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The therapeutic contributions of somatosensory feedback during exercise for those with Parkinson's disease

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THE THERAPEUTIC CONTRIBUTIONS OF SOMATOSENSORY FEEDBACK DURING EXERCISE FOR THOSE WITH PARKINSON'S DISEASE

by

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THESIS

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ABSTRACT

Previous research has proposed that the somatosensory feedback generated during exercise is a key component in regards to the mechanism underlying the therapeutic effects of exercise on the motor symptoms of Parkinson's disease (PD). This thesis aimed to further examine the contributions of different forms of somatosensory feedback during exercise in PD in order to understand the mechanism for symptom improvements that certain exercise studies report.

This randomized, controlled exercise study consisted of three treadmill groups, with the RATE and MAGNITUDE groups serving as the experimental conditions, while the CONTROL condition was an active comparator treadmill walking group. The RATE group attempted to elicit a rapid sampling rate from somatosensory afferents by having participants walk at a high cadence. The MAGNITUDE group attempted to generate a signal from somatosensory receptors that was larger or richer in magnitude by having participants wear ankle weights with the premise that the additional weight would cause tension sensitive golgi tendon organs to increase signaling. The CONTROL treadmill group served as an active comparator control group where participants walked regularly. Each condition finished with 13 participants with idiopathic PD.

All treadmill groups trained at the same aerobic intensity, duration, and frequency. however, only the RATE group improved in the primary outcome measure (motor section of the Unified Parkinson's Disease Rating Scale (UPDRS-III)) after exercise. Furthermore, this same condition improved on the upper limb

i

score of the UPDRS-III, possibly indicative of an overall improvement in basal ganglia (BG) functioning. Main effects of time were reported for step length in velocity across all treadmill training groups during both self-paced and maximal walking speeds. No changes in any measures of postural control were detected.

This study demonstrates that exercise that generates a high rate of somatosensory feedback from appears to be the most capable of improving motor symptoms of PD. Furthermore, gait improvements from treadmill training were independent of improvements in UPDRS-III, and are likely an effect of motor learning.

PROBLEM STATEMENT

Studies examining exercise interventions for the treatment of the motor symptoms in PD have been popular in the last decade, as the need for complementary strategies to pharmaceutical treatment has become more apparent. However, despite the body of research that has been conducted on exercise and PD, the actual mechanism(s) responsible for the therapeutic effect of that remain largely unknown. Furthermore, due to the lack of randomized, controlled exercise studies, current evidence of exercise as a reliable rehabilitation method remains limited.

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Lastly, and perhaps most importantly, thank you to the participants who worked tirelessly while they exercised for my research studies. Without their strong will to battle against PD and work hard, my research would not have been possible.

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Chapter 1: Prologue

AN OVERVIEW OF PARKINSON'S DISEASE

Parkinson's disease (PD) is a progressive neurological disorder that manifests when a substantial amount of dopaminergic neurons in the basal ganglia (BG) have died. Prevalence over the age of 70 is approximately 1 in 100, making PD the second most common neurodegenerative disease second only to Alzheimer's (Pringsheim, Jette, Frolkis & Steeves, 2014). Symptoms of PD are widespread, and are classified into motor and non-motor categories. Motor symptoms include tremor, bradykinesia, rigidity, postural instability, impaired gait, and poor proprioception (Guttman, Kish, & Furukawa, 2003; Rocchi, Chiari, & Horak, 2012; Schaafsma et al., 2003). Non-motor symptoms include, but are not limited to; mood disturbances, digestive complications, and autonomic system dysfunction (Park & Stacy, 2009). Symptoms worsen in severity as the disease progresses, eventually leading to loss of independence and a reduced quality of life.

