and medication dosage) in the experimental and control group to ensure that the individuals in the two groups were similar. The PD symptom (UPDRS, Kinesia ONE) and the mobility/balance outcome measures (TUG, mCTSIB) were analyzed with a 2x2 repeated measure ANOVA. If necessary, a paired samples $t$-test was used to assess for significant interactions to determine which session of data collection(s) contributed to an interaction. Descriptive statistics between these two groups were analyzed with an independent $t$-test. Lastly, a correlation between average heart rate during exercise and outcome (UPDRS and TUG) variables was performed. Heart rate and RPE were compared separately to each outcome variable. This analysis was done by calculating the change (pre and post) score for each outcome variable, and then correlating the average heart rate response to the change score of each outcome variable. For example, a change score for the UPDRS was calculated and then was correlated to the average heart rate response; a change score for TUG was calculated and then correlated to the average heart rate response. The purpose of this correlation was to examine if different exertion levels of the participant impacted the results of the outcome variables. Statistical significance was set at a 95% confidence interval, with a $p$ value = 0.05.
CHAPTER IV

THE EFFECTS OF REPEATED BOUTS OF DYNAMIC CYCLING ON MOTOR FUNCTION IN INDIVIDUALS WITH PD

Parkinson’s disease (PD) affects more than half a million people in the United States and this number is predicted to increase up to 1,260,000 people by the year 2040, with the economic cost estimated to be $7.2 billion (Kowal et al., 2013). PD, a progressive neurodegenerative disorder, is due to a decline in the production of dopamine, which helps to produce synchronized motor and sensory commands (Bartels & Leenders, 2009). The decrease in synchronized motor commands (i.e., motor control) results in decreasing functional status including daily tasks such as walking and rising from a chair (Ellis et al., 2005). The cause of PD is unknown, but treatment options consist of drug therapy or surgery. Both of these options decrease the symptoms, but do not cure the disease. It is important to identify additional interventions that may help manage the disease while maximizing Quality of Life (QOL) and functional status in individuals with PD (Ellis et al., 2005).

Several studies have shown that the optimal management of PD involves both pharmacologic treatment and exercise (Cakit et al., 2007; Cutson et al., 1995; David et al., 2012). Evidence indicates that exercise is beneficial in improving walking, balance, muscle strength, and the performance of activities of daily living in individuals with PD (Allen et al., 2012). Specifically, high-speed exercise (high velocity, complexity, repetition) is important in promoting activity-dependent neuroplasticity within the brain, which can produce alternative neural pathways in the central nervous system (CNS;
These alterations in the brain, due to activity-dependent neuroplasticity, may decrease the motor deficiencies of individuals with PD since different neural pathways are utilized. There are different types of high-speed exercise, such as dynamic (high cadence) cycling and treadmill training. Cycling, compared to treadmill walking, tends to be the preferred method of high-speed exercise because it is non weight-bearing which is physically less demanding (decreased impact and stress on the joints) on the individuals and results in decreased fatigue, which allows PD patients to be more active throughout the day (Elbers et al., 2009).

Recently, Ridgel and colleagues demonstrated that forced and assistive cycling is an effective method of treatment and management of PD symptoms (Ridgel et al., 2012; Ridgel et al., 2015; Ridgel et al., 2009). They demonstrated that eight weeks of forced exercise (30% more than individual’s preferred work rate) improved motor function in the upper limbs, which was measured by the Unified Parkinson’s Disease Rating Scale (UPDRS) and bimanual dexterity task (Ridgel et al., 2009). Another study found that 30 minutes of active-assisted cycling (AAC) improved tremor and bradykinesia in the upper extremity in individuals with PD while in the “off” medication state (Ridgel et al., 2012). Most recently, Ridgel and colleagues showed that three sessions of dynamic cycling for 40 minutes (75–85 revolutions per minute) improved the overall UPDRS III score by 13.9% and the Timed Up and Go test (TUG) by 16.5% (Ridgel et al., 2015).

It is clear that three sessions of dynamic cycling improves motor function in PD; however, there is still a need to determine how symptoms are altered immediately after a session of dynamic cycling and if additional sessions continue to provide improvements.
in symptoms. Therefore, this study investigates if increasing the number of dynamic cycling sessions correlates to an even greater improvement in motor function, and analyzes the immediate effects of dynamic cycling by assessing motor function immediately after each dynamic cycling session. It is hypothesized that repeated bouts of dynamic cycling will promote motor function improvement progressively with each exercise bout and that additional benefits will be seen after three exercise sessions.

**Methodology**

**Participants**

The inclusion criteria was a diagnosis of idiopathic PD, Hoehn and Yahr stages 1–3, individuals between 50–79 years of age, and no contraindications to exercise including untreated cardiovascular disease or stroke (Figure 6). Participants were evaluated in the “on” medication state, and were instructed to maintain their normal medication schedule. All subjects provided written informed consent as per the guidelines of the Kent State University Institutional Review Board.
Protocols

All eligible participants were asked to visit the exercise physiology laboratory at Kent State University on seven occasions. During the first session, participants completed motor function assessments, completed the designated treatment (dynamic cycling or stretching), and then completed the same motor function assessments again. During sessions 2–6, participants completed their designated treatment before completing...
the motor function assessments. On the seventh session, participants only completed the motor function assessments (Figure 7). Participants were asked to maintain their pre-enrollment physical activity level and medication schedule. To control for any changes in physical activity levels among individuals, all subjects wore a Mov Band, a wristband that counts daily steps and mileage, on their wrist throughout the duration of the study.

<table>
<thead>
<tr>
<th>Prior to Enrollment</th>
<th>Total 16: Screened potential subjects by inclusion and exclusion criteria; obtained health history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit 1 Baseline 1st Ex</td>
<td>Obtained informed consent. Performed baseline assessments. Primary Outcomes: UPDRS “ON” Meds and Kinesia ONE Administered intervention</td>
</tr>
<tr>
<td>Visits 2-6</td>
<td>Administered Exercise intervention Assessments after 5 minutes rest Primary Outcomes: UPDRS “ON” Meds and Kinesia ONE</td>
</tr>
<tr>
<td>Visit 7 Post-test</td>
<td>Performed Final assessments. Primary Outcomes: UPDRS “ON” Meds and Kinesia ONE</td>
</tr>
</tbody>
</table>

*Figure 7. Exercise protocol for participants.*
**Intervention**

All subjects in the dynamic cycling (Motomed Viva 2 movement therapy trainer) group completed six 40-minute exercise sessions, and all exercise sessions were separated by a day of rest. Each exercise session consisted of a 5-minute warm-up at 50 revolutions per minute (rpm), 30 minutes of dynamic cycling between 80–85 rpm, and a 5-minute cooldown at 50 rpm. During the dynamic cycling phase, participants were encouraged to cycle at 60–80% of their age-predicted maximum heart rate. Heart rate (bpm), Rating of Perceived Exertion (RPE), motor power, motor torque, and cadence (rpm) were recorded every five minutes by the researcher, and every second by the bike controller. Power and torque were recorded to assess the force produced by the bicycle motor during each revolution. Cadence was measured every second by the dynamic cycle control box through the total number of revolutions completed per minute. Participants were encouraged to overpower the motor to achieve a cadence between 80–85 rpm, otherwise the motor provided assistance to keep the cadence at 80 rpm (Ridgel et al., 2015). If participants achieved a cadence over 85 rpm then the motorized bike provided resistance. Motor assessment tests were completed approximately five minutes after each cycling session.

All subjects in the control group completed six 40-minute stretching sessions, and all stretching sessions were separated by a day of rest. Each stretching session consisted of a 5-minute warm-up on a Schwinn airdyne bicycle and 35 minutes of upper and lower body stretches. The stretches were done from a chair and all stretches were performed
twice and held for 20 seconds (Figure 4). Motor assessment tests were completed approximately five minutes after each stretching session.

**Motor Function Assessment Tests**

Motor assessment tests included the unified Parkinson’s Disease Rating Scale (UPDRS) part III motor exam and Kinesia ONE. UPDRS part III is a scale (0 to 4) used by clinicians that assess motor function and includes ratings for tremor, bradykinesia, rigidity, and balance. Kinesia ONE was used to evaluate tremor, bradykinesia, dyskinesia, and movement amplitude, rhythm, and speed. While performing the different motor tasks of the Kinesia ONE, participants wore a wireless finger sensor on their index finger that was most-affected by their symptoms, and were prompted by pictures on an iPad to perform each task. Each task was performed for 15 seconds and the wireless sensor transmitted information to the iPad where an algorithm analyzed the motor function movement and provided unbiased scores on a 0 to 4 scale. This device has been shown to be highly correlated to UPDRS clinical scores (Heldman, Espay, LeWitt, & Giuffrida, 2014). The iPad prompted participants to perform various upper body tasks, such as finger taps, touch nose, open and close hand, and palm rotation. In addition to prompting participants to perform motor tasks, the iPad also prompted the participants to perform resting measures so that resting tremor could be assessed. Resting tremor was assessed by having the participants rest with both hands in their lap, and by having participants maintain a position in which both arms completely extended out in front of their chest.
Statistical Analysis

Using IBM SPSS Statistics 20 (SPSS, Inc., Chicago, IL, 2005) an independent t-test was used to compare participant characteristics (age, height, weight, duration of PD, and physical activity level) between the two groups. A 2 x 2 (group-by-time) repeated measures analysis of variance (ANOVA) was performed to determine differences between groups and sessions for outcome variables. When necessary a paired sample t-test was used to determine differences between each session. Additionally, an interclass correlation was performed to compare the tremor and finger tap scores from the UPDRS and Kinesia ONE. Statistical significance was set at \( p \leq 0.05 \). All data was presented as mean ± standard deviation (SD).

