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**The effects of rigidity on energy expenditure during walking in Parkinson Disease**

by

Alexis Nelson

A Thesis

Submitted in Partial Fulfillment of the

Requirements for the Degree of

Master of Science

Major: Health Studies

The University of Memphis

May 2021

## **PREFACE**

The findings from this thesis will be submitted for publication to *Journal of Neuroscience Letters* and the formatted manuscript of this journal is presented in Chapter II. The formatting of this portion of the document is therefore reflexive of the submission requirements in this journal, however references will need to be in numerical format prior to submission.

## **ABSTRACT**

Nelson, Alexis K. The University of Memphis. May, 2021. The effects of rigidity on energy expenditure during walking and physical activity of daily living in Parkinson Disease and elderly adults. Advisor, Committee Chair: Dr. Douglas W. Powell.

Parkinson's disease (PD) is a neurodegenerative disorder associated with the loss of dopamine producing cells, resulting in motor symptoms including rigidity. There is little known on how the mechanical symptoms of PD are related to metabolic efficiency. The purpose of this study was to investigate the effects of rigidity on energy expenditure during walking. We hypothesized that rigidity would positively correlate to metabolic cost of walking. 20 participants were recruited (10 PD; 10 controls). Equipment involved included a metabolic cart to perform indirect calorimetry (TrueOne, ParvoMedics, Sandy, UT), and an isokinetic dynamometer for passive rigidity assessments (HUMAC, CSMi Inc, Boston, MA). PD observed significant differences in rigidity measurements where PD had higher rigidity compared to controls. No significant differences were observed for energy expenditure. A positive moderate correlation between total rigidity work score and absolute  $VO_2$  was observed, where greater rigidity relates to greater energy expenditure during walking.

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## ABBREVIATIONS

PD	Parkinson's Disease
CON	Healthy Age Matched Controls
QoL	Quality of Life
HRQoL	Health Related Quality of Life
SNc	Substantia Nigra pars Compacta
SR	Shortening Reaction
SII	Stretched-Induced Inhibition
COM	Center of Mass
MDS-UPDRS	Movement Disorders Society Unified Parkinson's Disease Rating Scale
MVIC	Maximum Voluntary Isometric Contraction
PFS-16	Parkinson's Fatigue Scale – 16
MMSE	Mini Mental State Exam

## CHAPTER I

### Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder associated with the loss of dopamine producing cells in the basal nuclei. In time, after 80% of neuronal apoptosis, the neurodegeneration leads to motor symptoms such as bradykinesia, postural instability, rigidity and tremor [82]. Overall, motor symptoms negatively impact the quality of life (QoL) and independence for PD patients [59]. A large contributor to a decreased QoL for PD stems from the cardinal symptoms as an inability to perform daily tasks such as walking.

Gait mechanics of PD are altered and continue to digress in the ability to maintain as the disease progresses. PD patients experience gait dysfunction through reduced gait velocity, variability, shortened step and stride lengths, reduced range of motion, reduced width variability and freezing of gait [23, 24, 32, 47, 63, 65, 68]. The previously mentioned adopted walking strategies reduce the mechanical efficiency of the system to perform the task [8]. This is partially due to the inability of the elastic musculotendon components to utilize energy conserving strategies. To conserve energy, the musculoskeletal system stores mechanical energy in the parallel and series elastic components during the early stages of gait. The series elastic component represents the tendon and the intrinsic elasticity of the myofilaments. Therefore, tendon compliance has a large influence on whole body metabolic efficiency [92] and further the ability of the tendon to perform its part in mechanical efficiency is compromised when the system is rigid. This mechanical inefficiency can potentially lead to an increase in metabolic demand.

PD patients exhibit greater metabolic costs of walking [16, 39]. In addition, higher  $\text{VO}_2$  are observed walking at preferred velocities in PD compared to healthy controls. Energy consumption while walking is higher in PD patients compared to healthy controls [51]. Further, energy expenditure during a 6-minute walk test has been correlated to physical activity levels for PD patients at home [38]. This increase in energy consumption during activities of daily living are well researched, however the connection to motor symptoms such as rigidity are not known.

In PD, an increase in energy expenditure has thought to be expressed through the symptom of fatigue [8]. In addition, for PD a potential mechanism behind mechanical inefficiency through the elastic components can be seen through the symptom of rigidity. Rigidity is defined as an increased resistance to passive movements created by hypertonia and increased intrinsic stiffness of passive connective tissues [22]. There is little research in PD on how mechanical and metabolic efficiency is connected. An increased understanding on the importance of the elastic components in mechanical efficiency, is necessary to identify the role of intrinsic stiffness in PD patients on the metabolic demand for gait. Therefore, the purpose of this study is to investigate the effects of parkinsonian rigidity on energy expenditure during walking in individuals with PD. We hypothesize that with increasing amount of rigidity, there will be a subsequent increase in energy expenditure during walking.

## CHAPTER II

### Literature Review

#### *Background*

Parkinson's disease (PD) is a progressive neurodegenerative disorder commonly characterized by motor symptoms such as bradykinesia, rigidity, tremor and postural instability [87]. Throughout the world, PD is most concentrated in the North American region [17]. Within the United States of America, PD is the second most prevalent neurodegenerative disorder [44]. Nationally, the burden of PD exceeded \$14.4 billion in 2010, leading to an estimated \$22,800 in healthcare costs per patient [44]. Not only is PD costly, but the projection of PD cases is estimated to grow substantially over the next two decades due to the increasing elderly population. More specifically, by 2040 from 2010 the PD population is estimated to double from the census of 630,000 patients that year [44]. The overall prevalence in the United States is small at 0.3% but, rates significantly increase to 1-2% in persons over the age of 65 and 4-5% for people of 85 [87]. With an increasing population with the disease, the estimates on national and individual debt are also bound to increase. Commonly the age of onset for PD is 60, but 10% of those affected are only 21 to 45 years [87]. Therefore, all adult groups are susceptible to PD. Individuals with PD experience numerous negative effects to their quality of life. Decreases in health-related quality of life (HRQOL) have been shown to have increases in disease severity [34].

#### *Etiology*

Overall, there are two types of PD; idiopathic and familial. 90% of neuropathologic PD are idiopathic, only 10% have a familial or genetic origin [87]. For the genetic origin, six gene mutations are currently known [87]. There are 18 chromosomal regions (termed PARK) that

have been found to be associated with PD onset but, research involving mutations in these areas are unreliable. PD-related mutations are said to affect proteins similar to alpha-synuclein and ligases like parkin as well as other molecular processes [9]. These genetic mutations are thought to forebode the pathology underlying PD. The pathology of idiopathic PD remains unclear but there are a few risk factors that have been identified. One factor within idiopathic PD is exposure to pesticides. This has been found to be an environmental risk factor to aid in the onset of PD [76].

Methods to how neuronal degeneration starts in PD are still in the research processes relating to both familial and idiopathic origination of the disease. Researchers found in PD oxidative stress, molecular changes and mitochondrial dysfunction contribute to neuronal apoptosis [52]. In a similar manner the above factors simultaneously enhance genotoxic agents, while increasing oxidative damage to proteins and lipids [54]. In idiopathic PD, an increase amount of  $\alpha$ -synuclein in the substantia nigra pars compacta (SNc) associates with the aggregation of proteins. This method of aggregation has also been found in an autosomal recessive form of familial PD formed from a mutation with the Parkin gene where the gene protects against the toxicity of the protein  $\alpha$ -synuclein [64]. With this mutation, a specific type of  $\alpha$ -synuclein is increased, making  $\alpha$ -synuclein a common factor in both origins of PD [54]. The accumulation of mutant  $\alpha$ -synuclein protein is involved with the generation of Lewy bodies. Lewy bodies simultaneously increase with pro-apoptosis factors. Functionally, Lewy bodies are known to either act as a cytoprotective response or act as an aid to neurodegenerative processes. Overall, Lewy bodies are an important marker to sight in the progression of PD.

### *Pathology of signs and symptoms*

Parkinson's can be described as a combination of motor problems of bradykinesia, resting tremor, rigidity, "freezing" and fatigue [22]. All of the symptoms named above stem from the basal ganglia dysfunction. The basal ganglia are a part of the subcortical nuclei that is made up of the caudate, putamen, globus pallidus (internal and external) and subthalamic nucleus (SNc). Functionally, the SNc works with the basal ganglia, but anatomically the SNc is a nucleus in the midbrain. Controls behind the basal ganglia include voluntary motor movements, procedural learning, eye movements, cognition and emotion. PD resides in the loss of dopaminergic neurons in the SNc. Motor symptoms such as rigidity or bradykinesia start to show when there is a 60% reduction in dopaminergic neurons in the putamen and an 80% reduction of dopamine [22]. The dorsal striatum, consists of the caudate and putamen, is the messenger pathway for the basal ganglia. This system receives excitatory afferent from the cortex and thalamus to form two pathways: indirect and direct. Both pathways are the most influential of the basal ganglia to control movement compared to other motor pathways [88]. Most of the cells in striatum are GABAergic (inhibits neural activity). The direct-pathway originates in the striatonigral which receives excitatory afferents from the sensorimotor cortex and thalamus. Direct pathways then project to GABAergic neurons in the internal globus pallidus and SNc which then send axons to the motor nuclei of the thalamus which offsets the inhibition signal. Direct pathways facilitate movement. Indirect-pathways originates from the striatopallidal and acts as an inhibitory synapse on GABAergic pallidal neurons and projects to the subthalamic nucleus. Subthalamic neurons sends axons to the internal globus pallidus and SNc which form excitatory synapse for the inhibitory output neurons [45]. The net effect of the indirect pathway is movement inhibition. An important role of dopamine is to regulate the two pathways through

two receptors: D1 and D2. D1 receptors facilitate firing in the striatum, where D2 receptors inhibit. Individuals with PD have trouble regulating the indirect and direct pathway due to the imbalance of dopaminergic neurons. PD reduces the dopamine receptors to activate which creates a downstream inhibition of the indirect pathway and decreased excitatory component of the direct pathway [22, 45].

### *Bradykinesia*

Bradykinesia is the slowness in a performed movement [7]. There are two elements to bradykinesia; hypokinesia, which explains the smaller range of motion with slowed movements and akinesia which refers to the late onset in order to initiate a movement [7]. Akinesia can be divided into three parts: (1) slowness and unskillfulness of movement secondary to rigidity, (2) absence of muscular weakness with lack of movement, and (3) difficulty to initiate movement. The first and second type of akinesia can be helped through Levodopa medications, and through stereotaxic thalamotomy within the ventrolateral nucleus of the thalamus [10]. The third type of akinesia has been shown to worsen through levodopa medication but helped through norepinephrine therapy.

In PD, one of the causes of bradykinesia is that motor units are slowed once fired and require a higher threshold than normal to fire [19]. Movement velocity correlates to the progression and severity of bradykinesia [10]. Bradykinesia is not inflicted by the motor control, but rather from the basal ganglia or by disrupted movement patterns [57]. In past research, following the disease, the initial least affected limb will grow to the same severity of the most affected limb with time [49]. In akinetic-rigid PD, deterioration of mental status parallels advancement in bradykinesia and independent from tremor [93]. Overall, this clarifies the reason behind two types of PD; tremor dominant PD, and akinetic-rigid PD where majority of the

symptoms are expressed independently from tremor. Bradykinesia is a symptom of akinetic-rigid PD.