Although there is not yet a cure for PD, treatment options do exist. Dopamine replacement therapy (DRT) consisting of the synthetic dopamine precursor Levodopa (L-DOPA) is the most common and accessible method for managing the motor symptoms of the disease (Sprenger & Poewe, 2013). Although the drugs ameliorate the symptoms, their use is associated with several unpleasant side effects such as dyskinesias, orthostatic hypotension, hallucinations, and on/off fluctuation (Fahn, 1996). Also of importance is the diminished therapeutic effect after prolonged usage as well as its possibility to be toxic to remaining dopaminergic neurons (Fahn, 1996;

Fahn et al. 2004). Furthermore, postural instability and gait dysfunction do not respond well to dopaminergic medication, leaving the two symptoms that are associated with the highest morbidity in PD mainly untreated (Sethi, 2008; Hely, Morris, Reid, & Trafficante, 2005). Thus, the value of determining if alternative treatment methods such as exercise are capable of improving these symptoms is important for the development of an ideal motor symptom improvement strategy.

The gold standard for assessing motor symptom severity is the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS-III), which is a battery of 14 tests performed by a trained assessor (Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease, 2003). Each test is scored on a scale from 0-4, with 0 representing normal or no impairment, and 4 representing extreme impairment/inability to perform the task. Although the test is subjective, the UPDRS III demonstrates high reliability and validity across all severities and is a universally accepted rating scale for patients with PD (Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease, 2003). The UPDRS-III is designed to assess the cardinal symptoms of PD: bradykinesia (slowness), postural instability and gait dysfunction, tremor, and akinesia (difficulty initiating movement). New pharmaceutical treatments are also assessed with the UPDRS-III (Jones & Murray 2014). If exercise should be considered worthy of prescription by medical practitioners as a complementary or alternative therapy, the efficacy of exercise to improve motor symptoms should be measured on the same scale to allow for a direct comparison.

EXERCISE AS THERAPY FOR THOSE WITH PD

Exercise has been shown to improve the condition of several chronic diseases and promote good health in general (Mattson, 2000; Haskell et al., 2007).   Naturally, the efficacy of exercise and physical activity to improve the motor symptoms of PD has been a popular area of research in recent years. However, despite the amount of research that has been conducted, fundamental questions about what specific forms of exercise are therapeutic for PD, and more importantly the mechanisms behind the therapeutic benefits remain largely unanswered. A more thorough understanding of which specific types of exercise are most efficacious will allow health practitioners to prescribe more successful exercise therapy for those with PD.   Specifically, understanding the actual traits (frequency, intensity, type and time) of exercise that provide motor symptom relief allows for more knowledge based exercise prescription.

EXERCISE AND ANIMAL MODELS OF PD

Initial studies involving exercise and Parkinson's disease have utilized rodent models which use either 6-hydroxydopamine (6-OHDA) or 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) as toxic agents. These agents act selectively on DA producing neurons, providing a reliable model to examine how exercise affects the dopaminergic system. Lau et al. (2011) examined the effects of a continuous treadmill based aerobic program in an MPTP rat model with aims to shed light on the exact mechanisms responsible for exercise-induced neuroprotection. Rats that exercised improved the function of nigrostriatal neurons, determined by synaptic

dopamine (DA) levels and dopamine active transporter (DAT) activity. An upregulation of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and Glial-derived neurotrophic factor (GDNF) were also noted, and has been reported in other works involving rat models (Tillerson, Caudle, Reveron & Miller, 2003).

Results from exercise in animal models of PD shed light upon the neural changes that may be responsible for motor symptom relief. It remains unclear if benefits from exercise and physical activity experienced in humans with PD can be attributed to these same factors, however, human studies examining acute bouts of aerobic exercise have shown an increase in synaptic DA concentration immediately after exercise (Wang et al., 2000). Although examining DA function is outside the scope of this thesis, animal models provide insight to the exercise derived neural changes responsible for symptom improvement.