Results

Sixteen subjects (9 males and 7 females; age 70 ± 7 years; Hoehn and Yahr score of 1.57 ± 0.51) with moderate idiopathic PD were randomized into a dynamic cycling or a control (stretching) group. Age, height, pre UPDRS, and duration of PD were not significant between groups; however, weight and Hoehn and Yahr scores were significantly different between groups (Table 1). It is important to note that these participants had smaller motor function deficiencies (baseline UPDRS score of 14.25 ±2.79, out of a maximum score of 108) when compared to previous participants (baseline UPDRS score of 28) of similar studies (Ridgel et al., 2012; Ridgel et al., 2015; Ridgel et al., 2009). All eight participants in the dynamic cycling group were able to complete all sessions, and cycled at an average of 51% (86.79 ± 21.06) of their age predicted maximum heart rate, which was calculated using the Karvonen formula (220-minus age =
age-predicted maximum heart rate; Karvonen et al., 1957). In addition, participants cycled at an average cadence of 78.91 (±2.24) rpm and the average motor power was 1.94 (±13.20) and torque 4.34 (±11.32; Table 2). For this study, power and torque was an indication of the motor power and torque, and didn’t reflect the amount of power the participants produced while cycling. A positive power and torque number indicated that the participants were doing more work than the motor, whereas a negative power and torque number indicated that the motor was doing more work than the participants.

Table 1

*UPDRS and Kinesia ONE Group Demographics*

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Dynamic</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>69.88±7.43</td>
<td>70.00±6.37</td>
<td>.972</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr (H&amp;Y)</td>
<td>1.34±0.52</td>
<td>1.88±0.35</td>
<td>.043*</td>
</tr>
<tr>
<td>Height (in)</td>
<td>68.25±2.43</td>
<td>69.13±3.94</td>
<td>.602</td>
</tr>
<tr>
<td>Weight (lbs)</td>
<td>170.62±20.95</td>
<td>207.50±42.27</td>
<td>.044*</td>
</tr>
<tr>
<td>Duration of PD (y)</td>
<td>4.50±1.6</td>
<td>6.38±2.56</td>
<td>.101</td>
</tr>
<tr>
<td>UPDRS pre treatment</td>
<td>14.13±2.1</td>
<td>14.38±3.5</td>
<td>.866</td>
</tr>
<tr>
<td>Hoehn and Yahr</td>
<td>1.38±0.52</td>
<td>1.88±0.35</td>
<td>.042*</td>
</tr>
</tbody>
</table>

Table values are mean ± standard deviations. The groups did not significantly differ from each other at baseline, besides H & Y and weight, as indicated by *. P values from independent t-test.
Table 2

*Average Dynamic Cycling Values*

<table>
<thead>
<tr>
<th>Exercise Variables</th>
<th>Exercise Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate (bpm)</td>
<td>86.79±21.06</td>
</tr>
<tr>
<td>Cadence (rpm)</td>
<td>78.91±2.24</td>
</tr>
<tr>
<td>Motor Power</td>
<td>1.94±13.2</td>
</tr>
<tr>
<td>Motor Torque</td>
<td>4.34±11.32</td>
</tr>
</tbody>
</table>

Abbreviations: bpm, beats per minute; rpm, revolutions per minute. Values are mean ± standard deviations.

Physical activity, as measured by the Mov Band, during the study was not significantly ($F = .871, p = .366$) different between groups (Figure 8). During the duration of the study, the participants in the dynamic cycling group took an average of 4,096.18 (± 2,995.99) daily steps and the average daily steps for the control group was 4,207.26 (± 3,115.45). One individual in the dynamic cycling group lost their Mov Band so their physical activity level was excluded from this analysis. In addition, one individual in the control group was extremely active during the study, which overestimated the average number of steps the control group achieved. When this particular individual was excluded from the data analysis, the control group achieved an average of 3,076.38 (±3,076.378) daily steps throughout the duration of the study. There was not a significant interaction for physical activity level between group ($F = 1.936, p = .186$) and time ($F = 2.872, p = .112$).
Figure 8. Physical activity levels for dynamic cycling and stretching group. Activity levels were measured by the Mov Band, for the dynamic cycling and stretching group throughout the study.

UPDRS

A significant ($p < 0.001$) group-by-time interaction occurred from pre- to post-testing for overall UPDRS Part III motor score in the dynamic cycling group (Figure 9). UPDRS score improved from pre- to post-testing by 17% in the dynamic cycling group. There was a significant main effect of time ($p = 0.030$) and main effect of group ($p = 0.001$). In the dynamic cycling group a paired samples $t$-test showed significant improvement between pre-testing and session 2 ($p = 0.010$), pre-testing and session 4 ($p = 0.001$), pre-testing and session 5 ($p = 0.001$), pre-testing and session 6 ($p = 0.002$), and pre-testing and session 7 ($p = 0.002$), session 3 and session 4 ($P = 0.014$), session 3 and session 5 ($p = 0.040$), session 3 and session 6 ($p = 0.021$), and session 3 and post-testing
The control group significantly improved UPDRS scores between session 1 and session 4 ($p = 0.038$), session 1 and session 6 ($p = 0.005$), session 1 and post-testing ($p = 0.005$), session 2 and session 3 ($p = 0.017$), session 2 and session 6 ($p = 0.010$), session 3 and post-testing ($p = 0.047$), session 4 and session 6 ($p = 0.030$), and session 4 and post-testing ($p = 0.030$). However, the control group significantly got worse in the UPDRS score from pre-testing to session 1 ($p = 0.011$), pre-testing to session 2 ($p = 0.004$), and pre-testing to session 3 ($p = 0.018$). As shown in Figure 9, the control group showed a lot of variability in between sessions, which can be explained by these individuals not receiving the dynamic cycling intervention.

**Figure 9.** Change in UPDRS score between the two groups from baseline testing to end of treatment. The dynamic cycling group significantly ($p = 0.030$) improved their UPDRS score from pre-testing to post-testing ($\pm 1.77$). Significant improvements in between sessions are indicated with an * ($p \leq 0.05$) or # ($p \leq 0.01$). Abbreviations: DY, dynamic cycling; CN, control group; EOT, end of treatment.
A change score (baseline values subtracted from post-testing values) was calculated for overall UPDRS scores in the dynamic cycling group and showed significant improvement ($F = 0.077, p = 0.0014$) in scores by 17%. The change score for each participant was matched to their corresponding heart rate during dynamic cycling to assess if a higher heart rate correlated to a greater improvement in UPDRS score. However, there does not appear to be any correlation between higher heart rate during dynamic cycling and UPDRS score (Figure 10).

![Figure 10](image)

*Figure 10. Comparison of heart rate during dynamic cycling to UPDRS change score from pre- to post-testing in the dynamic cycling group. This is displaying the change score, calculated from subtracting baseline UPDRS values from post-testing UPDRS values, in the dynamic cycling group and the corresponding average heart rate (bpm) during dynamic cycling. No relationship exists between heart rate during dynamic cycling and improvement in UPDRS scores. Equation $y = a + b*x$. Pearson’s $r = -0.504$ and adjusted R-square = 0.203.*
Kinetic Tremor

A significant ($p < 0.001$) group-by-time interaction occurred for kinetic tremor in the dynamic cycling group (Figure 11). Kinetic tremor in the dynamic cycling group improved by 53.03%, compared to 11.11% in the control group, from pre- to post-testing. There was a significant main effect of time ($p = 0.001$) and main effect of group ($p = 0.027$). Within the dynamic cycling group, a paired samples $t$-test showed significant improvements between pre-testing and session 3 ($p = 0.042$), pre-testing and session 4 ($p = 0.032$), pre-testing and session 5 ($p = 0.011$), pre-testing and session 6 ($p = 0.007$), pre-testing and post-testing ($P = 0.009$), session 2 and session 6 ($p = 0.024$). Kinetic tremor for the control group significantly improved from pre-testing to session 1 ($p = 0.022$), pre-testing and session 4 ($p = 0.040$), and pre-testing and session 5 ($p = 0.011$).

Figure 11. Kinetic tremor scores for each session in the dynamic cycling and stretching group. This is displaying the change in kinetic tremor scores between the two groups from baseline testing (pre-testing) to end of treatment (post-testing). The dynamic cycling group significantly ($p = 0.001$) improved their tremor score from pre-testing to post-testing ($±0.43$). Significant improvements in between sessions are indicated with an * ($p \leq 0.05$) or # ($p \leq 0.01$). Abbreviations: DY, dynamic cycling; CN, control group; EOT, end of treatment.
Hand Movement Amplitude

A significant ($p < 0.001$) group-by-time interaction occurred for hand movement amplitude in the dynamic cycling group (Figure 12). Hand movement amplitude in the dynamic cycling group improved by 35.68%, compared to 0% in the control group, from pre to post-testing. There was a main effect of time ($p = 0.006$) and main effect of group ($p = 0.005$). A paired samples $t$-test for dynamic cycling showed significant improvement between pre-testing and session 1 ($p = 0.036$), pre-testing and post-testing ($p = 0.013$), session 1 and post-testing ($p = 0.057$) and session 3 and post-testing ($p = 0.006$). In the control group the scores significantly got worse between session 1 and post-testing ($p = 0.040$), session 2 and session 4 ($p = 0.021$), session 2 and session 5 ($p = 0.009$), session 3 and session 4 ($p = 0.001$), session 3 and session 5 ($p = 0.052$), and session 3 and session 6 ($p = 0.038$). For the control group, hand movement amplitude scores significantly ($p = 0.047$) got worse between session 4 and session 6. Symptom variability seen in the control group can be explained by this group not receiving the dynamic cycling intervention.