### *Rigidity*

Muscle rigidity is defined as a uniformed resistance throughout an entire passive range of motion throughout the limb [67]. There are two elements of PD rigidity; (1) hypertonia, which is increased resistance of the joint to passive movement and (2) uniformity of the resistance, in which the resistance stays relatively constant across the ROM [67]. With the two elements, two mechanisms underlay uniformed muscle rigidity. The neural-mediated excitation of shortening muscles, i.e. the shortening reaction (SR) or the inhibition of stretched muscles i.e. stretched-induced inhibition (SII) help increase uniformed rigidity [66, 67]. There is a neural and non-neural contribution to rigidity. As stated above, neural contributions to rigidity are ascribed as some over-reaction of the stretch reflex mechanism. Specifically behind neural-rigidity mechanisms, the long-latency stretch reflexes are increased in size in PD due to the use of supraspinal pathways [73]. As a result, parkinsonian individuals should have a heightened long latency EMG magnitude during passive stretching when compared to age matched controls. In addition, PD experience high amounts of EMG activity during passive shortening of the muscle [5]. Both short and long latency reflexes have been shown in sagittal plane movements. Overall, this heightened long latency reflex and shortening reaction suggest that this reflex alteration contributes to neural components of parkinsonian rigidity and aid in an increase resistance to passive movements [5, 67]. The duration and magnitude of the long-latency reflex mostly contributes to increase hypertonia in PD [8]. Increased muscular activity at rest contributes to muscular rigidity in PD patients [8]. This is caused from brain efferent signals a need to the muscle to contract. Past research states that this symptom is due to neural components, but

current research is finding that non-neural components can be the cause of muscle rigidity [8, 67, 68]. Non-neural components include connective tissue, and increased stiffness in the tendons and muscles. All of the above including: an increased muscular signal at rest, an increase in stiffness at the tissue level, and an increased muscular effort show several mechanisms to show the abnormalities in muscular performance in PD patients.

### *Biomechanics of movement*

#### Muscular Effort / Peak Force Production and Rate of Force Development

In healthy older adults, muscular effectiveness already decreases with age; however, not at the equivalent rates with PD [43]. An early detection for PD has been speculated to be an increase in muscular weakness. Even in early stages of PD, power and work values compared to healthy age matched controls were significantly decreased in the lower extremity. In PD, previous research has shown that rate of force development, force steadiness and peak forces are altered [72, 78]. Rate of force development is hindered and also there is a reduction in peak maximum voluntary skeletal force output in PD patients [25, 31, 80, 81]. This has been shown through decreases in isokinetic force production in the lower extremity of PD patients [43, 81].

Specifically, PD shows a disparity in rate of force development in early to mild-to-moderate cases [31, 72]. In addition, with an increase in performance velocity, PD patient's performance decreases drastically compared to healthy controls. In healthy controls the trend is with increasing isokinetic velocity, a decline in muscle torque is expected. However, with Parkinson's patients this trend shows a greater disparity suggesting greater muscle weakness, and increasing disparity with disease progression [40, 58]. Anatomically, individuals with PD have been found to have less tendon elongation and muscle fascicle shortening, potentially having a connection to the decrease ability to produce force quickly [79]. Overall, in PD a trend shows

muscle weakness. This muscle weakness also affects several performance variables that affect activities of daily living. This reduction in muscle power has been associated with a greater fall risk and slower walking velocities [4]. In addition, Without the ability to develop force quickly, the risk of falling due to the inability of the patient to regain balance increases significantly [41]. Lower extremity muscles are important to perform activities of daily living such as balance, walking, showering, and many other examples. An inability to utilize large muscle groups at a short notice alters the quality of life of PD patients significantly. An origin for the inability to produce force quickly could be due to rigidity. Rigidity is the increase in resistance to move a limb through a range of motion. A way to quantify rigidity is through a work score.

Rigidity and work score have been correlated as a clinical quantitative assessment of rigidity. Work score helps to measure the elastic, viscous and inertial components of rigidity where velocity, length and acceleration all have a factor in resistance forces around the joint. Another way to quantify rigidity is through the use of angular impulse at a singular moment instead of throughout the movement [29]. Overall, PD patients show a reduction in muscle strength, power and alteration in the musculotendon mechanics creating a potentially inefficient system metabolically. There is an increased need to understand the relationship between how increases in physiological demand and reductions in mechanical efficiency affect the quality of life of PD patients. An inability to voluntarily reach a peak muscle activation could lead to muscle weakness, where overall could lead to alternate tendon mechanics leading to a less metabolically efficient system.

## *Energy Expenditure and Gait*

### Metabolic Demand

Whenever muscular work is performed, energy consumption is required. In order to move, mechanical patterns must be selected. Movement strategies are selected based on the metabolic cost of the action [3, 15, 56]. A reduced metabolic cost can be described as the conservation of energy exerted. Where an increased metabolic cost increases the amount of energy exerted through an increase in task demand. Breathing strategies depict one-way energy conservation can be quantified. A serial quick exchange of inhalation and exhalation of air can increase the energy needed for the task [60]. The longer the task is sustained or higher intensity the task needs, an increase in energy is required.

There is a ratio between breathing techniques and walking for energy consumption. During walking, a higher stride rate will equate to a higher energy consumption [70]. In addition, mechanical function can help define what physiological need is required. Human locomotion requires the body to progressively move through continuous displacement of the center of mass (COM). This displacement of COM in the lower extremity moves similar to an inverted pendulum. For instance, COM vertically oscillates throughout gait cycle. During the first stage of gait, COM projects in an upward motion for the body to fall forward. Once double support begins, COM falls and then heel strike abruptly raises COM to initiate the gait cycle again. In this paradigm, if movement is not impeded, the cyclical motion of the lower extremity will sustain with little to no mechanical work required [37, 46, 86]. With this stated, work is required during single limb stages of gait to redirect the COM [28], making the system require some energy consumption. However, energy to continue the pendulum of walking does not need the energy required as seen in previous research. Since the net mechanical work of the system is zero

without consideration of the single limb phase, additional energy conservation mechanisms must be in work.

Musculotendon units make up the elastic components which contribute to energy conservation during gait [28, 37]. Therefore, mechanically, tendon's help to decrease energy expenditure in walking and muscles are composed of contractile and elastic components, making up the energy consumption factors of walking. This relationship of musculotendon units can fluctuate, where tendon recoil can decrease the use of muscles during gait. For example, the Achilles tendon recoil helps decrease the use of the medial gastrocnemius during walking [48]. One way this ratio can be altered is through compliancy of the tissues. For instance, in order to perform optimally, tendons require an appropriate stiffness [30, 48]. Tendon stiffness is affected in PD patients, and ultimately can change the mechanisms behind musculotendon unit energy expenditure [67].

In addition to altered tendon tissue factures, altered gait strategies of PD patients could affect walking economy strategies as well. Compared to healthy age matched controls, PD individuals walk with shorter stride lengths. Shorter stride lengths has been known to increase walking economy in healthy individuals [53]. In addition, there is a greater walking economy in PD patients compared to healthy individuals [16]. However, walking economy has not been explained through parsing potential factors that aid in the increase of economy in PD patients compared to healthy individuals.

### Oxygen Consumption

With a higher metabolic demand, a higher consumption of oxygen is needed to continue the task. In walking PD patients have shown to have a higher oxygen cost of walking compared to health controls [38, 39]. Contrarily, in a study examining mild to moderate PD patients, no

rigidity requirement, aerobic capacity measures did not differ from predicted normal O<sub>2</sub> consumption levels during a maximal cycle ergometer. However these patients showed that their walking strategy was different compared to a healthy gait even when the velocities were in normal ranges [14]. However peak VO<sub>2</sub> was significantly lower in PD compared to healthy controls in a separate study later on [42]. This could be due to the inclusion material for not controlling for rigidity scores, and performing the aerobic capacity measures on an ergometer instead of a walking task. A walking task increases the stress to the system due to the difficulty for PD patients to perform the task.

Specifically, individuals who have PD and a shorter stride length demonstrate higher values of oxygen cost of walking. Oxygen consumption could be a physiological predictor of neurological walking dysfunction [39]. In PD patients, oxygen consumption averaged 64% at their preferred comfortable pace, indicating severe impairments for economy of gait [42, 77]. This is predicted to increase the energy demands to perform daily physical activities. In addition this all leads to a lower physiologic reserve where gait is performed at a high percentage of the patient's VO<sub>2</sub> [42]. With a higher metabolic demand, shown by an increase in oxygen consumption during a preferred walking pace, this should increase the fatigue of the PD patient during daily activities.

### *Fatigue*

Fatigue is frequently an early symptom of PD and approximately 58% of people with PD reported fatigue as one of their top 3 most disabling symptoms [26]. After a nine year follow up from the patients that reported severe fatigue symptoms showed a correlation between fatigue and the severity of the disease [27]. In comparison to healthy patients who reported significant fatigue: only 15% of healthy men and 29% of healthy women aged 65 to 102 years reported

significant fatigue [85]. PD-related fatigue has been described as an “overwhelming sense of tiredness” or “lack of energy” [2] and may be associated with a number of social, psychological and physiological factors including depression or anxiety [12].

Such wide-ranging descriptors of fatigue include subjective states that are independent of activity as well as activity-related decreases in force production. Findings from broad investigations of disease-associated fatigue are unclear and difficult to use in structuring treatment protocols. A common factor amongst people who report fatigue have a sedentary lifestyle. In a past study, 66% of men and 82% of women who reported fatigue, also reported a sedentary lifestyle [85]. There are two types of fatigue: fatigue and fatigability. Activity-induced fatigue is an important subcategory of fatigue which is more clearly identified by the term “fatigability” [21]. Fatigability is used to set apart activity- or exercise-induced changes that result in reduced muscle force production as opposed to the perception of fatigue which is manifested as a general state-of-being associated with an ongoing sense of tiredness or lack of energy. Fatigability is the result of substrate depletion at the muscle, or the inability to fire motor units (Mus) from the central structures. Peripheral fatigue will be caused from the intra-muscular inabilities to generate a movement in the same time as prior to the onset of fatigue, and central fatigue will result from the motor cortex’s inability to propagate a neural signal to the muscle [83]. Although fatigue is a prominent and disabling feature of PD, few studies have directly investigated the origins or mechanisms underlying PD-related fatigue.