EXERCISE IN HUMAN POPULATIONS WITH PD

Several modalities of exercise have been tested in human models of PD with mixed results. It appears that only certain forms of exercise are capable of providing post treatment reductions in UPDRS-III scores. Interventions that lead to reductions in overall UPDRS-III scores should be considered more successful than those that lead to improvements in an outcome measure that is similar to the training protocol. This is because improvements in UPDRS-III scores may be more indicative of improvements in the BG network (, rather than an improvement that can be explained by practice or motor control theories.

i. Treadmill based exercise

A variety of treadmill training (TT) interventions have been studied within the PD population comprising of varying intensities, speeds, and the use of body weight supported treadmill training (BWSTT). Benefits are dependent upon the actual type of TT intervention, but overall have shown to be a promising rehabilitative strategy for those with PD.

Fisher examined varying intensities of BWSTT with patients in early stages of PD. Patients in the high intensity group were trained at 75% of their age adjusted maximum heart rate (AAMHR), determined by the Karvonen formula (220-age). The low intensity group was trained at no greater than 50% of their AAMHR, and the zero intensity group attended educational sessions. The exercise based groups trained for 24 sessions over 8 weeks, while the zero intensity education group attended 4 separate information sessions. Outcome measures included the UPDRS III, self-selected and fast paced gait analysis, and a cortical excitability measure derived from transcranial magnetic stimulation (TMS). A slight, but non-significant improvement was reported in the UPDRS III. Significant improvements in spatiotemporal measures of gait including step length (1.48m to 1.56m, $p<.05$) and in both self-selected (1.46m/s to 1.52m/s, $p<.05$) and fast paced (1.91m/s to 2.00m/s, $p<.05$) walking velocities. Cortical excitability, determined by a TMS based cortical silent period (CSP) improved to levels that were closer to age-matched control participants, however, only in the high intensity training group. The authors attributed the improvements in cortical excitability to a possible upregulation of neurotrophic factors as a result of high intensity exercise. This study did not report average

walking speed or cadence of the actual training sessions, since maintaining a percentage of AAMHR was the main objective during training sessions.

Miyai et al. examined the effects of BWSTT in comparison to a traditional, gait based physiotherapy (PT) intervention not involving treadmill use. This study sampled moderately severe PD participants, and it was proposed that the body weight support (BWS) would allow them to train with a more proper gait pattern. The authors proposed that the proper gait pattern leads to a higher quality of afferent somatosensory feedback being sent to the CNS. The study was a crossover with the sample (n=10) being equally split into 4 weeks of each condition with 5 participants receiving BWSTT first, and 5 receiving traditional PT first. The BWSTT condition consisted of 12 sessions each lasting 45 minutes including 9 minutes of rest time. Body weight support was adjusted throughout each session starting with 20% for 12 minutes, 10% for 12 minutes, and finally 0% for the last 12 minutes. Speed was started at 0.5 km/hr and adjusted until 3.0km/hr as tolerated. The BWSTT intervention improved UPDRS III by 18% (18.2 to 15.0, $p<.001$), gait speed became quicker (10.0sec/10m to 8.3sec/10m, $p<.05$), and less steps were needed over a 10 metre walk (22.3 to 19.6, $p<.01$). Variability of gait was unable to be measured due to gait characteristics being obtained by stopwatch and counting. Although this study highlights the benefits of BWSTT, no comparison group of regular treadmill training was available.

To further examine the efficacy of BWSTT within PD, Toole [19] had three separate conditions consisting of a group that was not under any BWS, a group with 25% of their bodyweight unloaded, and lastly a group that trained with an additional

5% of their body weight. This study was conducted to determine if BWS has an influence on therapeutic effect of TT within PD. Participants trained 3 times a week for 6 weeks, with each session lasting 20 minutes. Intensity was relatively low, with patients in all groups training at 60% of their AAMHR. Despite what condition patients were in, improvements were observed in gait, UPDRS III, and balance measures. Reductions in UPDRS III scores were minimal (as only a 9% improvement was noted). This study concluded that the amount of body weight support during treadmill training does not affect symptom improvement.