Rapid Alternating Hand Movement Speed

A significant ($p < 0.001$) group-by-time interaction occurred for alternating hand movement speed within the dynamic cycling group (Figure 13). Rapid alternating hand movement speed in the dynamic cycling group improved by 22.9%, when compared to 0% in the control group, from pre to post-testing. There was a main effect of time ($p = 0.001$) and main effect of group ($p = 0.001$). In the dynamic cycling group, a paired samples $t$-test showed significant improvements between pre-testing and session 3 ($p = 0.036$), pre-testing and post-testing ($p = 0.013$), session 1 and post-testing ($p = 0.057$) and session 3 and post-testing ($p = 0.006$). In the control group the scores significantly got worse between session 1 and post-testing ($p = 0.040$), session 2 and session 4 ($p = 0.021$), session 2 and session 5 ($p = 0.009$), session 3 and session 4 ($p = 0.001$), session 3 and session 5 ($p = 0.052$), and session 3 and session 6 ($p = 0.038$). For the control group, hand movement amplitude scores significantly ($p = 0.047$) got worse between session 4 and session 6. Symptom variability seen in the control group can be explained by this group not receiving the dynamic cycling intervention.
0.037) and pre-testing and post-testing \((p = 0.003)\). In the control group scores significantly improved between session 1 and session 5 \((p = 0.034)\).

![Graph showing hand movement amplitude scores for each session in the dynamic cycling and stretching group](image)

Figure 12. Hand movement amplitude scores for each session in the dynamic cycling and stretching group. This is displaying the change in hand movement amplitude scores between the two groups from baseline testing (pre-testing) to end of treatment (post-testing). The dynamic cycling group significantly \((p = 0.006)\) improved their hand movement score from pre-testing to post-testing \((±1.25)\). Significant improvements in between sessions are indicated with an * \((p \leq 0.05)\) or # \((p \leq 0.01)\). Abbreviations: DY, dynamic cycling; CN, control group; EOT, end of treatment.

An intraclass correlation coefficient (ICC) compared the scores from the UPDRS and Kinesia ONE for tremor and finger tap speeds in both groups to assess how strongly the scores from the different methods resembled each other. Tremor ICC \((C = .945)\) was significant \((p < 0.001)\), with 89–98\% of the scores falling within the 95\% confidence interval. Finger tap ICC \((C = 0.920)\) was significant \((p < 0.001)\), with 85–97\% of the scores falling within the 95\% confidence interval. Thus, the UPDRS scores closely resembled the Kinesia ONE scores (Figures 14 and 15).
Figure 13. Rapid alternating hand movement speed scores for each session in the dynamic cycling and stretching group. This is displaying the change in rapid alternating hand movement speed scores between the two groups from baseline testing (pre-testing) to end of treatment (post-testing) (±0.66). The dynamic cycling group significantly \((p = 0.001)\) improved their hand movement score from pre testing to post-testing. Significant improvements in between sessions are indicated with an * \((p \leq 0.05)\) or # \((p \leq 0.01)\).
Abbreviations: DY, dynamic cycling; CN, control group; EOT, end of treatment.
Figure 14. Correlation between UPDRS and Kinesia ONE scores for tremor. This is displaying the relationship between the average scores for tremor between the UPDRS and Kinesia ONE amongst all participants. Tremor scores from UPDRS and Kinesia ONE are significantly correlated ($p = 0.000$), with a 95% confidence interval.
Abbreviations: UPDRS, Unified Parkinson’s disease Rating Scale; KO, Kinesia ONE.
Discussion

This study demonstrates that after six bouts of dynamic cycling motor function improves, and that these progressive improvements are seen immediately after each bout in individuals with idiopathic PD. Moreover, participants in the dynamic cycling group continued to show improvements in overall UPDRS motor score after three exercise sessions. The improvements reported in motor function did not appear to be related to exercise intensity, that is, individuals who cycled at a higher heart rate did not show greater improvements than individuals who cycled at a lower heart rate.

Participants improved their overall UPDRS Part III motor score from baseline to post-testing by 17%. Interesting, participants were still receiving additional benefits in
the overall UPDRS score past three exercise sessions which circles back to one of the purposes of this study in assessing if participants received additional benefits after three exercise sessions. These findings are similar with previous studies which showed eight weeks of forced exercise (FE) on a tandem bicycle significantly improved UPDRS Part III motor score from baseline to post-testing (Ridgel et al., 2009). Moreover, Ridgel and colleagues showed that three, 1-hour sessions of dynamic high-cadence cycling lead to a significant improvement on the UPDRS Part III motor exam (Ridgel et al., 2015).

In addition to improving overall UPDRS score, dynamic cycling significantly improved kinetic tremor from baseline to post-testing by 53% in individuals with PD. An explanation from the improvement in kinetic tremor could be the result of increasing the efficiency of dopamine within the basal ganglia, which is an area of the brain that responds to motor control. Previously, Ridgel and colleagues demonstrated that eight weeks of forced exercise (FE) on a tandem bicycle significantly improved upper extremity dexterity from baseline to post-testing (Ridgel et al., 2009).

Furthermore, six bouts of dynamic cycling significantly improved hand movement amplitude by 36% from baseline testing to post-testing in individuals with PD. Similar to improvements in kinetic tremor, hand movement amplitude may have improved due to increasing sensory feedback to the brain, which could alter cortical (part of the brain that produces coordinated, quick motor movements) excitability and therefore improve motor function. This is one of the first studies that assessed hand movement amplitude through the Kinesia ONE, and limits how these results compare to previous literature.
Lastly, six bouts of dynamic cycling significantly improved rapid alternating hand movement speed in the dynamic cycling group by 23% from baseline testing to post-testing. Improvements may be related to the increase in blood-oxygen-levels after acute bouts of high cadence exercise that supports the increased excitability in the cortical area which is the area as PD medications tend to target (Fisher et al., 2008).

This current study builds upon previous studies that found high intensity exercise improves motor function in individuals with PD (Ridgel et al., 2012; Ridgel et al., 2015; Ridgel et al., 2009), and that individuals with PD can tolerate high-speed exercise (Cakit et al., 2007; Fisher et al., 2008; Herman et al., 2007; Miyai et al., 2000). Of those studies that have examined the effects of high-intensity exercise on motor function in individuals with PD, all have been lower-extremity intervention based; therefore, there is a need to examine the effects of high-speed upper extremity exercise on the effects of motor function in individuals with PD. Likewise, future studies should investigate the impact of having participants dynamic cycle alone (without the presence of anyone in the room) compared to cycling in a group setting. From observation, the presence of people appears to impact a subject’s motivational level and attention while they are cycling. Additional studies should assess the effects of dynamic cycling on tremor during activities that physical/mentally (balancing, mental tasks, etc.) “stress” participants with PD.

Implications and Limitations

The results from this study show that when individuals with PD engage in six bouts of dynamic cycling for 30 minutes, there is significant improvement in overall UPDRS Part III motor scores, kinetic tremor, hand movement amplitude, and rapid
alternating hand movement speed. This study, along with others, demonstrates that individuals with PD can tolerate high-intensity exercise, which is important because most PD individuals are not pushed during rehabilitation programs and therapies (Onla-or & Weinstein, 2008). Importantly enough, dynamic cycling is unique in that it increases pedaling frequency without increasing fatigue (cardiovascular, pulmonary, etc.). Improvements in motor function may be evidence that high-speed exercise alters neural pathways, which may be due to dependent-neuroplasticity or changes within the cortical area (Fisher et al., 2008). Regardless, dynamic cycling can be utilized to better describe exercise prescriptions and rehabilitation services in individuals with PD.

Although this study did not use treadmills that required a harness, it still required specialized equipment that included a motorized, assistive recumbent bicycle. This piece of equipment requires a control box and an algorithm. In addition, a small sample size was used and this sample size showed minimal motor deficiencies when compared to other sample sizes of similar studies (Ridgel et al., 2012; Ridgel et al., 2015; Ridgel et al., 2009). When participants show minimal symptoms it is hard to show symptom improvements. Although this study had a post intervention follow-up of 48 hours after the last exercise session, the post follow-up did not look at how long (weeks, months, etc.) participants maintained their improvements in motor function, gait, and mobility.