### *Physical Activity*

Physical activity is considered to be one of the more important non-pharmaceutical strategies to improve quality of life. Physical activity is defined as any body movement that contracts skeletal muscle throughout the day that is unplanned, where planned physical activity is an exercise. For PD physical activity has been shown to improve the management of symptoms, and delay disease progression [11, 61,

75]. However, the majority of PD patients have reported significantly less physical activity levels compared to the general population [84]. In addition, PD population decreases physical activity more rapidly as they age compared to the healthy population [14]. A main concern for low physical activity rates is the effects of deconditioning. Deconditioning is associated with disuse-induced changes in muscle and bone due to a lack of load on the system, and a secondary effect of cardiometabolic risk factors that stem from low physical activity levels, that are exacerbated in neurological disabled populations [71]. This lack of participation in physical activities in PD patients has been predicted to correlate to their increase in energy consumption, leading an increase in symptoms of fatigue and to a subsequent decrease in physical activity. Through the use of accelerometer output and its association with energy expenditure in persons with mild-to-moderate Parkinson's disease, low physical activity levels demonstrated a strong correlation to energy expenditure [38]. Previous research shows that PD exhibits an increase in walking abnormalities, causing an increase in metabolic demand and a decrease in physical activity, however previous research has not shown if the symptom of rigidity could be a key factor that causing this cascade of secondary symptoms. The purpose of this study was to examine the effects of rigidity on metabolic cost in Parkinson's Disease during a walking task, to determine if rigidity and metabolic cost are correlated.

### **Research Question and Hypothesis**

*Question #1:* Is there a relationship between parkinsonian rigidity and energy expenditure during walking?

*Hypothesis #1:* We predict that increased rigidity will be positively correlated with increased metabolic cost during walking in PD patients.

## CHAPTER III

### **The effects of rigidity on energy expenditure during walking and physical activity of daily living in Parkinson Disease and elderly adults**

**Alexis K. Nelson, Deranda Lester, Melissa Puppa, Douglas W. Powell**

*Manuscript in preparation for Neuroscience Letters*

#### **INTRODUCTION**

Parkinson's disease (PD) is a movement disorder with motor symptoms of bradykinesia, tremor, postural instability and rigidity. PD motor symptoms affect the ability of the individual to perform activities of daily living substantially. Motor symptoms can help to drive non-motor symptoms. Motor symptoms have secondary effects, one being fatigue. Fatigue is reported as one of the most disabling nonmotor symptoms of PD [6]. Specifically, 50% of patients report fatigue as one of their most disabling symptoms [26]. In addition, fatigue could be a driving factor for a decrease in participation shown in recreational activities for PD, such as social, hobbies or sports, and leads to limited working hours [33]. Overall, fatigue limits the ability of individual to perform daily tasks, which decreases the quality of life.

Activity-induced fatigue is an important subcategory of fatigue which is more clearly identified by the term "fatigability" [21]. Fatigability is used to set apart activity- or exercise-induced changes that result in reduced muscle force production as opposed to the perception of fatigue which is manifested as a general state-of-being associated with an ongoing sense of tiredness or lack of energy. Fatigability is the result of substrate depletion at the muscle, or the inability to fire motor units (Mus) from the central structures. An increase in substrate depletion can stem from an increase in demand to the system.

Rigidity increases demand through increases in activation and resistance to move throughout joint ranges of motion. PD exhibits muscle activation at rest, and increased torque level initially and throughout motion [13, 67, 89, 91]. All of this states that rigidity leads to greater muscular effort to

perform similar tasks to healthy controls [36]. Increased muscle activation, potentially could increase the physiological response of the system to meet the demand.

PD patients exhibit greater metabolic cost of walking compared to healthy controls [16, 39]. Specifically, higher  $\text{VO}_2$  measurements compared to healthy controls at self-selected paces have been observed and an increase in oxygen consumption in PD [16, 42, 51]. Net economy of walking is greater in PD during walking [14, 39, 69]. Increases in metabolic demand has shown to correlate to decreases in physical activity at home [38]. However, there is a gap in the literature to compare if an increase in mechanical demand from rigidity correlates to metabolic measurements of walking.

Therefore, the purpose of this study was to find the relationship between rigidity and the metabolic cost of walking. We hypothesized that rigidity will positively correlate to walking, where greater rigidity will increase the metabolic cost in PD.

## **METHODS**

### *Participants*

20 participants (10 PD; 10 age-matched controls) between the ages of 50 to 75 years of age were recruited for this study. Inclusion criteria for individuals with PD will included: (1) being treated by dopaminergic medication, (2) having the presence of clinical rigidity ( $> 1$ , slight to mild to moderate or marked) in one or both limbs (legs) and (3) having a minimal tremor ( $< 1$ , slight and infrequently present). In addition, participants in the PD group had scores from the Motor Section (Part III) of the MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) as well as the Hoehn and Yahr scale less than 2.5 provided by their physician [22]. The Hoehn and Yahr score of 2.5 or less indicates that the patients are all within mild-moderate stages of PD. The Motor Section (Part III) of the UPDRS includes subjective assessments of rigidity, bradykinesia, postural instability and gait impairment. Part III motor score of greater than 15 to

indicate moderate showings of motor symptoms. All potential participants with PD were pre-screened by their movement disorders specialist on the patient's optimal-ON medication state. The UPDRS was designed by the Movement Disorder Society and is composed of four sections: intellectual function, activities of daily living, motor exam and motor complications [1]. Individuals with PD are given a score from a scale of 0 to 4 with 0 being normal or no problems and 4 being severe problems for each question on the exam. During the motor assessment, physicians are taught to move the patients' limb passively through a range of motion and rate the evoked resistance using the previously mentioned scale with 4 meaning the "range of motion [is] achieved with difficulty". Based on UPDRS scores and physician feedback, individuals with PD were classified by disease severity. Additional exclusion criteria included any comorbidities such as any cardiovascular diseases, dementia, etc. from being able to perform the protocol in addition to any lower extremity injuries within the previous 6 months.

Control subjects were age – matched to participants with PD and will have no history of neurological disorders. Healthy controls performed the motor section (Part III) of the MDS- Unified Parkinson's Disease Rating Scale to indicate that all participants were "healthy" and did not exhibit any motor symptoms. A score of 0 for all of Part III MDS-UPDRS were required from healthy participants in order to participate. Any participant with an ankle range of motion smaller than 35 degrees or knee range of motion smaller than 60 degrees or a history of lower extremity condition that would affect ankle or knee joint ranges of motion were excluded. Any musculoskeletal injuries or health related disabilities that would affect the participant's walking pattern in the lower extremity within the recent 6 months were also excluded for participation.

### *Experimental Protocol*

Participants visited the Musculoskeletal Analysis Laboratory (MAL) once for examination and testing. Individuals were screened for inclusion in this study, screening will include the Mini-Mental State Exam, and provide written informed consent. Following screening and consent, testing will occur in the following order: (1) complete the Parkinson's Fatigue Survey (PFS-16), anthropometric measurements (measurements will include: age, sex, height and weight) (2) completion of maximal voluntary isometric contractions at the knee (3) rigidity testing at the knee and repeat steps (2) and (3) for the ankle (4) completion of over ground walking task of three trials at a preferred and maximal self-selected pace (5) placement of reflective markers and (6) treadmill walking at a pace equal to their over ground walking self-selected preferred pace for 6 minutes with the use of the metabolic cart, and (7) distribution of the accelerometer.

### *Rigidity Testing*

Following anthropometric assessments, each participant will perform a maximal voluntary isometric contraction (MVIC) in an isokinetic dynamometer (HUMAC, CSMi Inc, Boston, MA) for ankle and knee flexors and extensors. All rigidity testing were performed on the most affected limb for PD patients and the dominant limb for controls. The MVIC were used to identify peak force output and rate of force development of the extensors and flexors of the ankle and knee. Participants were asked to "push as hard as you can" against the dynamometer arm and strapped into the device to minimize risk of excess movement and injury. Participants remained in the dynamometer for passive compliance testing at the ankle and knee. This protocol allows for quantification of rigidity in a similar manner that physicians diagnose patients. During this portion, the isokinetic dynamometer moved the participant's passive limb through a range of

motion while recording the resistance torques applied by the lower extremity soft tissues. Given that the participant is passive, the resulting torque measured by the dynamometer would be a result of the resistance applied by passive tissues. Previous literature suggests that this method of testing adequately quantifies both the neural simultaneously as non-neural contributions to rigidity because the application to the joints allows for activation without muscle input. Therefore this 'activation' is a representation of passive tissue deformation during a range of motion [62, 74, 90]. This would be classified as the non-neural part of rigidity and would in turn be the resulting contribution to the passive torque. At the ankle joint, participants will be moved through a range of motion equal to 30 degrees (15 degrees of dorsiflexion; 15 degrees of plantarflexion) and at the knee joint with a range of motion equal to 60 degrees (60 degrees flexion; 0 degrees extension). The dynamometer will perform the continuous passive motion (flexion/extension) at each joint for a period of 45 seconds at two velocities: 60 deg/sec and 180 deg/sec.

### *Over Ground Walking*

Following rigidity testing, a total of six over ground walking trials will be performed across a 3-meter walkway for the preferred walking velocity (three trials) and maximal walking velocity (three trials). A pair of infrared timing gates (Lafayette Instruments) were used to determine the walking speed of the participant over the center 3 meters of the walkway. An average of the three trials will be used as the participant's self-selected walking pace and maximal walking pace. The preferred walking pace was maintained during the treadmill walking trials. Following over ground walking trials, participants rested as needed prior to continuation of the experimental protocol.

### *Experimental Equipment*

Following overground walking, retro-reflective markers were placed bilaterally on the participant's upper and lower extremity including; pelvis, thigh, shank and feet to measure individual segment motion during treadmill walking trials using a 9-camera motion capture system (150 Hz, Qualisys AB, Goteburg, Sweden). For static markers, retroreflective markers were placed on the first and fifth metatarsal heads, the medial and lateral placement of the malleolus for the ankle and epicondyles of the knee, and the iliac crest of the pelvis and greater trochanter of the hip.

### *Treadmill Walking*

Once the markers were placed, participants walked for six minutes at the participants preferred velocity on a force imbedded treadmill to record ground reaction forces (GRFs; 1500 Hz, Bertec Inc., Columbus, Ohio USA), three-dimensional kinematics and indirect calorimetry using a metabolic measurement system (TrueOne, ParvoMedics, Sandy, UT). The ground reaction forces collected in the walking trial were used to find internal joint moments. Indirect calorimetry compares the concentrations of gases within the room to the concentrations of gases expired by the participant to determine the quantity of oxygen consumed by the participant during a given task. Participants performed a 6-minute treadmill walking task while three-dimensional kinematics and energy expenditure is recorded. Gait kinematics were recorded in 60 second intervals starting at the beginning of each minute during the 6-minute treadmill walking task while energy expenditure was collected continuously throughout the treadmill walking protocol.

### *Data Analysis*

Key outcome variables of the study included parkinsonian rigidity, metabolic cost of walking, and physical activity. Parkinsonian rigidity was quantified by the rigidity work score, angular impulse and slope of the extension and flexion angle. Angular impulse was calculated as the torque value integrated with respect to time ( $\text{Nm} \cdot \text{sec}$ ). Angular impulse used the negative slope angle determined by the start and stop of the extension or flexion of the joint movement (ankle or knee), which is calculated as the passive resistance torque integrated with respect to joint angle. Rigidity work score is calculated by the integral of torque with respect to joint angle ( $\text{Nm} \cdot \text{deg}$ ).

Metabolic cost of walking was quantified as the average volume of oxygen consumed during the third to sixth minutes of treadmill walking task. Metabolic cost data from the first two minutes were discarded as the data represent acute metabolic responses to activity and are not reflective of a stable metabolic cost of the treadmill walking task.