To determine the effect of high velocity treadmill walking, Herman employed a progressive and speed dependent TT program under the premise that bradykinesia and hypokinetic gait can be remedied by practicing to walk at a fast velocity. The program was 6 weeks long, and sessions ran four times a week. Patients were harnessed in order to prevent falling, but bodyweight was not unloaded. Treadmill speed was dependent on comfortable overground walking speed, which was assessed at the start of every week. During the first 2 weeks, patients trained at speeds at or below overground walking speed. By week 3, PD participants walked at speeds ranging from 5-10% greater than their overground walking speed. A large reduction in UPDRS III was noted (scores improved by 25% (29 to 22, $p<.05$)). Measures of gait also improved, as self-paced gait became faster (1.11m/s to 1.26m/s, $p<.05$) after TT, most likely due to greater stride length (1.17m to 1.25m, $p<.05$). This study was based upon progressively increasing walking speed and provided the actual gait velocity in which participants were trained at. However, it is important to consider that the study lacked a control group, and was an open label design.

The immediate (Pohl et al., 2003) and long-term (Cakit, Saracoglu, Hakan & Erdem, 2007) effects of fast paced treadmill programs have also been studied in the PD population. Although the previously mentioned Herman study was also based upon progressive speed dependent training, percentages relative to comfortable pace were used. The following studies differ because the speed was based upon percentages of *maximal* overground walking speed, rather than comfortable walking speed. After one bout of maximal speed dependent treadmill training, increases were reported in self-paced gait velocity, alongside a reduction in percentage of gait spent in double support. To investigate the long term effects of maximal speed training, an 8 week, 16 session intense speed dependent treadmill training demonstrated an increase in maximal tolerated walking speed from 1.9km/h (+/-0.75km/h) to 2.6km/h (+/-0.77km/h) $p<.001$ (Cakit et al., 2007). Unfortunately, UPDRS III was only measured at baseline, so the effect of maximal speed training on motor symptom severity remains unknown.

Despite there being several previous TT interventions published for PD, several fundamental questions remain. It appears that nearly every sort of treadmill training despite speed, intensity or use of BWSTT has the ability to improve gait. However, only UPDRS III improvements and changes in cortical excitability were reported in high intensity protocols (Herman, 2007; Fisher, 2008). TT interventions that alter cadence but match intensity (% of MHR) between training groups are needed to determine if the rate of exercise has an interaction with the intensity in regards to providing therapeutic benefit for motor symptoms of the PD.

ii. Forced Exercise

Ridgel, Vitek & Alberts define forced exercise (FE) as exercise that is augmented mechanically to assist the participant in achieving and maintaining an exercise rate greater than their preferred rate of exercise. The group utilized a stationary tandem bicycle setup where a trainer would pedal at the front of the cycle, effectively controlling the cadence of the rear cranks. By forcing the participant on the back of the cycle to maintain the cadence set by the trainer, the participant would be able to achieve and maintain a rate of exercise (in regards to cadence) greater than they could on their own while providing the same amount of effort. This group was the first to adapt an FE paradigm that originally showed promise in rodent and animal models of PD (Lau, 2011; Tillerson, 2003). Their FE intervention resulted in a within group 35% decrease in total UPDRS-III score, in contrast to a control cycling group which saw no change, despite exercising at a matched duration, frequency and intensity (% of MHR). The only identified difference between the successful FE group and the control condition was a difference in pedaling cadence. Improvements in the FE group were also seen in upper limb outcome measures unrelated to the training protocol, leading researchers to conclude that the exercise may have caused global improvements in BG functioning. A separate study by the same group showed that even a single bout of FE was capable of reducing bradykinesia and tremor (Ridgel, Peacock, Fickes & Kim, 2012). These results demonstrated that not all exercise that is matched by aerobic intensity is equal in its therapeutic effect. Since pedaling cadence was the only reported difference between groups, the authors proposed that faster sampling rates of afferent somatosensory information

experienced by FE group could be responsible for the improvement in BG functioning.

iii. Body awareness/other - Is somatosensory training the missing link?