**Conclusion**

The results of this study showed upper extremity motor function improvements after six bouts of dynamic cycling, while also showing immediate, progressive improvements after sessions in UPDRS, kinetic tremor, hand movement amplitude, and
rapid alternating hand movement speed. High speed, high cadence exercise is beneficial for individuals with Parkinson’s disease, which may increase sensory information back to the brain and reinforce existing connections within the central system or create new pathways within this system. This mode of exercise is tolerated by individuals with PD, and is a mode of exercise that does not exhausted them, which is important so that they can stay active throughout the day to help manage their symptoms. Exercise intensity (percentage of heart rate reserve or percentage of age-predicted maximum heart rate) at which individuals with PD should exercise is still unknown, but these individuals gain benefit from high repetition exercise such as dynamic cycling or treadmill training. High-cadence exercise, along with drug therapy, may help individuals with Parkinson’s disease manage their symptoms.
CHAPTER V
THE EFFECTS OF REPEATED BOUTS OF DYNAMIC CYCLING ON GAIT, MOBILITY, AND BALANCE IN INDIVIDUALS WITH PD

Parkinson’s disease (PD) is an incurable, neurological condition, which affects the brain and results in loss of motor function. Motor function deficiencies affect individual’s dependency due to activities of daily living (ADLs) becoming increasingly more difficult, such as walking, standing, and maintain postural stability. The loss of postural instability is often related to an increased risk of falls leading to reduced mobility, physical activity, and decreased quality of life (QOL; Crouse, Phillips, Jahanshahi, & Moustafa, 2016). The incidence and prevalence of PD is increasing and is estimated to affect more than half a million of people in the United States with the expectations that this number will rise to over 1 million people by the year 2040 (Kowal et al., 2013). PD is commonly treated with medication but over time, individuals become immune to the medication, which results in further increasing the dosage of drug therapy, or the drug therapy begins to lose its effectiveness. Therefore, there is a need to identify additional interventions that may help manage PD and provide individuals with a better Quality of Life (QOL; Ellis et al., 2005).

Exercise is frequently prescribed to individuals with PD, in addition to the drug therapy. The benefits from exercising involve improvement in motor function, which help individuals complete ADLs (Allen et al., 2012). In particular, high-speed exercise, defined as high velocity, complexity, and repetition, has been shown to improve motor function in individuals with PD (Cakit et al., 2007; Fisher et al., 2008; Herman et al.,
2007; Miyai, Fujimoto, Yamamoto, Ueda, Saito, Nozaki, & Kang, 2002; Pohl, Rockstroh, Ruckriem, Mrass, & Mehrholz, 2003; Ridgel et al., 2012; Ridgel et al., 2015; Ridgel et al., 2009). Improvements in motor function from high-speed exercise may occur due to promoting activity-dependent neuroplasticity within the brain (Fisher et al., 2008). Specifically, activity-dependent neuroplasticity may alter neural pathways within the central nervous system that allow different neural pathways in the brain to be utilized. Much of the high-speed exercise is performed on a treadmill because that mode of exercise allows participants to exercise at a higher intensity than what they typically would.

Previous treadmill training studies have shown improvements in lower extremity motor function in individuals with PD (Cakit et al., 2007; Herman et al., 2007; Miyai et al., 2002; Pohl et al., 2003). Pohl and colleagues reported that one session of speed-dependent treadmill training (STT; progressive increase in walking speed) and limited progressive treadmill training (LTT; walking speed does not increase) improved gait and walking phases in individuals with PD (Pohl et al., 2003). Miyai and colleagues (2002) found that body weight-supported treadmill training (BWSTT) for 45-minutes, three times a week, for 1 month had a significant effect on ambulation speed and short-step gait in individuals with PD. Likewise, Herman and colleagues (2007) demonstrated that after 24 sessions, consisting for 30 minutes of progressive (walking speed was increased weekly) treadmill walking improved QOL measures on Parkinson’s Disease Questionnaire (PDQ-39), Unified Parkinson’s Disease Rating Scale (UPDRS) scores, increased gait, and decreased swing time variability (while walking). Alike, Cakit and
colleagues (2007) demonstrated that sixteen 30-minute sessions of progressive (speed was increased every 5 minutes by 0.6kmh) treadmill training significantly improved walking distance and speed in individuals with PD.

Treadmill training has also shown to increase postural stability in individuals with PD. Toole and colleagues found that after six weeks of walking on a treadmill for 20 minutes, three times a week, significantly improved dynamic posturography (uses a computerized dynamic posturography that measures anterior and posterior center of gravity displacement) and the Berg Balance Scale score (Toole, Maitland, Warren, Hubmann, & Panton, 2005). Alike, Cakit and colleagues (2007) demonstrated that sixteen 30-minute sessions of progressive (speed was increased every 5 minutes by 0.6kmh) treadmill training significantly improved scores on the Berg Balance Scale test in individuals with PD. The underlying reason for postural instability in PD remains unclear, and only a few studies have assessed the effects of high-speed exercise on balance in individuals with PD.

To the same token as treadmill training, dynamic high cadence cycling performed on an assistive, motorized recumbent bicycle has improved mobility in individuals with PD. Ridgel and colleagues (2015) found that having subjects perform three sessions of dynamic cycling for 40 minutes of dynamic cycling (75–85 revolutions per minute) improved the Timed Up and Go test (TUG). It remains unclear if dynamic cycling improves postural stability in individuals with PD. Cycling, in comparison to treadmill walking, is physically less demanding in that it is a non weight-bearing exercise which decreases the stress and impact on the bones and joints; therefore, it results in decreased
fatigue, which allows PD patients to be more active throughout the day (Elbers et al., 2009).

Previous dynamic cycling research showed that three sessions of dynamic cycling significantly improved mobility in individuals with PD; however, it is unclear if additional exercise sessions will continue to provide improvement in mobility, as well as significantly improve gait and balance. The primary purpose of this study is to investigate if six bouts of dynamic cycling lead to improvements in gait, mobility, and balance, and if the improvements occur immediately after the bouts of dynamic cycling in individuals with idiopathic PD. A secondary purpose of this study is to assess if participants gain additional benefits after three exercise sessions. It is hypothesized that repeated bouts of dynamic cycling will promote gait and mobility improvement, seen immediately after the bout and progressively between each bout, and improve balance in individuals with PD. Additionally, participants will gain additional benefits in gait, mobility, and balance after three exercise sessions.

Methodology

Participants

The inclusion criteria was a diagnosis of idiopathic PD, Hoehn and Yahr stages 1–3, individuals between 50–79 years of age, and no contraindications to exercise including untreated cardiovascular disease or stroke (see Figure 6). Exclusion criteria consisted of individuals diagnosed with PD but were identified as “high risk,” who had unpredictable motor fluctuations, uncontrolled dyskinesia, and had a history of any neurological (stroke, multiple sclerosis), cardiovascular (recent heart surgery,
pacemaker), hematological, or orthopedic condition that limits their ability to participate in dynamic cycling. The participants were instructed to remain their normal medication schedule and were evaluated in the “on” medication state. All subjects provided written informed consent as per the guidelines of the Kent State University Institutional Review Board.

**Protocols**

All eligible participants were asked to visit the exercise physiology laboratory at Kent State University on seven occasions. The first visit was a familiarization session, which consisted of participants completing gait, mobility, and balance assessment tests, completing the designated treatment (dynamic cycling or stretching), and then completing the same assessment tests again. On sessions 2–6, participants completed their designated treatment before completing gait, mobility, and balance assessments. The seventh session consisted of participants only completing gait, mobility, and balance assessment tests (see Figure 16). Participants were instructed to not change their pre-enrollment physical activity levels or medication schedule. To monitor the participant’s physical activity levels throughout the duration of the study, each subject was given a Mov Band, a wristband that counts daily steps and mileage, and each was instructed to wear this device for the entirety of the study.
Prior to Enrollment

Total 16: Screened potential subjects by inclusion and exclusion criteria; obtained health history

↓

Visit 1 Baseline 1st Ex

Obtained informed consent.

Performed baseline assessments.

Primary Outcomes: Kinesia One “ON” Meds, TUG, and mCTSIB

Administered intervention

Visits 2-6

Administered Exercise intervention

Assessments after 5 minutes rest

Primary Outcomes: Kinesia One “ON” Meds, TUG, and mCTSIB

Visit 7 Post-test

Performed Final assessments.

Primary Outcomes: Kinesia One “ON” Meds, TUG, and mCTSIB

Figure 16. Gait, mobility, and balance exercise protocol.

Interventions

Subjects within the dynamic cycling group completed six 40-minute sessions on a motorized (Motomed Viva 2 movement therapy trainer), stationary bicycle. Each session consisted of a 5-minute warm-up at 50 revolutions per minute (rpm), 30 minutes of dynamic cycling between 80–85 rpm, and a 5-minute cooldown at 50 rpm, and all sessions were separated by a day of rest. While dynamic cycling, participants were encouraged to keep their heart rate between 60–80% of their age-predicted maximum
heart rate. During the dynamic, high cadence cycling the following variables were recorded: heart rate (HR), Rating of Perceived Exertion (RPE), motor power, motor torque, and cadence were recorded. The cadence was evaluated to ensure that participants were staying within the prescribed range of rpm, which is the total number of revolutions completed per minute. The bike controller recorded the variables every second, and the researcher recorded the variables every five minutes. To achieve the dynamic, high cadence cycling participants were encouraged to overpower the assistive motor by keeping their cadence above 80 rpm. If a cadence over 85 rpm was achieved, then the motorized bicycle provided resistance. However, if participants were not able to maintain 80 rpm then the motor provided assistance to keep the cadence at 80 rpm (Ridgel et al., 2015). Gait, mobility, and balance assessment tests were completed approximately five minutes after each cycling session.