### *Statistical Analysis*

To investigate relationships between independent variables (metabolic cost of walking and rigidity) and determine significant differences in walking velocity, energy expenditure and rigidity score one-tailed independent sample  $t$  tests were performed with significance level set at  $\alpha = 0.05$ . Cohen's  $d$  effect sizes will be computed to determine the magnitude of differences in dependent variables. For Cohen's  $D$  of effect sizes: small  $d < 0.6$ , moderate:  $0.6 < d < 1.2$ , and large:  $d > 1.2$  [35]. A correlation analysis was used to quantify the relationship of energy expenditure and rigidity scores.  $R$  – squared will be quantified if a meaningful moderate or above correlation were found to find an explanation for the variance.

## RESULTS

[Table 1 here]

Table 1 shows participant information summaries. Our findings observed that within our sample, height and weight were significant with a large effect size ( $p = 0.01$ ,  $d = 1.15$ , and  $p = 0.01$ ,  $d = 1.26$ , respectively) where both height and weight were greater in the PD group compared to the healthy controls. In addition, the UPDRS part three motor examination were also significant with a large effect size ( $p < 0.01$ ,  $d = 6.11$ ) where PD had a greater score than the control condition.

[Table 2 here]

Table 2 summarizes all velocity measurements; overground and treadmill. Our findings observed no difference between groups for the participant's preferred or maximum walking during the overground session ( $p = 0.22$ ,  $d = 0.37$ , and  $p = 0.40$ ,  $d = 0.12$ ). However, treadmill preferred walking velocity showed significant differences with a moderate effect size between the groups where the controls preferred to walk faster than the PD group ( $p = 0.05$ ,  $d = 0.8$ ). Further, both the PD and control group observed significant differences between their overground and treadmill walking velocities where the treadmill speed was slower than the preferred overground velocities (PD  $p < 0.01$ ; Control  $p = 0.02$ ).

[Table 3 here]

Table 3 summarizes all metabolic measurements. For energy consumption, no significant differences were found between  $VO_2$  measured in ml/kg/min or  $VO_2$  in L/min, or  $VO_2$  normalized to treadmill velocity in meters per second (mps). However, a moderate effect size was observed for the efficiency of the task of  $VO_2 \cdot \text{mps}^{-1}$  ( $d = 0.62$ ). Effect sizes were not

notable for  $\text{VO}_2$  measured as  $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  ( $d = 0.45$ ), or  $\text{VO}_2$  measured as  $\text{L} \cdot \text{min}^{-1}$  ( $d = 0.23$ ).

[Table 4 here]

Ankle rigidity measures are stated in Table 4. Rigidity measurements included rigidity work score, slope, impulse, peak dorsiflexion and plantarflexion in degrees. At the ankle all variables observed statistically significances, except for extension impulse, and peak degree measurements, extension and flexion ( $p = 0.126$ ,  $d = 0.55$ ,  $p = 0.269$ ,  $d = 0.29$ , and  $p = 0.168$ ,  $d = 0.44$ , respectively). Total rigidity work score, and components to calculate total rigidity work score (extension and flexion) observed statistically significances with a large effect size ( $p = 0.014$ ,  $d = 1.1$ ,  $p = 0.034$ ,  $d = 0.91$ , and  $p = 0.007$ ,  $d = 1.29$ , respectively). Flexion impulse observed statistically significance with a moderate effect size ( $p = 0.050$ ,  $d = 0.80$ ). Extension and flexion slope observed statistically significances with a large effect size ( $p = 0.019$ ,  $d = 1.02$  and  $p = 0.007$ ,  $d = 1.26$ ).

[Table 5 here]

In table 5, knee rigidity measurements are observed. At the knee, all measurements were statistically significant and had a large effect size. For rigidity work score, total, flexion and extension work scores were statistically significant with a large effect size ( $p < 0.01$ ,  $d = 1.84$ ,  $p < 0.01$ ,  $d = 1.48$ , and  $p < 0.01$ ,  $d = 1.67$ , respectively). Extension and flexion impulse were statistically significant with a large effect size ( $p < 0.01$ ,  $d = 1.48$  and  $p < 0.01$ ,  $d = 1.67$ ). Extension and flexion slope were statistically significant with a large effect size ( $p = 0.026$ ,  $d = 0.99$  and  $p < 0.01$ ,  $d = 1.80$ ).

[Table 6 here]

Table 6 reports the correlation analysis between metabolic and rigidity measurements at the ankle. Positive moderate correlations were observed between rigidity work score measurements (total, flexion and extension), and flexion impulse for all metabolic measurements in the PD group and a  $p$  value was run for the total rigidity work score from the Pearson product correlation coefficient for all metabolic measures (*total*:  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$ :  $r = 0.69$  and  $p = 0.044$ ,  $0.60$ ,  $0.76$ , and  $0.69$ ;  $\text{VO}_2 \cdot \text{mps}^{-1}$   $r = 0.67$  and  $p = 0.048$ ,  $0.60$ ,  $0.72$ , and  $0.67$ ;  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ :  $r = 0.49$  and  $p = 0.188$ ,  $0.42$ ,  $0.56$ , and  $0.49$ ;  $\text{VO}_2 \cdot \text{mps}^{-1} \cdot \text{kg}^{-1}$ :  $r = 0.49$  and  $p = 0.197$ ,  $0.43$ ,  $0.54$ , and  $0.48$ , respectively). Positive weak correlations were observed between ankle slope measurements, extension and flexion, compared to all metabolic measurements in the PD group (*Extension*:  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$ :  $r = 0.23$ ,  $0.28$ ;  $\text{VO}_2 \cdot \text{mps}^{-1}$   $r = 0.28$ ,  $0.30$ ,  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ :  $r = -0.03$ ,  $0.08$ ;  $\text{VO}_2 \cdot \text{mps}^{-1} \cdot \text{kg}^{-1}$ :  $r = 0.07$ ,  $0.12$ , respectively). For controls, all correlations were weak except for flexion work observed a moderate correlation in  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$  and  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  ( $r = 0.31$ ,  $0.32$ , respectively). Only statistically significant rigidity measurements were included in the correlation to metabolic measures. A  $p$  value was determined for total rigidity work measurements for all  $\text{VO}_2$  measurements from the Pearson product correlation analysis ( $\text{AVO}_2 \text{ L} \cdot \text{min}^{-1}$   $p = 0.245$ , absolute  $\text{AVO}_2 \cdot \text{mps}^{-1}$   $p = 0.386$ ,  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$   $p = 0.740$ ,  $\text{VO}_2 \cdot \text{mps}^{-1}$   $p = 0.865$ ).

[Table 7 here]

In table 7 reports all observed correlations at the knee for rigidity and metabolic measures. At the PD knee group, A positive moderate correlations were observed between total rigidity work score and two metabolic measures of  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$  and efficiency of  $\text{VO}_2 (\text{L} \cdot \text{min}^{-1} \cdot \text{mps}^{-1})$  in the PD group ( $r = 0.43$ ,  $p = 0.433$  and  $r = 0.33$ ,  $p = 0.386$  respectively). A positive

moderate correlation was observed for extension rigidity work score two metabolic measures of  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$  and efficiency of  $\text{VO}_2 (\text{L} \cdot \text{min}^{-1} \cdot \text{mps}^{-1})$  in the PD group ( $r = 0.45$  and  $r = 0.32$ , respectively). For the controls, a positive moderate correlation was observed between extension rigidity work score and impulse for  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  ( $r = 0.31$  and  $r = 0.31$ , respectively). A positive moderate correlation was observed between flexion work score and  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$  in the PD group ( $r = 0.31$ ), and the controls observed a negative moderate correlation between flexion work and efficiency of  $\text{VO}_2$  in two measures  $\text{L} \cdot \text{min}^{-1} \cdot \text{mps}^{-1}$  and  $\text{VO}_2 \cdot \text{mps}^{-1} \cdot \text{kg}^{-1}$  ( $r = -0.36$ ,  $-0.32$ , respectively). For extension impulse, a moderate correlation was observed for  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$  and  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1} \cdot \text{mps}^{-1}$  ( $r = 0.45$  and  $r = 0.32$ , respectively) and for controls, a moderate positive correlation was observed for  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  ( $r = 0.31$ ). For flexion impulse a positive moderate correlation was found for  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$  ( $r = 0.31$ ) in the PD group and for the controls for  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1} \cdot \text{mps}^{-1}$  and  $\text{VO}_2 \cdot \text{mps}^{-1} \cdot \text{kg}^{-1}$  found a negative moderate correlation ( $r = -0.36$  and  $-0.32$ , respectively). For extension slope, between all metabolic measures found a negative moderate correlation, ( $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$ :  $r = -0.44$ ,  $\text{VO}_2 \cdot \text{mps}^{-1}$   $r = -0.43$ ,  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ :  $r = -0.36$ ,  $\text{VO}_2 \cdot \text{mps}^{-1} \cdot \text{kg}^{-1}$ :  $r = -0.36$ , respectively). All correlations observed weak positive or negative relationships in the controls between extension slope and all metabolic measurements ( $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$ :  $r = 0.17$ ,  $\text{VO}_2 \cdot \text{mps}^{-1}$   $r = 0.15$ ,  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ :  $r = -0.11$ ,  $\text{VO}_2 \cdot \text{mps}^{-1} \cdot \text{kg}^{-1}$ :  $r = -0.04$ , respectively). Flexion slope in the PD group observed negative moderate correlations for  $\text{VO}_2 \text{ L} \cdot \text{min}^{-1}$  and  $\text{VO}_2 \cdot \text{mps}^{-1}$  ( $r = -0.47$ , and  $r = -0.44$ , respectively) and a positive moderate correlation for the control group between  $\text{VO}_2 \cdot \text{mps}^{-1}$  ( $r = 0.51$ ). All other measures between PD and controls for flexion slope and metabolic measures were weak correlations. A  $p$  value was determined for total rigidity work measurements for all  $\text{VO}_2$  measurements from the Pearson product correlation analysis ( $\text{AVO}_2 \text{ L}$

$\cdot \text{min}^{-1} p = 0.044$ , absolute  $\text{AVO}_2 \cdot \text{mps}^{-1} p = 0.048$ ,  $\text{VO}_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} p = 0.188$ ,  $\text{VO}_2 \cdot \text{mps}^{-1} p = 0.197$ ).

## **Discussion**

### *Purpose and Major Findings*

The purpose of this study was to examine the effects of rigidity on metabolic cost in Parkinson's Disease during a walking task, to determine if rigidity and metabolic cost are correlated. The major findings of the current study demonstrate that Parkinson's patients on optimal-ON medications do not exhibit significant differences in metabolic cost compared to healthy controls, however, there is a moderate positive correlation between metabolic cost and rigidity where an increase in rigidity will subsequently increase the metabolic cost of walking.