The contributions of somatosensory feedback during exercise are highlighted in the next few exercise programs, which are neither aerobic, intense, or speed based. Improvements in UPDRS-III scores have been reported in interventions such as Tai Chi (Yang, Li, Gong & Zhu, 2014), PD SAFEx (Sage & Almeida, 2009, Sage & Almeida, 2010), and Qi Gong (Schmitz-Hubsch, Pyfer, Kielwen, Fimmers, & Klockgether, 2006). These interventions focus on body awareness, and force Parkinson's patients to rely heavily on somatosensory information to maintain balance and stability. The mechanisms responsible for the improvement of symptoms are still unknown for body awareness based exercises, however, an improvement in the processing of somatosensory information may in part be responsible for the improvements in motor symptoms (Sage, 2008; Sage, 2009). Work that has examined sensory feedback during movement in PD have supported that the processing of somatosensory information is disrupted in Parkinson's disease (Abbruzzese & Berardelli, 2003; Zia et al. 2000; Konczak et al., 2007). Additionally, other research has proposed that the deficits in sensory processing may actually contribute to the motor symptoms of PD (Jacobs & Horak, 2006; Abbruzzese, 2004). Due to the possibility that poor processing of somatosensory information within the BG contributes to the motor symptoms of the disease, an improvement in integration of somatosensory information could be a causal factor in regards to improvements in motor symptoms.

MUSCLE SPINDLE AND GOLGI TENDON ORGAN FUNCTION/PHYSIOLOGY

The term somatosensory feedback refers to the afferent sensory message provided by proprioceptors in the body that allow for the detection of movement, muscle tension and physical location in space. The two primary proprioceptors discussed in this thesis are muscle spindles and Golgi tendon organs (GTO). Muscle spindles are stretch-sensitive mechanoreceptors that are found in virtually all mammalian skeletal muscle. Their function is to provide the central nervous system with information about length and changes in length of a muscle (Proske, 1997). In regards to the afferent signal that is created sent to the CNS, as the muscle is lengthened, the spindle increases its frequency of discharge in proportion to the length of the sarcomere (Burke, Hagbarth & Löfstedt, 1978).

The other proprioceptor discussed in this thesis is the GTO, which provides the CNS with information regarding the tension that a muscle fiber is subject to. GTO's are very sensitive to changes in tension, as the activation threshold for this particular proprioceptor is very low (Jami, 1992). As the GTO is put under more strain, the output of action potentials becomes more frequent, providing the CNS information that the muscle is under greater load. Furthermore, as more motor units are recruited to perform a task that requires more tension, a greater quantity of GTOs will begin to discharge (Horcholle-Bossavit, Jami, Petit, Vejsada & Zytnicki, 1988).

In the middle section of this thesis, the terms RATE and MAGNITUDE are used as descriptors for somatosensory feedback that the exercise programs are intended to generate. During regular walking, the CNS is receiving information from

both the GTO's and muscle spindles as muscles extend and contract while being subjected to varying tension. The RATE group, which consists of walking at a fast cadence causes length sensitive muscle spindles to discharge more frequently, as a greater amount of gait cycles are occurring in a given period of time. This more frequent discharge from length sensitive muscle spindles is the basis for the RATE title, as the CNS receives this stretch/shortening message more frequently. The treadmill program that was deemed "MAGNITUDE" was intended to generate a greater discharge from tension sensitive GTO's. This was accomplished by having participants wear ankle weights during walking in an effort to elicit greater tension at the flexors of the hip and extensors of the knee during walking. Assuming that the ankle weights lead to greater muscle tension during gait, the greater amount of discharge from GTO's particularly during toe off and swing would provide a signal to the CNS that is greater in magnitude. Thus, compared to regular treadmill walking the feedback from GTO's would be of greater magnitude due to the use of the ankle weights.