Subjects in the control group completed six 40-minute sessions of upper and lower body stretches (Figure 4). Each stretching session consisted of a 5-minute warm-up on a Schwinn airdyne; then 35 minutes of stretches performed from a chair, and all sessions were separated by a day of rest. The stretches were performed twice and held for 20 seconds. Gait, mobility, and balance assessment tests were completed approximately five minutes after each stretching session.

Gait, Mobility, and Balance Assessment Tests

Gait, mobility, and balance tests included the Kinesia ONE, Timed Up and Go (TUG) and Modified Clinical Test of Sensory Interaction in Balance (mCTSIB). Kinesia ONE was used to evaluate gait and freezing of gait (FOG). FOG is a sudden gait
disturbance that results in individuals having difficulty completing or continuing locomotion. Participants wore a wireless sensor on the shoe that was most-affected by their symptoms, and were prompted by pictures on an iPad on how to perform each task. The wireless sensor marked the angular velocity for each forward step during the leg swing for gait and FOG (Heldman et al., 2012). During gait mean angular velocity and coefficient of variation of time during leg swing was analyzed, and during FOG all previous variables were recorded in addition to the time it took the participant to complete a half turn which was measured through angular velocity and rotation time (Heldman et al., 2012). The gait and FOG test required participants to walk 15 feet (4.572 meters) in a straight line during which the information from the wireless sensor was analyzed by the algorithm and then provided unbiased scores on a 0 to 4 (0 indicating symptom free and 4 indicating severe symptoms) scale, which has been shown to be highly correlated to UPDRS clinical scores (Heldman et al., 2014).

Mobility in the participants was evaluated through the TUG test. Participants began in a seated position in a chair and when the researcher said “go,” the participant got up from the chair and walked at a preferred speed for 3 meters, turned around a cone, walked back to the chair, and sat down. The researcher recorded the amount of time it took the participant to walk 3 meters and sit back down in the chair. Time started when the researcher said “go” and time stopped when the participant sat back down in the chair. Participants completed two trials and the average time of those trials was used for analysis. Time taken to complete the test is strongly correlated to level of functional mobility (Shumway-Cook et al., 2000).
mCTSIB was used to evaluate balance, and was performed on the Biodex Balance System (BBS). The BBS is a multi-axial device that objectively measures and records an individual’s ability to stabilize joints in the anter-posterior and medial-lateral positions simultaneously (Parraca et al., 2011). To reduce the risk of falling, participants wore a safety harness. Each session consisted of four different conditions (eyes open firm surface, eyes opened soft surface, eyes closed firm surface, eyes closed soft surface), and each condition was 30 seconds, with a 10 second break between each condition. Dedicated software (Biodex, Version 1.08, Biodex Inc.) analyzed the degree of tilt in each axis, providing an average sway score (Parraca et al., 2011). All visual feedback from the BBS was turned off, and participants stood bipedal on the circular platform (with shoes off) during the session. Participant’s foot position was recorded through coordinates on the platform’s grid to ensure same foot place throughout all sessions (Parraca et al., 2011).

**Statistics**

Using IBM SPSS Statistics 20 (SPSS, Inc., Chicago, IL, 2005) an independent $t$-test was used to compare participant characteristics (age, height, weight, duration of PD, and physical activity level) between the two groups. A 2 x 2 (group-by-time) repeated measures analysis of variance (ANOVA) was performed to determine differences between groups and sessions for outcome (gait, mobility, and balance) variables. When necessary a paired sample $t$-test was used to determine differences between each session. Statistical significance was set at $p \leq 0.05$ and all data was reported as mean ± standard deviation.
**Results**

Participants did not significantly differ between groups in age, height, and duration of PD; however, weight and Hoehn and Yahr scores were significantly different between groups (see Table 3). All participants \( n = 8 \) in the dynamic cycling group completed each session and cycled at an average of 51\% (86.79±21.06) of their age predicted maximum heart rate at an average speed of 78.91 (±2.24) rpm. In addition, the average motor power and torque was 1.94 (±13.20) and 4.34 (±11.32), respectively (see Table 2). For this study, power and torque were an indication of the motor power and torque, and didn’t reflect the amount of power and torque the participants produced while cycling. A positive power and torque number indicated that the participants were doing more work than the motor, whereas a negative power and torque number resulted in the motor doing more work than the participant.

Average steps, as measured by the Mov Band, during the study did not significantly \( F = .871, p = .366 \) differ between groups. Participants in the dynamic cycling group averaged 4,096.18 (± 2,995.99) number of steps daily, and participants in the control group averaged 4,207.26 (± 3,115.45) daily steps. Since each group consisted of 8 participants, the average number of daily steps for each group may have been influenced by individuals who were extremely active or sedentary. One individual in the dynamic cycling group lost their Mov Band so their physical activity level was excluded from this analysis. In addition, one individual in the control group was extremely active during the study, which overestimated the average number of steps in the control group. Even when this particular participant’s physical activity levels were excluded from the
Table 3

_Gait, Mobility, and Balance Group Demographics_

<table>
<thead>
<tr>
<th>Demographics</th>
<th>DY</th>
<th>CN</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>69.88±7.43</td>
<td>70.00±6.37</td>
<td>.972</td>
</tr>
<tr>
<td>Height (in)</td>
<td>68.25±2.43</td>
<td>69.13±3.94</td>
<td>.602</td>
</tr>
<tr>
<td>Weight (lbs)</td>
<td>170.62±20.95</td>
<td>207.50±42.27</td>
<td>.044*</td>
</tr>
<tr>
<td>Duration of PD (y)</td>
<td>4.5±1.6</td>
<td>6.38±2.56</td>
<td>.101</td>
</tr>
<tr>
<td>Hoehn and Yahr</td>
<td>1.38±0.52</td>
<td>1.88±0.35</td>
<td>.043*</td>
</tr>
</tbody>
</table>

Abbreviations: DY, dynamic cycling; CN, control group; Y, years; In, inches; Lbs, pounds; H&Y, Hoehn and Yahr.
Values are mean ± standard deviations. The groups did not significantly differ from each other at baseline, besides weight and H & Y, as indicated by *.
P values from independent t-test.

analysis, there still was not a significant difference between groups in activity levels.

There was not a significant interaction for physical activity level and improvement in symptoms between group (F = 1.936, p = .186) and time (F = 2.872, F = .112). Although it was not significant, the dynamic cycling group progressively increased their physical activity levels throughout the study, whereas the control group progressively decreased their physical activity levels (Figure 8).

**Gait**

A significant \( p < 0.001 \) group by time interaction occurred from pre- to post-testing for gait in the dynamic cycling group (Figure 17). Gait in the dynamic cycling group improved by 59.11%, compared to 3.06% in the control group, from pre- to post-testing. There was a significant main effect of time \( p = 0.004 \) and main effect of
group \((p = 0.008)\). In the dynamic cycling group, a paired samples \(t\)-test showed significant improvement between pre-testing and session 7 \((p = 0.012)\), session 1 and session 7 \((p = 0.051)\), session 3 and session 7 \((p = 0.058)\), session 5 and session 7 \((p = 0.036)\), and session 6 and session 7 \((p = 0.057)\). The control group showed no significant differences between sessions in gait. There was no significant difference in freezing of gait from pre- to post-testing in either group.

![Figure 17. Gait scores for each session in the dynamic cycling and stretching group. This is displaying the change in gait scores between the two groups from baseline testing (pre-testing) to end of treatment (post-testing) (±1.31). The dynamic cycling group significantly \((p < 0.001)\) improved their gait score from pre-testing to post-testing. Significant improvements in between sessions are indicated with an * \((p \leq 0.05)\). Abbreviations: DY, dynamic cycling; CN, control group; EOT, end of treatment.](image-url)
**Mobility**

A significant ($p < 0.001$) group by time interaction occurred from pre- to post-testing for TUG time in the dynamic cycling group (Figure 18). TUG time in the dynamic cycling group improved by 21.87%, compared to 1% in the control group, from pre to post-testing. There was a significant main effect of time ($p = .012$) and main effect of group ($p = .019$). In the dynamic cycling group, a paired samples t-test showed significant improvement between baseline testing and session 3 ($p = 0.035$), baseline testing and session 4 ($p = 0.030$), baseline testing and session 5 ($p = 0.019$), baseline testing and session 6 ($p = 0.019$), baseline testing and session 7 ($p = 0.016$), session 1 and session 3 ($p = 0.040$), session 1 and session 4 ($p = 0.020$), session 1 and session 5 ($p = 0.004$), session 1 and session 6 ($p = 0.003$), session 1 and session 7 ($p = 0.002$), session 2 and session 5 ($p = 0.015$), session 2 and session 6 ($p = 0.029$), session 2 and session 7 ($p = 0.012$), session 3 and session 7 ($p = 0.039$), and session 4 and session 7 ($p = 0.044$). The control group showed no significant differences between sessions.