### *Rigidity*

PD patients showed greater rigidity compared to healthy controls. Previous research shows rigidity work score, slope and impulse were greater in PD compared to healthy controls during similar methods in protocol for the wrist instead of the ankle or knee [67]. In optimal-ON medication states, previous findings show that PD has steeper slope values for extension and flexion for rigidity at the wrist, similar to our findings at the ankle and knee [91]. This potentially is due to the counter effect of the stretch reflex overcoming rigidity force with optimal-ON medication states to lower overall rigidity work score. Rigidity work score closely correlates to clinical assessments of rigidity, however elastic forces are not included when measuring work values [18, 20]. Angular impulse and rigidity slope measurements are component of the rigidity work score. Angular impulse has been stated to reflect the relationship between total resistive torque and time, by inclusion of all components of the resistive torque. This indicates that elastic and non-elastic components are a part of rigidity [29]. However

previous literature examined angular impulse during medication “off period” for at least 12 hours prior to data collection. Levodopa medications have been shown to offset the severity of rigidity score in previous literature [91]. This should indicate differences in our results where our patients were on optimal-ON medication diminishing some rigidity symptoms, however at ankle and knee impulse measurements were still statistically different compared to the healthy controls.

### *Metabolic Measurements*

PD group had similar energy expenditure rates compared to healthy controls. Comparing our results to previous literature, our results show different outcomes for metabolic measurements due to our studies inclusion of “optimal-ON” medication timing for data collections. Our  $\text{VO}_2$  results compared to previous research are similar in controls to comfortable pace, however PD patients varied compared between the two studies where our average  $\text{VO}_2$  was  $9.30 \pm 3.93$  and theirs  $11.5 \pm 2.8$  for their slower and comfortable pace  $\text{VO}_2$   $13.1 \pm 2.8$  [38]. This difference could be due to the task demand between the groups were not the same physiologically. This difference could be potentially due to the difficulty of walking for PD patients mechanically inhibiting the ability for patients to walk at the pace that is needed to reach a physiological increase in demand compared to controls, which is also shown through the difference in treadmill speed between the groups.

Further, compared to a separate study where  $\text{VO}_2$  measured as  $\text{ml} \cdot \text{kg}^{-1} \text{min}^{-1}$  during an ergometer max test showed similar results where PD did not show significant differences from healthy controls. This lack of difference shown could be due to the demand of the disease was not significant enough in an ergometer task to show metabolic differences and exonerated PD disease walking symptoms from the task to overall lower the demand from patients; similar to

lowering treadmill velocity, decreasing the demand of the task in the PD group compared to controls [14, 69]. The lack of controls for physical activity levels, medication state of the PD group and a difference in protocol due to velocity deficits all help to explain differences in findings to previous literature.

### *Metabolic Relation to Rigidity*

It was hypothesized that an increase in rigidity would positively correlate to an increase in energy expenditure. While no statistical significance was observed between groups for metabolic measurements alone, our findings support our hypothesis where an increase in rigidity positively correlated to an increase in energy expenditure for PD. By normalizing for weight and velocity we observe a positive moderate correlation between rigidity and metabolic measures at the ankle (**Figure 1**) and knee (**Figure 2**). Therefore, we postulate that due to the difference in velocity between the PD and Healthy controls, this is a measure of the efficiency of the system to perform the walking task. In PD there is less efficiency to perform a similar task to the healthy controls when normalizing for velocity on the treadmill.

[Figure 1 here]

[Figure 2 here]

Greater rigidity work scores positively correlate to  $VO_2$  in PD patients. Comparing to previous literature our findings are similar. There is a gap in the literature examining rigidity correlations to metabolic measurements in PD patients, however in healthy older adults, greater stiffness values in lower extremity joints have correlated to an increase in metabolic work in older adults [55]. As rigidity is a passive stiffening of the tissues instead of an active stiffness value, rigidity increases stiffness around the joint and therefore the larger rigidity work score at

the knee and ankle could potentially contribute to the higher energy expenditure in Parkinson's patients.

### *Comments and Limitations*

There are several limitations to this study. The sample that was recruited was not gender-matched evenly for PD and controlled groups. This could affect metabolic data for men and women have different reported averages for several metabolic measures [50]. In addition, our statistical power could be inefficient to see statistical differences for metabolic measurements due to our small sample size.

### *Conclusions and Future Research*

Overall, rigidity affects metabolic cost of walking where greater rigidity increases the metabolic cost. During daily activities PD patients utilize more energy compared to healthy controls to complete everyday tasks such as walking. This potentially could increase the amount of fatigue PD patients experience daily and have reported in previous literature to be one of the most disabling symptoms of the disease [26]. However, analyzing rigidity to energy expenditure during walking only explains part of fatigue. Future research should compare walking mechanics on a treadmill in PD compared to healthy controls. The metabolic demand between PD and healthy controls were not different, however potentially the mechanical demand differed between the two groups to equate to similar  $VO_2$  findings where mechanical demand is defined by differences seen in treadmill velocity. In addition, this study was performed on optimal-ON medication states, future research should expand to off-medication states or non-optimal on to notice the effects of PD during non-optimal settings to better correlate to experiences of patients who experience dyskinesia. Further, inclusion of physical activity levels to correlate to in-

laboratory experiences could benefit the progress of how rigidity effects metabolic measures of walking outside of laboratory settings.

## REFERENCES

- [1] S.F. (Ed.), Recent developments in Parkinson's disease, Macmillian Healthcare, Florham, NJ (1987) pp. 629-634.
- [2] S. Abudi, Y. Bar-Tal, L. Ziv, M. Fish, Parkinson's disease symptoms--patients' perceptions, *J Adv Nurs* 25 (1997) 54-59.
- [3] R.M. Alexander, Optimization and gaits in the locomotion of vertebrates, *Physiol Rev* 69 (1989) 1199-1227.
- [4] N.E. Allen, C. Sherrington, C.G. Canning, V.S. Fung, Reduced muscle power is associated with slower walking velocity and falls in people with Parkinson's disease, *Parkinsonism Relat Disord* 16 (2010) 261-264.
- [5] C.J. Andrews, D. Burke, J.W. Lance, The response to muscle stretch and shortening in Parkinsonian rigidity, *Brain* 95 (1972) 795-812.
- [6] P. Barone, A. Antonini, C. Colosimo, R. Marconi, L. Morgante, T.P. Avarello, E. Bottacchi, A. Cannas, G. Ceravolo, R. Ceravolo, G. Cicarelli, R.M. Gaglio, R.M. Giglia, F. Iemolo, M. Manfredi, G. Meco, A. Nicoletti, M. Pederzoli, A. Petrone, A. Pisani, F.E. Pontieri, R. Quatralo, S. Ramat, R. Scala, G. Volpe, S. Zappulla, A.R. Bentivoglio, F. Stocchi, G. Trianni, P.D. Dotto, P.s. group, The PRIAMO study: A multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease, *Mov Disord* 24 (2009) 1641-1649.
- [7] A. Berardelli, J.C. Rothwell, P.D. Thompson, M. Hallett, Pathophysiology of bradykinesia in Parkinson's disease, *Brain* 124 (2001) 2131-2146.
- [8] A. Berardelli, A.F. Sabra, M. Hallett, Physiological mechanisms of rigidity in Parkinson's disease, *J Neurol Neurosurg Psychiatry* 46 (1983) 45-53.
- [9] L. Bertram, R.E. Tanzi, The genetic epidemiology of neurodegenerative disease, *J Clin Invest* 115 (2005) 1449-1457.
- [10] J.W. Blaszczyk, Motor deficiency in Parkinson's disease, *Acta Neurobiol Exp (Wars)* 58 (1998) 79-93.
- [11] P. Borriore, E. Tranchita, P. Sansone, A. Parisi, Effects of physical activity in Parkinson's disease: A new tool for rehabilitation, *World J Methodol* 4 (2014) 133-143.
- [12] R.G. Brown, A. Dittner, L. Findley, S.C. Wessely, The Parkinson fatigue scale, *Parkinsonism Relat Disord* 11 (2005) 49-55.
- [13] D. Burke, K.E. Hagbarth, B.G. Wallin, Reflex mechanisms in Parkinsonian rigidity, *Scand J Rehabil Med* 9 (1977) 15-23.
- [14] C.G. Canning, J.A. Alison, N.E. Allen, H. Groeller, Parkinson's disease: an investigation of exercise capacity, respiratory function, and gait, *Arch Phys Med Rehabil* 78 (1997) 199-207.
- [15] G.A. Cavagna, P. Franzetti, The determinants of the step frequency in walking in humans, *J Physiol* 373 (1986) 235-242.
- [16] C.L. Christiansen, M.L. Schenkman, K. McFann, P. Wolfe, W.M. Kohrt, Walking economy in people with Parkinson's disease, *Mov Disord* 24 (2009) 1481-1487.
- [17] G.P.s.D. Collaborators, Global, regional, and national burden of Parkinson's disease, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016 17 (2016) 939-953.
- [18] W. DD, A method of measuring the dynamic characteristics of muscle rigidity, strength, and tremor in the upper extremity, IRE

Trans Med Electron (1959) 159-164.

- [19] P.J. Delwaide, J. Schoenen, [Clinical neurophysiology in the evaluation and physiopathology of Parkinson's disease], *Rev Neurol (Paris)* 141 (1985) 759-773.
- [20] T.C. Duggan, D.L. McLellan, Technical contribution. Measurement of muscle tone: a method suitable for clinical use, *Electroencephalogr Clin Neurophysiol* 35 (1973) 654-658.
- [21] B.A. Eldadah, Fatigue and fatigability in older adults, *PM R* 2 (2010) 406-413.
- [22] S. Fahn, Description of Parkinson's disease as a clinical syndrome, *Ann N Y Acad Sci* 991 (2003) 1-14.
- [23] M. Faist, J. Xie, D. Kurz, W. Berger, C. Maurer, P. Pollak, C.H. Lucking, Effect of bilateral subthalamic nucleus stimulation on gait in Parkinson's disease, *Brain* 124 (2001) 1590-1600.
- [24] M. Ferrarin, M. Rizzone, B. Bergamasco, M. Lanotte, M. Recalcati, A. Pedotti, L. Lopiano, Effects of bilateral subthalamic stimulation on gait kinematics and kinetics in Parkinson's disease, *Exp Brain Res* 160 (2005) 517-527.
- [25] J.P. Folland, B. Haas, P.C. Castle, Strength and activation of the knee musculature in Parkinson's disease: effect of medication, *NeuroRehabilitation* 29 (2011) 405-411.
- [26] J. Friedman, H. Friedman, Fatigue in Parkinson's disease, *Neurology* 43 (1993) 2016-2018.
- [27] J.H. Friedman, H. Friedman, Fatigue in Parkinson's disease: a nine-year follow-up, *Mov Disord* 16 (2001) 1120-1122.
- [28] T. Fukunaga, K. Kubo, Y. Kawakami, S. Fukashiro, H. Kanehisa, C.N. Maganaris, In vivo behaviour of human muscle tendon during walking, *Proc Biol Sci* 268 (2001) 229-233.
- [29] V.S. Fung, J.A. Burne, J.G. Morris, Objective quantification of resting and activated parkinsonian rigidity: a comparison of angular impulse and work scores, *Mov Disord* 15 (2000) 48-55.
- [30] R.I. Griffiths, Shortening of muscle fibres during stretch of the active cat medial gastrocnemius muscle: the role of tendon compliance, *J Physiol* 436 (1991) 219-236.
- [31] K.G. Hammond, R.F. Pfeiffer, M.S. LeDoux, B.K. Schilling, Neuromuscular rate of force development deficit in Parkinson disease, *Clin Biomech (Bristol, Avon)* 45 (2017) 14-18.
- [32] J.M. Hausdorff, Gait dynamics in Parkinson's disease: common and distinct behavior among stride length, gait variability, and fractal-like scaling, *Chaos* 19 (2009) 026113.
- [33] K. Herlofson, B.M. Kluger, Fatigue in Parkinson's disease, *J Neurol Sci* 374 (2017) 38-41.
- [34] K. Herlofson, J.P. Larsen, The influence of fatigue on health-related quality of life in patients with Parkinson's disease, *Acta Neurol Scand* 107 (2003) 1-6.
- [35] W. Hopkins, *Effect Statistics A New View of Statistics* vol. 2016 (2014).
- [36] Y.Z. Huang, F.Y. Chang, W.C. Liu, Y.F. Chuang, L.L. Chuang, Y.J. Chang, Fatigue and Muscle Strength Involving Walking Speed in Parkinson's Disease: Insights for Developing Rehabilitation Strategy for PD, *Neural Plast* 2017 (2017) 1941980.
- [37] M. Ishikawa, P.V. Komi, M.J. Grey, V. Lepola, G.P. Bruggemann, Muscle-tendon interaction and elastic energy usage in human walking, *J Appl Physiol* (1985) 99 (2005) 603-608.