THERAPEUTIC CONTRIBUTIONS OF SOMATOSENSORY FEEDBACK

Recently, the contributions of afferent, somatosensory feedback from muscle spindles, golgi tendon organs and joint receptors has been proposed to be a mechanism responsible for the therapeutic effects of exercise for those with PD (Alberts et al., 2011; Ridgel et al., 2012). This hypothesis is supported by research that shows that afferent feedback has the ability to alter corticomotor excitability (Coxon, Stinear & Byblow, 2005; Cheng J, Brooke JD, Misiaszek JE, Staines WR, 1995). Furthermore, work reporting therapeutic effects from whole body vibration

therapy in PD has also proposed somatosensory feedback as the mechanism responsible for motor symptom improvement (King, Almeida & Ahonen, 2009; Haas CT, Turbanski K, Kessler K & Schmidtbleicher, 2006). The incoming somatosensory feedback may reset or perturb the abnormally slow neural rhythms that occur in the Parkinsonian brain (King, Almeida & Ahonen, 2009). Exercise based evidence for this hypothesis stems from forced exercise studies where training variables such as heart rate and output (watts) are matched between groups, while cadence differs (Alberts et al., 2011). Only groups that trained at fast cadences received therapeutic benefits, leading the authors to conclude that a higher rate of sampling from somatosensory afferents was the only difference between groups.

Although the argument that high rates of sampling of somatosensory information is what leads to therapeutic benefits of high cadence exercise, it is important to consider that the previously mentioned body awareness and resistance based exercises that have also been shown to be capable of improving the motor symptoms rely on somatosensory information, but in a different manner. Body awareness based exercises are not quick or high rate in nature, but rather are slow and generate high magnitudes of somatosensory feedback. Therefore, it is possible that exercise interventions that generate greater magnitudes of somatosensory feedback by increasing the discharge frequency from GTO's may be just as effective as those that are based upon generating high rates of somatosensory feedback in regards to their therapeutic qualities.

THESIS OBJECTIVES

       The objective of this thesis is to explore the therapeutic capability of three different treadmill exercise programs. The first treadmill condition is deemed the RATE group, and will have participants walk while maintaining a fast cadence. The next treadmill condition is the MAGNITUDE group, where participants will walk with ankle weights. Lastly, a CONTROL treadmill exercise program consisting of participants walking at their voluntary speed will serve as an active comparator. The variations in types of treadmill training programs were carefully manipulated with the intention to vary the type of somatosensory feedback they generate. This work will hopefully provide insight to the therapeutic contributions of somatosensory feedback during exercise, and allow for a further understanding of which specific traits of exercise for those with PD are beneficial.

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Chapter 2

The therapeutic contributions of somatosensory feedback during exercise in Parkinsons disease; a randomized, controlled trial.

ABSTRACT

Background: Somatosensory feedback generated from exercise has been hypothesized to be in part responsible for the therapeutic effects of forced-exercise in Parkinson's disease (PD). *Objective:* To explore the influence of different forms of somatosensory feedback and their contribution to motor symptom improvement from exercise in PD. *Methods:* 48 patients with idiopathic PD were randomized into 3 different treadmill exercise programs (RATE, MAGNITUDE, CONTROL). Participants were evaluated before and after the program using the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS-III) and objective measures of both gait and postural control. All programs lasted 6 weeks with sessions occurring 3 times a week. *Results:* Baseline measurements revealed no statistical differences between groups. 9 participants withdrew. Despite all groups exercising at a matched intensity, frequency and duration, only the RATE group significantly reduced their UPDRS-III (23.35 ± 8.13 to 18.85 ± 7.17, P<.01). Furthermore, this group improved on an upper limb subsection of the UPDRS-III (12.00 ± 5.39 to 9.15 ± 4.14, P<.01). *Conclusion:* A high sampling rate of somatosensory feedback appears to be a trait of exercise that contributes to its therapeutic effect in PD. Those exercising for therapeutic benefit with PD should consider including activity that is rapid and repetitive in nature.