A change score (baseline values subtracted from post-testing values) was calculated for TUG time in the dynamic cycling group and showed significant improvement ($F = 8.313$, $p = 0.012$) in walking speed by 28%. The change score for each participant was matched to his or her corresponding heart rate during dynamic cycling to assess if a higher heart rate correlated to a greater improvement in walking speed during the TUG. Although not a significant ($p = .236$), positive correlation there does appear to be greater improvement in TUG time with a higher dynamic cycling heart rate (Figure 19).
Figure 18. TUG times for each session in the dynamic cycling and stretching group. This is displaying the change in TUG times between the two groups from baseline testing (pre-testing) to end of treatment (post-testing). The dynamic cycling group significantly ($p < 0.001$) improved their TUG time from pre testing to post-testing ($±2.26$). Significant improvements in between sessions are indicated with an * ($p \leq 0.05$). Abbreviations: TUG, Timed Up-and-Go; DY, dynamic cycling; CN, control group; EOT, end of treatment.
Figure 19. Relationship between TUG time and heart rate during dynamic cycling. This is displaying the change score, calculated from subtracting baseline TUG times from post-testing TUG times, in the dynamic cycling group and the corresponding average heart rate (bpm) during dynamic cycling. No significant ($p = .236$) relationship exists between heart rate during dynamic cycling and improvement in TUG time. Equation $y = a + b \times x$. Pearson’s $r = 0.527490$ and adjusted R-square $= 0.15795$. The TUG change score intercept $= -1.3710$ ($\pm 2.44345$) and slope $= 0.0400$ ($\pm 0.02636$). Abbreviations: TUG, Timed Up-and-Go test; bpm, beats per minute.

Balance

There was no significant difference in balance for eyes open firm surface ($F = 2.375, p = .146$), eyes closed firm surface ($F = .115, p = .740$), eyes open foam surface ($F = .087, p = .772$), and eyes closed foam surface ($F = .014, p = .908$) in either the dynamic cycling or the control group. An interesting observation was seen during static balance involving the individuals in the dynamic cycling group who appeared to have less of a tremor while balancing than those individuals in the control group. In fact, it appeared
that those individuals in the control group had a noticeable tremor during the static balance.

**Discussion**

This study demonstrates that after six bouts of dynamic cycling, gait and TUG time improve, and that these progressive improvements were seen after each bout in individuals with idiopathic PD. Additionally, participants in the dynamic cycling group continued to show improvements in gait and mobility when the number of exercise sessions was extended past three sessions. However, balance did not improve after six bouts of dynamic cycling. Exercise intensity in the dynamic cycling group did not affect the improvements seen in gait and mobility; that is, individuals who cycled at a higher heart rate did not see greater improvements in symptoms than those individuals who cycled at a lower heart rate.

Participants in the dynamic cycling group improved their gait, as measured by the Kinesia ONE, from baseline to post-testing by 60%. Additionally, participants were still improving their gait after three exercise sessions, which one purpose of this study was to assess if participants still gained benefits after three exercise sessions. However, participants in the dynamic cycling group did not improve Freezing of Gait (FOG). The wireless accelerometer that was worn on the participant’s shoe measured the angular velocity during the leg swing phase of each step for gait and FOG, in addition to another variable that was measured during FOG which was the time it took the participant to complete a half turn (Heldman et al., 2012). The half turn time was measured through rotation time; therefore, this study did not improve rotation time after six bouts of
dynamic cycling. To our knowledge, this is the first dynamic cycling intervention that showed an improvement in gait. Gait may have improved due to an increase in cortical excitability, which appears to be dependent on high-speed exercise because there is an increase in sensory information leading back to the brain. The cortical area of the brain controls motor movement; therefore, if there is an increase in the activation within this part of the brain, then motor function (such as gait) could be improved. Another possible explanation for the improvement in gait is that participants received one-on-one supervision from the researcher while high cadence cycling. This close supervision may have increased the participant’s motivational level while exercising which could translate to an increase in exercise intensity when compared to previous dynamic cycling interventions. Previous studies that have assessed treadmill training on gait have seen significant improvements in gait. A study done by Herman and colleagues (2007) found that six weeks of intensive treadmill training significantly improved gait speed and lowered gait variability in individuals with PD. Moreover, Miyai and colleagues (2000) found that 4 weeks of treadmill training improved UPDRS scores and gait walking, while decreasing shuffling of gait.

In addition to improvement in gait, participants in the dynamic cycling group improved their mobility, as measured by TUG, from baseline to post-testing by 28%. Likewise to gait, participants were still improving their TUG time after three exercise sessions, which shows that participants gain additional benefits after three exercise sessions. Improvements in mobility may be a result of an increase in the efficiency of dopamine, which may be reinforcing connections within the brain and therefore leading
to improvements in mobility. This result is similar to a previous finding in which three bouts of dynamic cycling improved TUG time from pre-testing to post-testing (Ridgel et al., 2015). Treadmill training interventions have also showed improvements in mobility with individuals with PD (Pohl et al., 2003; Miyai et al., 2002; Ridgel et al., 2015). For example, Pohl and colleagues (2003) found that 3 one-hour gait training sessions significantly improved 10-m walk speed and double stance walking phase. Moreover, Miyai and colleagues (2002) demonstrated that body weight-supported treadmill training significantly improved ambulatory speed and the number of steps taken at a 1 month follow-up intervention.

In light of the significant improvements seen in gait and mobility, six bouts of dynamic cycling did not improve balance in individuals with PD. Dynamic cycling may not affect balance due to the lack of stimulating the specific neurophysiology and weight-bearing components used in postural stability. Dynamic cycling is a non weight-bearing mode of high-speed exercise, which decreases the amount of proprioception feedback to the brain when compared to weight-bearing exercise. Additionally dynamic cycling does not increase stability in the ankle and hip joints, which are joints used during balancing. Nonetheless weight-bearing exercise, such as treadmill training, is capable of increasing the stability and strength of the ankles and hips, which may convert into improvements in balance. Cakit and colleagues (2007) demonstrated that 16 sessions of incremental speed-dependent treadmill training significantly improved walking distance, walking speed, and balance in individuals with PD. Another study by Cakit and colleagues demonstrated that progressive, increase in walking speed on the treadmill improved static
balance. Toole and colleagues (2005) found that six weeks of treadmill training increased dynamic balance in individuals with PD. Interestingly, both of these high-speed studies were performed on the treadmill; therefore, it is difficult to distinguish if the improvements in balance are due to neural improvements within the brain or due to the muscles supporting the ankle and hip joints increasing in strength. As noted by Ridget and colleagues (2009), a limitation to treadmill training is the possibility that motor function improvement may occur due to the repetitive motor practice the lower body receives during these programs. High cadence dynamic cycling is unique, when compared to treadmill training, in that the motor assessments are different than the motor training (Ridgel et al., 2009). The effects of high-speed exercise on balance in individuals with PD still remain unclear and warrant further investigation.

Numerous studies demonstrate that individuals with PD can tolerate high-speed exercise (Cakit et al., 2007; Fisher et al., 2008; Herman et al., 2007; Miyai et al., 2000). High speed exercise leads to motor, gait, and balance improvement in individuals with PD, which may be a result of increasing sensory feedback to certain areas of the brain. Specifically, this increased sensory feedback may alter cortical excitability, which is primarily responsible for producing coordinated, quick motor movements. Fisher and colleagues (2008) proposed that high intensity exercise leads to activity-dependent neuroplasticity, which was discovered with a transcranial magnetic stimulation that showed blood-oxygen-levels increased after acute bouts of forced cycling, and these improvements occurred in areas of the brain, which are targeted by PD medications. Likewise, a study performed by Ridget et al. (2012) showed that assistive adaptive
cycling (AAC) resulted in immediate improvement in motor function, which suggests that global central nervous system is effected after high intensity exercise.

This current study builds upon previous studies that found high-speed exercise improves gait and mobility in individuals with PD (Fisher et al., 2008; Herman et al., 2007; Miyai et al., 2000; Cakit et al., 2007; Ridelg et al., 2015). Of those studies that have examined the effects of high-speed exercise on gait and mobility function in individuals with PD, all have been lower-extremity intervention based; therefore, there is a need to examine the effects of high-speed upper extremity exercise on the effects of gait and mobility function in individuals with PD. Likewise, future studies should investigate the impact of having participants dynamic cycle alone (without the presence of anyone in the room) compared to cycling in a group setting. From observation, the presence of people appears to impact a subject’s motivational level and attention while they are cycling. Additional studies should assess the effects of dynamic cycling on tremor during activities that physical/mentally (balancing, mental tasks, etc.) “stress” participants with PD.

**Implications and Limitations**

The results from this study show that when individuals with PD engage in six bouts of dynamic cycling for 30 minutes, there are significant improvements in gait and TUG time. This study, along with others, demonstrates that individuals with PD can tolerate high-cadence exercise which is important in rehabilitation programs because a report from Winston laboratory suggests that most PD patients are not pushed during therapy and exercise programs (Onla-or & Winston, 2008). Importantly enough,
dynamic cycling is unique in that it increases pedaling frequency without increasing fatigue (cardiovascular, pulmonary, etc.) due to this mode of exercise being non-weight-bearing in which the body does not encounter as much impact (pounding) when compared to weight-bearing exercise. Improvements in gait and TUG function may be evidence that high-cadence exercise alter neural pathways, which may be due to dependent-neuroplasticity or changes within the cortical area (Fisher et al., 2008). Regardless, dynamic cycling may be utilized to better describe exercise prescriptions and rehabilitation services for individuals with PD. It is still important to find a regimen that increases postural stability since this is becoming an increasing concern with the progression of the disease and is not improved with medication (Lefaivre & Almeida, 2015).

Although this study did not use a harness, it still required specialized equipment, which includes a motorized, assistive recumbent bicycle. This piece of equipment requires a control box and an algorithm. In addition, a small sample size was used and this sample size showed minimal motor deficiencies when compared to other sample sizes of similar studies (Ridgel et al., 2012; Ridgel et al., 2015; Ridgel et al., 2009).