- [38] B. Jeng, K.L.J. Cederberg, B. Lai, J.E. Sasaki, M.M. Bamman, R.W. Motl, Accelerometer output and its association with energy expenditure in persons with mild-to-moderate Parkinson's disease, *PLoS One* 15 (2020) e0242136.
- [39] B. Jeng, K.L.J. Cederberg, B. Lai, J.E. Sasaki, M.M. Bamman, R.W. Motl, Oxygen cost of over-ground walking in persons with mild-to-moderate Parkinson's disease, *Gait Posture* 82 (2020) 1-5.
- [40] S. Kakinuma, H. Nogaki, B. Pramanik, M. Morimatsu, Muscle weakness in Parkinson's disease: isokinetic study of the lower limbs, *Eur Neurol* 39 (1998) 218-222.
- [41] T. Kamo, R. Asahi, M. Azami, H. Ogihara, T. Ikeda, K. Suzuki, Y. Nishida, Rate of torque development and the risk of falls among community dwelling older adults in Japan, *Gait Posture* 72 (2019) 28-33.
- [42] L.I. Katzel, F.M. Ivey, J.D. Sorkin, R.F. Macko, B. Smith, L.M. Shulman, Impaired economy of gait and decreased six-minute walk distance in Parkinson's disease, *Parkinsons Dis* 2012 (2012) 241754.
- [43] W. Koller, S. Kase, Muscle strength testing in Parkinson's disease, *Eur Neurol* 25 (1986) 130-133.
- [44] S.L. Kowal, T.M. Dall, R. Chakrabarti, M.V. Storm, A. Jain, The current and projected economic burden of Parkinson's disease in the United States, *Mov Disord* 28 (2013) 311-318.
- [45] A.C. Kreitzer, R.C. Malenka, Striatal plasticity and basal ganglia circuit function, *Neuron* 60 (2008) 543-554.
- [46] A.D. Kuo, J.M. Donelan, A. Ruina, Energetic consequences of walking like an inverted pendulum: step-to-step transitions, *Exerc Sport Sci Rev* 33 (2005) 88-97.
- [47] M.J. Kurz, J.G. Hou, Levodopa influences the regularity of the ankle joint kinematics in individuals with Parkinson's disease, *J Comput Neurosci* 28 (2010) 131-136.
- [48] G.A. Lichtwark, A.M. Wilson, Is Achilles tendon compliance optimised for maximum muscle efficiency during locomotion?, *J Biomech* 40 (2007) 1768-1775.
- [49] S. Louie, M.M. Koop, A. Frenklach, H. Bronte-Stewart, Quantitative lateralized measures of bradykinesia at different stages of Parkinson's disease: the role of the less affected side, *Mov Disord* 24 (2009) 1991-1997.
- [50] J.R. Lytle, D.M. Kravits, S.E. Martin, J.S. Green, S.F. Crouse, B.S. Lambert, Predicting Energy Expenditure of an Acute Resistance Exercise Bout in Men and Women, *Med Sci Sports Exerc* 51 (2019) 1532-1537.
- [51] M.A. Maggioni, A. Veicsteinas, S. Rampichini, E. Ce, R. Nemni, G. Riboldazzi, G. Merati, Energy cost of spontaneous walking in Parkinson's disease patients, *Neurol Sci* 33 (2012) 779-784.
- [52] L.J. Martin, A.C. Price, K.B. McClendon, N.A. Al-Abdulla, J.R. Subramaniam, P.C. Wong, Z. Liu, Early events of target deprivation/axotomy-induced neuronal apoptosis in vivo: oxidative stress, DNA damage, p53 phosphorylation and subcellular redistribution of death proteins, *J Neurochem* 85 (2003) 234-247.
- [53] P.E. Martin, D.W. Morgan, Biomechanical considerations for economical walking and running, *Med Sci Sports Exerc* 24 (1992) 467-474.
- [54] K.S. McNaught, C.W. Olanow, Protein aggregation in the pathogenesis of familial and sporadic Parkinson's disease, *Neurobiol Aging* 27 (2006) 530-545.

- [55] O.S. Mian, J.M. Thom, L.P. Ardigo, M.V. Narici, A.E. Minetti, Metabolic cost, mechanical work, and efficiency during walking in young and older men, *Acta Physiol (Oxf)* 186 (2006) 127-139.
- [56] A.E. Minetti, C. Capelli, P. Zamparo, P.E. di Prampero, F. Saibene, Effects of stride frequency on mechanical power and energy expenditure of walking, *Med Sci Sports Exerc* 27 (1995) 1194-1202.
- [57] M.E. Morris, R. Ianseck, T.A. Matyas, J.J. Summers, The pathogenesis of gait hypokinesia in Parkinson's disease, *Brain* 117 ( Pt 5) (1994) 1169-1181.
- [58] H. Nogaki, S. Kakinuma, M. Morimatsu, Movement velocity dependent muscle strength in Parkinson's disease, *Acta Neurol Scand* 99 (1999) 152-157.
- [59] R.L. Nussbaum, C.E. Ellis, Alzheimer's disease and Parkinson's disease, *N Engl J Med* 348 (2003) 1356-1364.
- [60] A.B. Otis, W.O. Fenn, H. Rahn, Mechanics of breathing in man, *J Appl Physiol* 2 (1950) 592-607.
- [61] T. Paillard, Y. Rolland, P. de Souto Barreto, Protective Effects of Physical Exercise in Alzheimer's Disease and Parkinson's Disease: A Narrative Review, *J Clin Neurol* 11 (2015) 212-219.
- [62] B.K. Park, Y. Kwon, J.W. Kim, J.H. Lee, G.M. Eom, S.B. Koh, J.H. Jun, J. Hong, Analysis of viscoelastic properties of wrist joint for quantification of parkinsonian rigidity, *IEEE Trans Neural Syst Rehabil Eng* 19 (2011) 167-176.
- [63] A. Peppe, M. Pierantozzi, C. Chiavalon, F. Marchetti, C. Caltagirone, M. Musicco, P. Stanzione, A. Stefani, Deep brain stimulation of the pedunclopontine tegmentum and subthalamic nucleus: effects on gait in Parkinson's disease, *Gait Posture* 32 (2010) 512-518.
- [64] L. Petrucelli, C. O'Farrell, P.J. Lockhart, M. Baptista, K. Kehoe, L. Vink, P. Choi, B. Wolozin, M. Farrer, J. Hardy, M.R. Cookson, Parkin protects against the toxicity associated with mutant alpha-synuclein: proteasome dysfunction selectively affects catecholaminergic neurons, *Neuron* 36 (2002) 1007-1019.
- [65] M. Plotnik, N. Giladi, J.M. Hausdorff, A new measure for quantifying the bilateral coordination of human gait: effects of aging and Parkinson's disease, *Exp Brain Res* 181 (2007) 561-570.
- [66] D. Powell, N. Hanson, A.J. Threlkeld, X. Fang, R. Xia, Enhancement of parkinsonian rigidity with contralateral hand activation, *Clin Neurophysiol* 122 (2011) 1595-1601.
- [67] D. Powell, A.J. Threlkeld, X. Fang, A. Muthumani, R. Xia, Amplitude- and velocity-dependency of rigidity measured at the wrist in Parkinson's disease, *Clin Neurophysiol* 123 (2012) 764-773.
- [68] D.W. Powell, S.E. Blackmore, M. Puppa, D. Lester, N.G. Murray, R.J. Reed-Jones, R.P. Xia, Deep brain stimulation enhances movement complexity during gait in individuals with Parkinson's disease, *Neurosci Lett* (2018) 133588.
- [69] E.J. Protas, R.K. Stanley, J. Jankovic, B. MacNeill, Cardiovascular and metabolic responses to upper- and lower-extremity exercise in men with idiopathic Parkinson's disease, *Phys Ther* 76 (1996) 34-40.
- [70] B. Ressler, J. Kohl, Analysis of coordination between breathing and walking rhythms in humans, *Respir Physiol* 106 (1996) 317-327.
- [71] J.H. Rimmer, W. Schiller, M.D. Chen, Effects of disability-associated low energy expenditure deconditioning syndrome, *Exerc Sport Sci Rev* 40 (2012) 22-29.