INTRODUCTION

Parkinson's Disease (PD) is a progressive movement disorder with motor symptoms such as tremor, bradykinesia, rigidity, postural instability, and gait impairment (Guttman, Kish & Furukawa, 2003; Rocchi, Chiari & Horak, 2002). Dopamine replacement therapy (DRT) is the most common and accessible treatment for motor symptom management (Rascol, Payoux, Ory, Ferreira, Brefel-Courbon & Monastruc, 2003; Parkinson Study Group, 2000). Although DRT ameliorates cardinal motor symptoms, its use is commonly accompanied by bothersome physical and mental side effects (Fahn, 1996; Fahn et al., 2004). Furthermore, postural instability and gait dysfunction respond minimally to DRT, leaving two symptoms associated with the high morbidity in PD minimally treated (Sethi, 2008; Hely, Morris, Reid & Trafficante, 2005). The compromising and incomprehensive aspects of DRT stress the importance of developing alternative and complimentary methods of motor symptom management in PD.

Exploring the efficacy of exercise and physical activity to improve the motor symptoms of PD has been a popular area of research in recent years. (Ridgel, Peacock, Fickes & Kim, 2012; Herman, Giladi, Gruendlinger & Hausdorff, 2008; Alberts, Linder, Penko, Lowe & Phillips, 2011; Sage & Almeida, 2009; Sage & Almeida, 2010; Yang et al., 2014; Li, Harmer & Fitzgerald, 2012; Corcos et al., 2013, Miyai et al., 2000). Aerobic exercise on treadmill, bicycle, resistance training, and body awareness exercises such as Tai Chi, and Sensory Attention Focused Exercise (PD SAFEx) have been shown to be successful in providing motor symptom relief,

measured by the motor subscale of the Unified Parkinson's Disease Rating Scale (UPDRS-III). However, despite the amount of research that has been conducted on exercise and PD, which specific qualities and traits of exercise responsible for evoking a therapeutic response remain largely unknown.

Recently, somatosensory feedback generated during exercise from muscle spindles, golgi tendon organs and joint receptors has been proposed to contribute to the therapeutic of exercise on the motor symptoms of PD (Ridgel et al., 2012; Alberts et al., 2011) This is concurrent with research demonstrating that varying somatosensory afferent feedback alters corticomotor excitability (Coxon, Stinear & Byblow, 2005; Cheng, Brooke, Misiaszek & Staines, 1995). Furthermore, work reporting therapeutic effects from whole body vibration therapy in PD has also proposed somatosensory feedback as the mechanism responsible for motor symptom improvement (King, Almeida & Ahonen, 2009; Turbanski, Haas, Schmidtbleicher, Friedrich & Duisberg, 2005). The incoming somatosensory message relays through the thalamus, and may reset or perturb abnormally slow and asynchronous neural rhythms that occur in the Parkinsonian brain (Levy, Ashby, Hutchison, Lang, Lozano & Dostrovsky, 2002; Brown, Olivviero, Mazzone, Insola, Tonali & Di Lazzaro, 2002; Marsden, Limousin-Dowsey, Ashby, Pollak). Applied exercise based evidence for this hypothesis stems from forced exercise (FE) studies where participants are assisted to achieve an exercise intensity that they would not be capable of maintaining on their own. In FE, variables such as heart rate and output (watts) are matched between groups, while only cadence differs. Only the rapid cadence FE group received therapeutic benefits leading to the possibility that a high rate of

somatosensory sampling generated from FE was partly responsible for motor symptom improvement reported (Alberts et al., 2011).