**Conclusion**

This study shows that six bouts of dynamic cycling improved gait and mobility in individuals with idiopathic Parkinson’s disease. These improvements were seen immediately following the bout of dynamic cycling, and at the end of the treatment. In light of the improvements in gait and mobility, six bouts of dynamic cycling did not significantly improve balance. The lack of improvement in balance may highlight the
importance of exercises (tai chi, tango dancing, treadmill walking, etc.) that strengthen the muscles at the hip and ankle joints. Individuals with PD can participate in a high-speed exercise program, which can be done on a traditional recumbent bicycle, to seek the benefits of an exercise program. The ideal exercise intensity (percentage of heart rate reserve or percentage of age-predicated maximum heart rate) is still unknown; however, individuals may still receive benefits from repetitive movements, such as high-speed cycling on a recumbent bicycle or high-speed treadmill training. High-speed exercise, in conjunction with drug therapy, may help individuals with Parkinson’s disease manage their symptoms.
CHAPTER VI

SUMMARY

The decline of dopamine in the basal ganglia leads to the motor symptomatology, and typically results in individuals with Parkinson’s disease being less physically active and deconditioned. As the disease progresses, there are physical implications including decreases in muscular strength and physical inactivity but physical activity has a positive impact on quality of life (QOL) for individuals with PD (Paula, Salmela, Faria, Brito, & Cardoso, 2006). Though the symptoms often prevent PD individuals from exercising, exercise is safe, feasible, and often provides symptom relief that counteracts the pathology. In particular, high intensity exercise is beneficial because of the cortical and activity-dependent neuroplasticity that may occur within the central nervous system, which could minimize the symptoms of PD. Likewise, lower extremity high intensity exercise results in upper and lower extremity motor improvement.

This study demonstrated that overall UPDRS Part III motor exam, kinetic tremor, hand movement speed, rapid alternating hand movement amplitude, gait, and TUG time were significantly improved after six bouts of dynamic cycling, and showed progressive improvement after each bout of cycling. The overall UPDRS Part III motor exam score improved from baseline to post-testing by 17% in the dynamic cycling group. Similarly, TUG time improved from baseline to post-testing by 28% in the dynamic cycling group. Improvements in motor function usually correlate with decreased symptom severity.

Despite the significant improvements that were found in overall UPDRS Part III motor scores, kinetic tremor, hand movement speed, rapid alternating hand movement
amplitude, gait, and TUG time there was no significant improvement in static balance as measured by the Biodex Balance System. Through visual observation, it appeared that individuals in the dynamic cycling group had less tremor while performing the static balance conditions than the participants in the control group.

The current study is not without limitations. The sample size was small, and participants had minimal motor and symptom deficiencies. The researcher performing the UPDRS was not blinded, which may have led to bias scoring. However, the intraclass correlation coefficient was significant when comparing the UPDRS and Kinesia ONE scores for tremor and finger tap speed. Due to the assistive nature of the motorized bike, it is very difficult and challenging to have participants elevate their heart rate to 60–80% of their maximum heart rate, thus, participants in this study dynamic cycled at an average of 51% of their age predicted maximum heart rate.

There is a need for future research to explore the optimal exercise prescription program for individuals with PD, focusing on intensity, duration, and mode of exercise. Of those studies that have examined the effects of high-intensity exercise on motor and gait function in individuals with PD, all have been lower-extremity intervention based; therefore, there is a need to examine the effects of high-intensity upper extremity exercise on the effects of motor, gait, mobility, and balance function in individuals with PD. Similarly, future studies should investigate if participant’s motivational level is influenced by the presence of other individuals while dynamic cycling. Lastly, there is a need to assess if high intensity exercise affects tremor in individuals with PD during stressful physical or mental tasks, such as balancing or cognitive tests.
APPENDICES
APPENDIX A

INFORMED CONSENT FORM
Appendix A

Informed Consent Form

Informed Consent to Participate in Research Study

Study Title: The effects of dynamic cycling on gait and balance in individuals with Parkinson’s disease

Principal Investigator: Angela Ridgel, PhD

Co-Investigator: Dana Ault, MS; Brandon Pollock, PhD; Sara Harper, MS

You are being invited to participate in a research study. This consent form will provide you with information on the research project, what you will need to do, and the associated risks and benefits of the research. Your participation is voluntary. Please read this form carefully. It is important that you ask questions and fully understand the research in order to make an informed decision. You will receive a copy of this document to take with you.

Purpose: The purpose of this study is to better understanding how repeated sessions of dynamic cycling can help motor function and balance in individuals with Parkinson’s disease.

Procedures: If you choose to participate in this study then you will be asked to visit Kent State University’s Laboratory for 7 sessions. You will be randomly assigned to the dynamic cycling or stretching group. You will complete the tests listed below before and after the cycling/stretching intervention.

Cardiovascular Testing: Your resting heart rate and blood pressure will be recorded. This will take about 10 minutes.

Motor Performance (UPDRS): The researcher will ask you to complete different motor tasks like making a fist and walking. This will take 5 minutes to complete this test.
Kinesia ONE: This is a computer program that records movement while you are wearing a small sensor on your finger (see picture). This test will take 5 minutes.

Balance: We will ask you to stand quietly on a device under four different conditions: eyes open while standing on a firm surface, eyes closed while standing on a firm surface, eyes open while standing on a foam surface, and eyes closed while standing on a foam surface. A safety harness will be used to prevent falling (see picture). This will take 10 minutes. To test balance, a piece of equipment will be used that is called the Biodex Balance system.

TUG: This test (5 mins) measures mobility by having you walk 3 meters (10 feet) around a cone and returning to a seated position.

If you are assigned to the stretching group you will be asked to attend 7 sessions.

- Each visit will be separated by a day of rest.
- On session 1, we will record your resting heart rate and blood pressure. Then, you will complete the tests described above before completing the stretching routine.
- The stretching routine will consist of a 5 minute warm-up on a stationary bicycle and then different upper and lower body stretches will be performed. Session 1 will take about 75 minutes to complete.
- You will be given a Mov Band (activity watch) to wear on your wrist for the length of the study that will record your activity level. For sessions 2-6, you will perform the stretching routine before completing test again. These sessions will take about 60 minutes to complete.
- On session 7, the tests will be completed one last time. Session 7 will take about 60 minutes.

If you are assigned to the dynamic cycling group you will be asked to attend 7 sessions and testing will be the same as described above. However, you will complete 40 minutes of dynamic cycling instead of stretching.

- Each visit will be separated by a day of rest.
- Dynamic cycling will include a 5 minute warm-up pedaling at 50 revolutions per minute (rpm), 30 minutes of dynamic cycling at 75-85 rpm, and a 5 minute cool down at 50 rpm.
You will be given a Mov Band (activity watch) to wear on your wrist for the length of the study that will record your activity level.

Criteria for Inclusion/Exclusion:
Inclusion: To be included in this study you must be diagnosed with idiopathic Parkinson’s disease and be between the ages of 50-79 years. In addition, you may not have any medical conditions such as cardiovascular disease or stroke, and you need to be able to follow simple instructions.

Exclusion: You will not be eligible to participate in this study if you have unpredictable motor movements, and any history of neurological (stroke, multiple sclerosis), cardiovascular (recent heart surgery, pacemaker), or orthopedic condition (broken bone, bone fracture) that limits your ability to participate in dynamic cycling or stretching.

Benefits
Both the exercise and stretching group will benefit from information given to them regarding their movement and balance during testing. For the dynamic cycling group, your participation may provide improvements in your motor function and increase your stability. Other benefits may include improved fitness, health, and quality of life. The results of this study will provide important information on the effect of dynamic cycling on motor function and balance in individuals with Parkinson’s disease.

Risks and Discomforts
There are risks and discomforts associated with exercising, such as heart attack, stroke, muscle injury, and muscle soreness. Every effort will be made to minimize these risks by using the information you provide in your pre-exercise medical screening. The research personnel are trained in basic cardiac life support and there is an Automatic External Defibrillator (AED) in the laboratory. If the exercise intensity is too hard you will be permitted to rest at any time. Your exercise intensity will be continuously monitored by a heart rate monitor worn around your chest and you will be asked about your level of exertion. If at any time you experience a sensation that is unusual and uncomfortable please inform the research personnel and they will stop the exercise session. Emergency services will be called for injuries or any other circumstances. Your medical insurance will be billed for any emergency services that are performed by medical staff.

Privacy and Confidentiality
All results will be kept confidential. Any identifying information will be kept in a secure location and only the researchers will have access to this information. Individuals who participate in this study will not be identified in any publication or presentation of research results. Your personal information, such as your name and date of birth, will be removed as soon as possible. Only information you have disclosed to the researchers will be collected, such as your healthy history. Your research information may, in certain circumstances, be disclosed to the Institutional Review
Board (IRB), which oversees research at Kent State University, or to certain federal agencies. Confidentiality may not be maintained if you indicate that you may do harm to yourself or others.

**Compensation**
If you take part in this research study, you will be compensated $10.00 for each session (for a total of $70.00).

**Voluntary Participation**
Taking part in this research study is entirely up to you. You may choose not to participate or you may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled. You will be informed of any new, relevant information that may affect your health, welfare, or willingness to continue your study participation.