- [72] M.H. Rose, A. Lokkegaard, S. Sonne-Holm, B.R. Jensen, Tremor irregularity, torque steadiness and rate of force development in Parkinson's disease, *Motor Control* 17 (2013) 203-216.
- [73] J.C. Rothwell, J.A. Obeso, M.M. Traub, C.D. Marsden, The behaviour of the long-latency stretch reflex in patients with Parkinson's disease, *J Neurol Neurosurg Psychiatry* 46 (1983) 35-44.
- [74] B. Sepehri, A. Esteki, E. Ebrahimi-Takamjani, G.A. Shahidi, F. Khamseh, M. Moinodin, Quantification of rigidity in Parkinson's disease, *Ann Biomed Eng* 35 (2007) 2196-2203.
- [75] S. Sharififar, R.A. Coronado, S. Romero, H. Azari, M. Thigpen, The effects of whole body vibration on mobility and balance in Parkinson disease: a systematic review, *Iran J Med Sci* 39 (2014) 318-326.
- [76] T.B. Sherer, R. Betarbet, J.T. Greenamyre, Pesticides and Parkinson's disease, *ScientificWorldJournal* 1 (2001) 207-208.
- [77] L.M. Shulman, L.I. Katzel, F.M. Ivey, J.D. Sorkin, K. Favors, K.E. Anderson, B.A. Smith, S.G. Reich, W.J. Weiner, R.F. Macko, Randomized clinical trial of 3 types of physical exercise for patients with Parkinson disease, *JAMA Neurol* 70 (2013) 183-190.
- [78] J.W. Skinner, E.A. Christou, C.J. Hass, Lower Extremity Muscle Strength and Force Variability in Persons With Parkinson Disease, *J Neurol Phys Ther* 43 (2019) 56-62.
- [79] R.R. Smart, C.M. Richardson, D.J. Wile, B.H. Dalton, J.M. Jakobi, Importance of Maximal Strength and Muscle-Tendon Mechanics for Improving Force Steadiness in Persons with Parkinson's Disease, *Brain Sci* 10 (2020).
- [80] G.E. Stelmach, N. Teasdale, J. Phillips, C.J. Worringham, Force production characteristics in Parkinson's disease, *Exp Brain Res* 76 (1989) 165-172.
- [81] J. Stevens-Lapsley, B.M. Kluger, M. Schenkman, Quadriceps muscle weakness, activation deficits, and fatigue with Parkinson disease, *Neurorehabil Neural Repair* 26 (2012) 533-541.
- [82] S. Sveinbjornsdottir, The clinical symptoms of Parkinson's disease, *J Neurochem* 139 Suppl 1 (2016) 318-324.
- [83] J.L. Taylor, S.C. Gandevia, Transcranial magnetic stimulation and human muscle fatigue, *Muscle Nerve* 24 (2001) 18-29.
- [84] M. van Nimwegen, A.D. Speelman, E.J. Hofman-van Rossum, S. Overeem, D.J. Deeg, G.F. Borm, M.H. van der Horst, B.R. Bloem, M. Munneke, Physical inactivity in Parkinson's disease, *J Neurol* 258 (2011) 2214-2221.
- [85] S. Vestergaard, S.G. Nayfield, K.V. Patel, B. Eldadah, M. Cesari, L. Ferrucci, G. Ceresini, J.M. Guralnik, Fatigue in a representative population of older persons and its association with functional impairment, functional limitation, and disability, *J Gerontol A Biol Sci Med Sci* 64 (2009) 76-82.
- [86] R.L. Waters, S. Mulroy, The energy expenditure of normal and pathologic gait, *Gait Posture* 9 (1999) 207-231.
- [87] D. Weintraub, C.L. Comella, S. Horn, Parkinson's disease--Part 1: Pathophysiology, symptoms, burden, diagnosis, and assessment, *Am J Manag Care* 14 (2008) S40-48.
- [88] T. Wichmann, M.R. DeLong, Functional and pathophysiological models of the basal ganglia, *Curr Opin Neurobiol* 6 (1996) 751-758.
- [89] R. Xia, K. Markopoulou, S.E. Puumala, W.Z. Rymer, A comparison of the effects of imposed extension and flexion movements on Parkinsonian rigidity, *Clin Neurophysiol* 117 (2006) 2302-2307.

- [90] R. Xia, A. Muthumani, Z.H. Mao, D.W. Powell, Quantification of neural reflex and muscular intrinsic contributions to parkinsonian rigidity, *Exp Brain Res* 234 (2016) 3587-3595.
- [91] R. Xia, W.Z. Rymer, The role of shortening reaction in mediating rigidity in Parkinson's disease, *Exp Brain Res* 156 (2004) 524-528.
- [92] K.E. Zelik, T.W. Huang, P.G. Adamczyk, A.D. Kuo, The role of series ankle elasticity in bipedal walking, *J Theor Biol* 346 (2014) 75-85.
- [93] W.J. Zetuskys, J. Jankovic, F.J. Pirozzolo, The heterogeneity of Parkinson's disease: clinical and prognostic implications, *Neurology* 35 (1985) 522-526.

## APPENDICES

### Appendix A: Tables

**Table 1.** Participant Information (mean  $\pm$  SD).

Group	PD	CON	<i>p</i> value, Cohen's D
Height	177.6 $\pm$ 9.7	165.2 $\pm$ 11.7	0.01*, 1.15
Weight	97.9 $\pm$ 19.8	74.1 $\pm$ 17.3	0.01*, 1.26
Age	64.8 $\pm$ 7.9	66.1 $\pm$ 4.5	0.33, 0.2
Sex	8 M: 2F	4 M: 6 F	---
MMSE	29.3 $\pm$ 0.8	29.7 $\pm$ 0.5	0.13, 0.54
PFS-16	0.90 $\pm$ 1.66	0.67 $\pm$ 1.66	0.38, 0.14
UPDRS- Motor	31.3 $\pm$ 7.2	0.0 $\pm$ 0.0	< 0.01*, 6.11

Table 1 Demographics Summary. Height measured in centimeters (cm). Weight measured in kilograms (kg). UPDRS- Motor only includes the part three motor examination.

**Table 2.** Walking Velocity (mean  $\pm$  SD).

Group	PD	CON	<i>p</i> value, Cohen's D
Preferred	1.14 $\pm$ 0.18	1.20 $\pm$ 0.11	0.22, 0.37
Maximum	1.63 $\pm$ 0.33	1.60 $\pm$ 0.32	0.40, 0.12
Treadmill	0.93 $\pm$ 0.24	1.10 $\pm$ 0.16	0.05*, 0.8

Table 2 Walking Velocity Summary. All velocity stated above is measured in meters per second (m/s). The data is the average of all the PD patients and the control groups.

**Table 3.** Metabolic Summary (mean  $\pm$  SD).

Metabolic Measurement	PD	CON	<i>p</i> value, Cohen's D
VO <sub>2</sub> L · min <sup>-1</sup>	0.92±0.43	0.83±0.36	0.31, 0.23
VO <sub>2</sub> · mps <sup>-1</sup>	1.05±0.58	0.76±0.34	0.10, 0.62
VO <sub>2</sub> ml · kg <sup>-1</sup> min <sup>-1</sup>	9.30±3.93	10.89±3.05	0.17, 0.45
VO <sub>2</sub> · mps <sup>-1</sup>	10.7±5.6	9.1±4.1	0.17, 0.45

Table 3 Metabolic Summary. VO<sub>2</sub> is measured in two ways: in L · min<sup>-1</sup> and ml · kg<sup>-1</sup> min<sup>-1</sup>. Metabolic efficiency is measured as VO<sub>2</sub> in L · min<sup>-1</sup> or ml · kg<sup>-1</sup> min<sup>-1</sup> over meters per second (mps).

**Table 4.** Ankle Rigidity (mean  $\pm$  SD).

Rigidity Measurement		PD	CON	<i>p</i> value, Cohen's D
Rigidity Work Score Nm · deg	Extension	97.9 $\pm$ 33.5	73.7 $\pm$ 17.5	0.034*, 0.91
	Flexion	71.0 $\pm$ 21.6	48.8 $\pm$ 11.1	0.007*, 1.29
	Total	169.91 $\pm$ 53.02	122.46 $\pm$ 24.2	0.014*, 1.13
Impulse Nm· s	Extension	1.68 $\pm$ 0.58	1.38 $\pm$ 0.49	0.126, 0.55
	Flexion	1.27 $\pm$ 0.42	0.95 $\pm$ 0.40	0.050*, 0.80
Slope Nm · deg <sup>-1</sup> · s <sup>-1</sup>	Extension	0.202 $\pm$ 0.132	0.017 $\pm$ 0.221	0.019*, 1.02
	Flexion	0.286 $\pm$ 0.149	0.116 $\pm$ 0.118	0.007*, 1.26
	DF	-11.504 $\pm$ 4.039	-12.489 $\pm$ 2.542	0.269, 0.29
Peak Deg	PF	19.503 $\pm$ 0.040	19.169 $\pm$ 1.066	0.168, 0.44

Table 4 Ankle Rigidity Summary. Extension and Flexion values for Slope measured in Nm · deg<sup>-1</sup> s<sup>-1</sup>, Impulse in Nm · s, and Rigidity work score in Nm · deg in flexion, extension and total for mean, standard deviations, and statistical measures. Deg = degrees, DF = dorsiflexion, PF = plantarflexion.

**Table 5.** Knee Rigidity (mean  $\pm$  SD).

Rigidity Measurement		PD	CON	<i>p</i> value, Cohen's D
Rigidity Work Score Nm · deg	Extension	102.88 $\pm$ 25.34	72.00 $\pm$ 14.84	< 0.01*, 1.49
	Flexion	129.83 $\pm$ 39.86	75.82 $\pm$ 22.43	<0.01*, 1.67
	Total	232.71 $\pm$ 54.48	147.82 $\pm$ 35.57	<0.01*, 1.84
Impulse Nm · s	Extension	1.72 $\pm$ 0.42	1.20 $\pm$ 0.25	< 0.01*, 1.49
	Flexion	2.17 $\pm$ 0.67	1.27 $\pm$ 0.37	< 0.01*, 1.67
Slope Nm · deg <sup>-1</sup> s <sup>-1</sup>	Extension	-0.38 $\pm$ 0.14	-0.27 $\pm$ 0.06	0.026*, 0.99
	Flexion	-0.45 $\pm$ 0.12	-0.26 $\pm$ 0.09	<0.01*, 1.80

Table 5 Knee Rigidity Summary. Extension and Flexion values for Slope measured in Nm · deg<sup>-1</sup> s<sup>-1</sup>, Impulse in Nm · s, and Rigidity work score in Nm · deg in flexion, extension and total for mean, standard deviations, and statistical measures.

**Table 6.** Correlation Ankle Analysis (r values).

Metabolic Measure	Group	Rigidity Work Score	Ext Work	Flex Work	Flex Impulse	Ext Slope	Flex Slope
AVO <sub>2</sub> L · min <sup>-1</sup>	PD	0.69	0.60	0.76	0.69	0.23	0.28
	CON	0.35	0.15	0.31	0.27	0.20	-0.08
AVO <sub>2</sub> · mps	PD	0.67	0.60	0.72	0.67	0.28	0.30
	CON	0.15	0.21	0.00	-0.03	0.10	0.02
VO <sub>2</sub> mL · kg <sup>-1</sup> · min <sup>-1</sup>	PD	0.49	0.42	0.56	0.49	-0.03	0.08
	CON	0.23	0.13	0.32	0.22	-0.03	-0.10
VO <sub>2</sub> · kg <sup>-1</sup> · min <sup>-1</sup>	PD	0.49	0.43	0.54	0.48	0.07	0.12
	CON	-0.03	-0.04	0.00	-0.01	-0.04	-0.11

Table 6. Correlation Analysis showing the relationship between Metabolic and Rigidity Measurements at the ankle. Only statistically significant rigidity measurements were included in the correlation to metabolic measures. A *p* value was determined for total rigidity work measurements for all VO<sub>2</sub> measurements from the Pearson product correlation analysis (AVO<sub>2</sub> L · min<sup>-1</sup> *p* = 0.245, absolute AVO<sub>2</sub> · mps<sup>-1</sup> *p* = 0.386, VO<sub>2</sub> mL · kg<sup>-1</sup> · min<sup>-1</sup> *p* = 0.740, VO<sub>2</sub> · mps<sup>-1</sup> *p* = 0.865).