**Contact Information**
If you have any questions or concerns about this research, you may contact Dr. Angela Ridgel at 330.672.7495 or Dana Ault at 513.519.4481. This project has been approved by the Kent State University Institutional Review Board. If you have any questions about your rights as a research participant or complaints about the research, you may call the IRB at 330.672.2704.

**Consent Statement and Signature**
I have read this consent form and have had the opportunity to have my questions answered to my satisfaction. I voluntarily agree to participate in this study. I understand that a copy of this consent will be provided to me for future reference.

___________________________________ Date: _____________________
Participant Signature
APPENDIX B

PRE-PARTICIPATION PHONE SCREENING
Appendix B

Pre-Participation Phone Screening

Prospective participants that have expressed interest in participating in a Parkinson’s disease study will receive a telephone call from the researcher. The following telephone script will be used:

“Hello, I received your name because you have expressed interest in participating in the Parkinson’s disease study. This study will be taking place at Kent State University and is evaluating the effectiveness of repeated bouts of dynamic cycling on motor function and balance in individuals with Parkinson’s disease. If you choose to participate in this study, you will be asked to visit the exercise laboratory at Kent State University for 6 sessions of dynamic cycling. Are you interested in hearing more about the study?”

- At this point, if the individual does not have an interest in participating in the study then the prospective participant will be thanked for their time and the researcher will provide their contact information in case the individual has a change in mind. The telephone call will then be ended.
- If the participant has an interest in participating in the study then the telephone call will continue as follows:

“Participants will come to the exercise laboratory at Kent State University for a total of 7 sessions. On your first visit you can expect to have your resting heart rate, blood pressure, and rating of perceived exertion recorded, as well as, your physical fitness level, motor function, and balance tested through simple assessments. You will also be given a small physical activity monitor to wear every day on your wrist during the study. This monitor will track and record your physical activity levels throughout the day. All techniques that are performed are non-invasive.

When all assessments have been completed you will be randomly assigned to either a dynamic cycling group or a stretching group- that means you will not be able to choose which group you are a part of. The dynamic cycling group will partake in 6 sessions of cycling, which will consist of a 5 minute warm-up, 30 minutes of dynamic cycling, and a 5 minute cool down. After the cycling is completed you will be asked to complete different motor and balance assessment tests. Each session will approximately take two hours to complete. The stretching group will partake in 6 sessions of various upper and lower body stretching exercises. Each session will approximately take 60 minutes to complete. Regardless of the group that you have been assigned to, each visit will be separated by a day of rest.

The last visit of the study will consist of recording your resting heart rate, blood pressure, and rating of perceived exertion, as well, asking you to complete motor and balance assessment tests. When this visit has been completed you will have finished this research study. Are you interested in seeing if you are a candidate for this study?”
• If the prospective individual is not interested in this study then they will be thanked for their time and the telephone call will be ended.

• If the prospective individual is interested in the study then these additional questions will be asked:
  _________________ Have you been diagnosed with Idiopathic Parkinson’s disease?
  _________________ Are you between the age of 50-79 years old?
  _________________ Do you have physician approval to participate in this study?
  _________________ Do you have a history of non-Parkinson’s disease related neurological disorder or brain injury such as stroke?
  _________________ Do you have an orthopedic injury that would limit your ability to exercise?
  _________________ Do you have a history of non-Parkinson’s disease related cardiovascular disease such as recent heart surgery or pacemaker?
  _________________ Are you able to move around without, or minimal use, of ambulatory equipment?
  _________________ Do you have unpredicted motor fluctuations?

• If the individual does not meet the inclusion/exclusion criteria then they will be thanked for their time and the telephone call will end. If the individual meets the inclusion/exclusion criteria then they are eligible to participate in the study with physician approval, and the telephone conversation will continue as follows: “Would you like to schedule an appointment for the first testing visit?”
  • If no, then the researcher would thank the individual for their time.
  • If yes, an appointment will be scheduled, or develop a timeline to schedule.

“You will be required to sign an inform consent form prior to participating in this study. Also, please bring your physician approval to participate in this study with you to your first appointment. You should wear comfortable clothing that allows you to exercise and wear tennis shoes to all your sessions.”

• If the individual does not have physician approval yet, then the participant will be informed the following:
  “In order to participate in this study you will be required to get clearance from your physician. Please have your physician write their approval on documented paper.”
APPENDIX C

PHYSICIAN CLEARANCE FORM
Appendix C

Physician Clearance Form

Physician’s Clearance for Exercise Participation

Kent State University-Dept. of Exercise Physiology

Patient’s name:
Address:
Telephone number:

Dear Doctor--

Your patient, ____________________, has expressed an interest in participating in a dynamic cycling aerobic exercise study in individuals with Parkinson’s disease (pending KSU IRB approval ____________). The objective of this study is to examine the effectiveness of repeated bouts of dynamic cycling on motor function and balance in individuals with Parkinson’s disease.

The participant will complete 6 sessions of dynamic cycling. Each session includes a 5 minute warm up, 30 minutes of dynamic cycling at 60-80% age-adjusted maximum heart rate, and a 5 minute cool down. The exercise sessions will last 40 minutes. We will examine motor and balance parameters before and after the exercise program.

Below is a clearance form to be filled out and signed by you.

Physician’s recommendation (check the appropriate line)
a.________ There is no contraindication for participation in this exercise research project.
b.________ Because of the following diagnosis, participation in this exercise research program is inadvisable.

Physician’s name: _____________________________________________
Signature: ______________________________________________________
Date: __________________________________________________________
Address: _________________________________________________________
Telephone: _______________________________________________________
Fax: ____________________________

Dear Patient: Please retain this form and give to the researchers of the Parkinson’s disease exercise study.

Thank you!
APPENDIX D

DATA SHEETS
Appendix D

Data Sheets

**TUG**

SUBJECT CODE:______________ DATE:____________ SESSION #:__________

**Instructions:**
1. Gather stop watch, safety cones, a chair with arms, and Kinesia ONE sensor.
2. Place the back of the chair against a sturdy wall.
3. Place the safety cone 3 meters away from the chair (in a straight line).
4. Have the subject sit in the chair and attach the Kinesia ONE sensor to the back of the subject’s shoe.
5. Time the subject from sitting, stand up, walk 3 meters to cone, walk back, and sit down.
6. Subjects start on word “GO” and should be instructed to walk at a ‘comfortable/normal’ pace.

<table>
<thead>
<tr>
<th>TUG trial</th>
<th>TUG Time</th>
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<tr>
<td>Trial 1</td>
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<td>Trial 2</td>
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</table>

Data Collector: ____________________________ (initial)
Kinesia ONE

SUBJECT CODE:________________ DATE:____________ SESSION #:________

Instructions:
1. Log into [https://kinesia.GLNeuroTech.com](https://kinesia.GLNeuroTech.com)
2. The login is aridge11 and password is password1

<table>
<thead>
<tr>
<th>Session #</th>
<th>Resting Tremor</th>
<th>Postural Tremor</th>
<th>Kinetic Tremor</th>
<th>Finger Tap Speed</th>
<th>Finger Tap Amplitude</th>
<th>Finger Tap Rhythm</th>
<th>Finger Tap count</th>
<th>Hand Movement Speed</th>
<th>Hand Movement Amplitude</th>
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<th>Rapid Alternating Movement Amplitude</th>
<th>Rapid Alternating Movement Rhythm</th>
<th>Dyskinesia</th>
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<td>Dyskinesia</td>
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Data Collector: ______________________________ (initial)
mCTSIB

SUBJECT CODE: ______________ DATE: ______________ SESSION #: __________

Instructions:
1. Touch display screen to turn on the Biodex system
2. On the display screen, touch the testing box
3. Then touch the mCTSIB box
4. Enter in the subject’s demographic information
5. Identify the subject’s foot position. This will consist of the subject’s foot angle and then heel position
   a. The foot angle is determined by selecting the angle of degree on the platform that runs parallel to the specific foot
   b. The foot position is determined by selecting the letter and number that matches the subject’s internal heel position.
   R. foot angle _______ L. foot angle _______ R. heel position _______ L. heel position _______
6. Hit confirm on the display screen
7. Hit begin testing and the display screen will begin to count down from 3 seconds.
8.

<table>
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<tr>
<th>Condition</th>
<th>EO; firm</th>
<th>EC; firm</th>
<th>EO; foam</th>
<th>EC; foam</th>
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<tr>
<td>Sway</td>
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Data Collector: ____________________________ (initial)
**Dynamic Cycling**

SUBJECT CODE: _______________ DATE: ______________ SESSION #: __________

Instructions:
1. Log into the lab top computer.
2. Click on the KSU Bike project.
3. When the first error box appears hit yes.
4. After a few seconds another box will appear, make sure to hit yes.
5. Click the dynamic button and set appropriate cadence (50 rpms for warm-up, 80 rpms for dynamic)
6. Touch the display screen on the display box of the cycle.
7. Tap the dynamic cycling box until it says activated

<table>
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<tr>
<th>Time</th>
<th>Tag 0= Power</th>
<th>Tag 1= Torque</th>
<th>Tag 2= HR</th>
<th>Tag 4= RPM</th>
<th>RPE</th>
<th>BP</th>
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<tr>
<td>Pre warm-up (0:00)</td>
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<td>40:00 mins (end cool down)</td>
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BP after 30 minutes of cycling ________________________________
REFERENCES
REFERENCES