**Table 7.** Knee Correlation Analysis (r values).

Metabolic Measure	Group	Rigidity Work Score	Ext Work	Flex Work	Ext Impulse	Flex Impulse	Ext Slope	Flex Slope
$AVO_2L \cdot \text{min}^{-1}$	PD	0.43	0.45	0.31	0.45	0.31	-0.44	-0.47
	CON	-0.23	-0.11	-0.21	-0.11	-0.12	0.17	0.28
$AVO_2 \cdot \text{mps}^{-1}$	PD	0.33	0.32	0.25	0.32	0.25	-0.43	-0.44
	CON	-0.18	0.11	-0.36	0.11	-0.36	0.15	0.51
$VO_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$	PD	0.13	0.29	-0.01	0.29	-0.01	-0.36	-0.24
	CON	0.06	0.31	-0.11	0.31	-0.11	-0.11	0.15
$VO_2 \cdot \text{mps}^{-1}$	PD	0.07	0.20	-0.03	0.20	-0.03	-0.36	-0.21
	CON	-0.18	0.06	-0.32	0.06	-0.32	-0.04	0.20

Table 7. Correlation Analysis showing the relationship between Metabolic and Rigidity Measurements at the knee. Only statistically significant rigidity measurements were included in the correlation to metabolic measures. A *p* value was determined for total rigidity work measurements for all  $VO_2$  measurements from the Pearson product correlation analysis ( $AVO_2L \cdot \text{min}^{-1}$  *p* = 0.044, absolute  $AVO_2 \cdot \text{mps}^{-1}$  *p* = 0.048,  $VO_2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  *p* = 0.188,  $VO_2 \cdot \text{mps}^{-1}$  *p* = 0.197).

## Appendix B: Figures

**Figure 1.** Knee Correlation Analysis

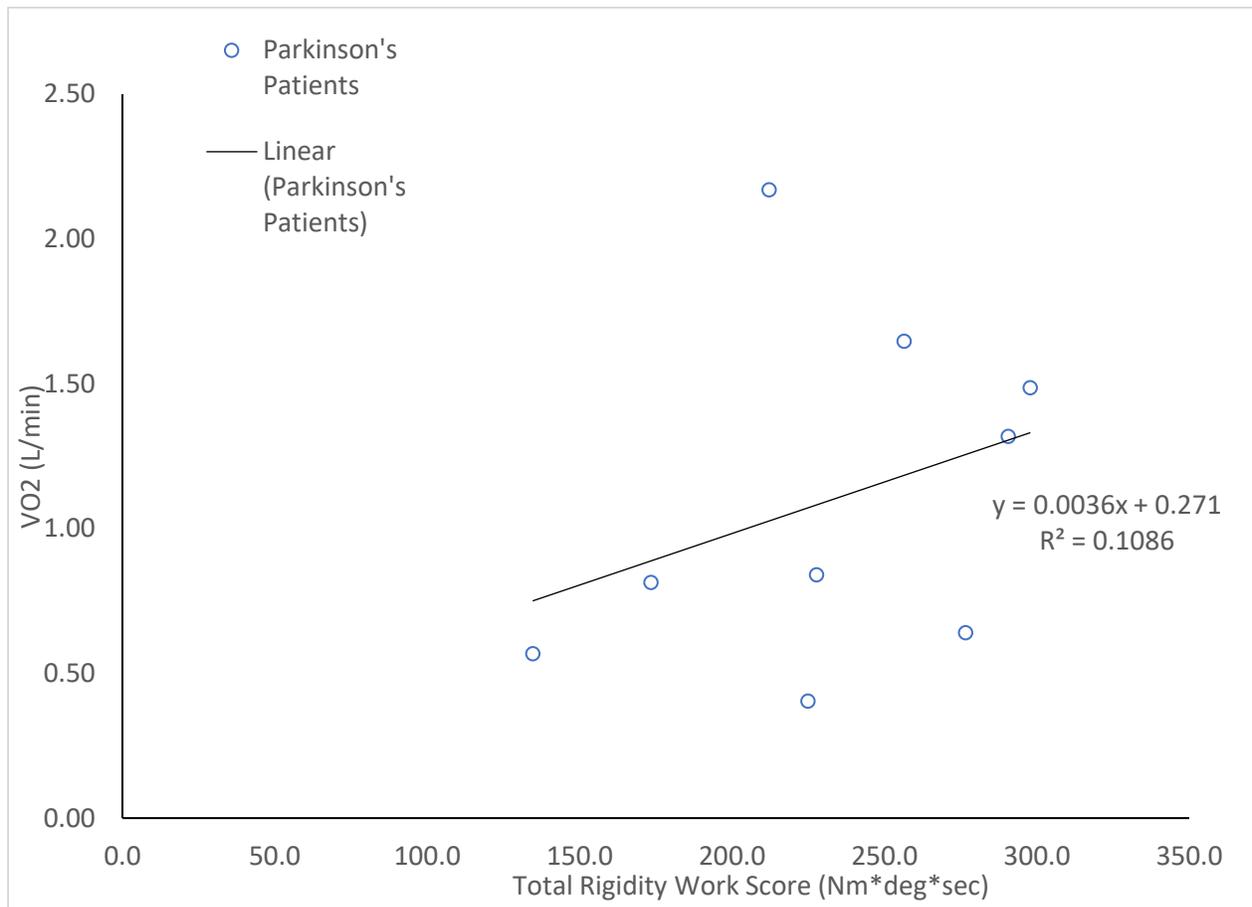


Figure 1 Summary. Knee  $VO_2$  measured in L / min / mps correlated to total rigidity work score measured in Nm · deg.

**Figure 2.** Ankle Total Rigidity by  $VO_2 \text{ L} \cdot \text{min}^{-1}$

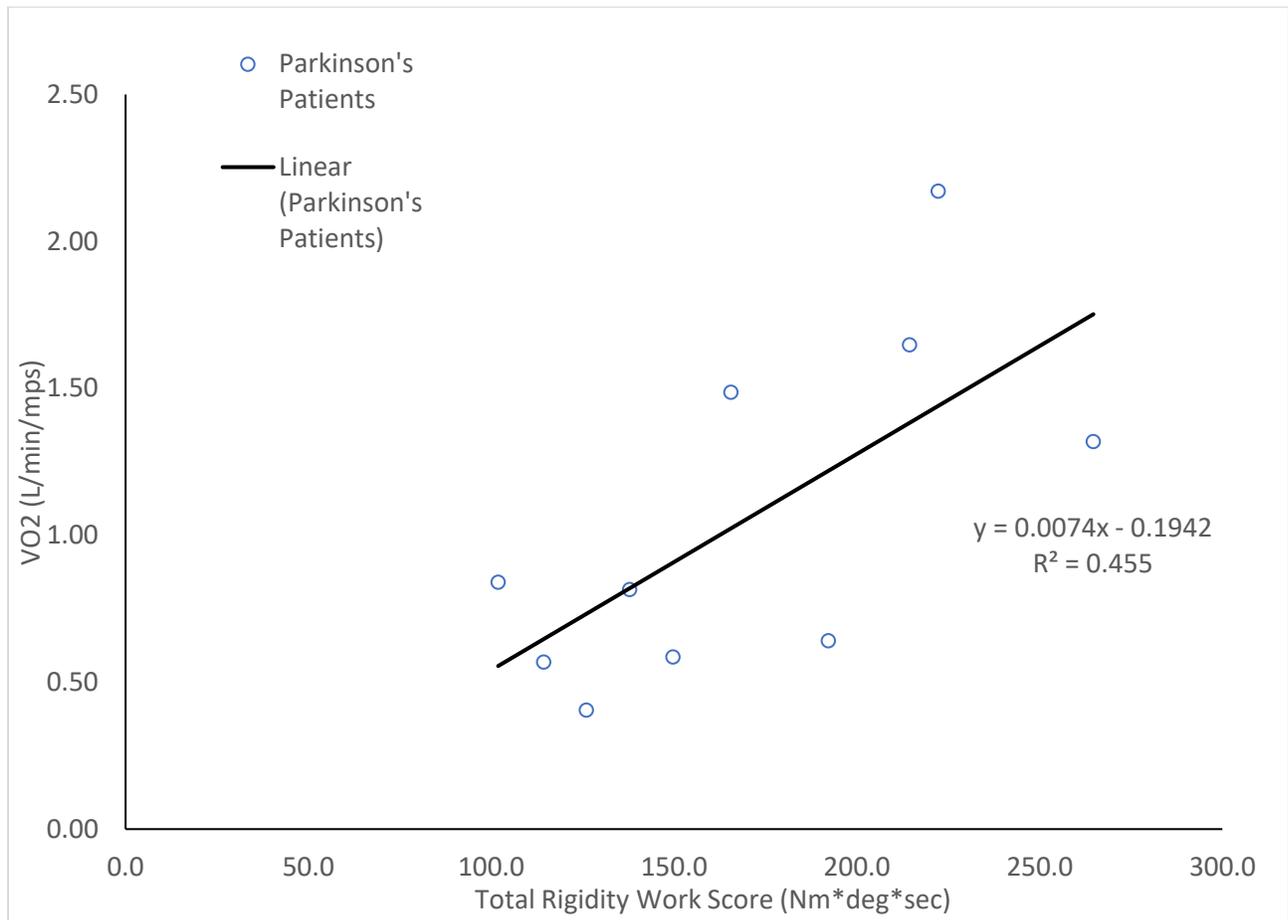


Figure 2 Summary. Ankle  $VO_2$  measured in L / min / mps correlated to total rigidity work score measured in Nm · deg.



Institutional Review Board  
Division of Research and Innovation  
Office of Research Compliance  
University of Memphis  
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PI: Douglas Powell  
Co-Investigator: Mark LeDoux  
Advisor and/or Co-PI: Melissa Puppa  
Department: College of Health Sciences  
Study Title: Relationship between parkinsonian rigidity, metabolic cost of locomotion and physical activity  
IRB ID: PRO-FY2019-188  
Submission Type: Renewal  
Level of Review: Full Board

IRB Meeting Date: Sep 25, 2020 12:00 PM CDT  
Decision: Approved  
Approval Date: September 25, 2020  
Expiration Date: September 25, 2021

**Findings: A modification must be submitted to provide the procedures for protecting human subjects from COVID-19, to continue data collection. The procedures should describe what the research team will do.**

The IRB has reviewed the renewal request. The University of Memphis Institutional Review Board, FWA00006815, has reviewed your submission in accordance with all applicable statuses and regulations as well as ethical principles.

Approval of this project is given with the following obligations:

1. If this IRB approval has an expiration date, an approved renewal must be in effect to continue the project prior to that date. If approval is not obtained, the human subjects consent form(s) and recruiting material(s) are no longer valid and any research activities involving human subjects must stop.
2. When the project is finished a completion form must be completed and sent to the board.
3. No change may be made in the approved protocol without prior board approval, whether the approved protocol was reviewed at the Exempt, Expedited or Full Board level.
4. Exempt approval are considered to have no expiration date and no further review is necessary unless the protocol needs modification.

5. Human subjects training is required every 2 years and is to be kept current at [citiprogram.org](http://citiprogram.org).

Thank you,  
James P. Whelan, Ph.D.  
Institutional Review Board Chair  
The University of Memphis.

*Note: Review outcomes will be communicated to the email address on file. This email should be considered an official communication from the UM IRB.*