Although it is possible that a high rate of afferent sampling is a contributing factor towards the therapeutic benefits of exercise, it is important to consider that rapid, high cadence exercise is not the only type of exercise that has reported UPDRS-III improvements. Previously mentioned body awareness and strength training exercises are not quick or high rate in nature, but rather are slow and methodical. In regards to afferent feedback, these types of exercise would generate high magnitudes rather than high rates of somatosensory feedback. Therefore, if somatosensory feedback generated from exercise is a contributing factor for therapeutic benefit, it is possible that generating a high magnitude of feedback may also be beneficial. This raises the need for a randomized, controlled study which matches intensity, type, and duration of exercise while manipulating the characteristics of somatosensory feedback that the participant receives. One way of manipulating somatosensory feedback while keeping other training variables constant is by using body weight supported treadmill training (BWSTT), as more body weight can be removed to facilitate high rate exercise that would otherwise be difficult or impossible for a Parkinson's patient to maintain.

The aim of the current study was to explore the therapeutic contribution of various forms of somatosensory feedback generated during exercise. It is hypothesized that exercise that generates a high RATE of somatosensory feedback will improve motor symptoms of the disease. Furthermore, the therapeutic effect of somatosensory feedback that is greater in MAGNITUDE during exercise was

explored. The objective is to provide those responsible for exercise prescription in PD an indication of how somatosensory feedback may contribute to the therapeutic improvements reported from certain forms of exercise in PD.

METHOD

Participants

Participants were recruited from the Sun Life Financial Movement Disorders Research and Rehabilitation Centre (MDRC) at Wilfrid Laurier University in rolling fashion from October 2013 to June 2014. Inclusion criterion included a diagnosis of idiopathic PD, the ability to walk without the aid of an assistive device for 10 metres, no history of cerebral or myocardial infarction, and no musculoskeletal issues in the lower limbs or back that would affect ability to walk for sustained periods of time. All participants provided PARmed-X forms that were signed by a physician to ensure that they were fit for exercise. Participants were removed from the analysis if they missed more than 2 sessions or changed medication at any time during the intervention. Informed written consent was provided prior to any participation or assessment. The study was approved by the Wilfrid Laurier University ethics board and was registered with clinicaltrials.gov ID #NCT01987557.

Sample Size Calculation

A sample size of 13 was required to detect a 3.5 point change in the UPDRS-III with an assumption of 80% power. This chosen value was conservative estimate based off of a minimally clinical important change (MCIC) which has been reported to be between 2.4 and 2.7 points (Shulman et al., 2010)

Randomization

Participants were randomized into 1 of 3 training groups by a random number generator after initial assessments were completed to ensure that groups would be comparable by UPDRS-III (*Figure 1*). Randomization was done by a researcher who was not responsible for any assessments that were subjective in nature.

Outcome Measures

All tests were conducted within one week of the start of the intervention (Pre), and again during the week following the cessation of the intervention (Post). All assessments were done in the "On" state of Parkinsonian medication.

i. Unified Parkinson's Disease Rating Scale (motor section)

The primary outcome measure was the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS-III). An upper limb subscore (UPDRS-III UL) was generated using items 20-25 of the UPDRS-III. A posture and gait subscore (UPDRS-III PG) was generated with items 27-31. The UPDRS-III was conducted by a certified clinical assessor who was blinded to group assignment.

ii. *Spatiotemporal Aspects of Gait*

Spatiotemporal aspects of gait were generated from a 7.9m GaitRITE walkway (CIR Systems Inc, Havertown, PA) during self-selected, then maximal overground walking speeds. The mean from 5 trials for each walking speed were used for analysis.

iii. Postural Control

Postural control was assessed on a Balance SD system (Biodex, Shirley, NY) using the Postural Stability Test (PST) and modified Clinical Test of Sensory Integration on Balance (m-CTSIB) modes. The postural stability mode assessed how well a participant could maintain their centre of balance during quiet stance. This test was repeated 3 times for 20 seconds each on platform stability level 8, which has been validated in previous research (Arnold & Schmitz, 1998). The m-CTSIB assessed the ability to integrate various forms of sensory feedback which has been shown to be deficient in PD (Rinalduzzi et al., 2015). The m-CTSIB included 4 conditions that were each tested once for 30 seconds. Baseline (eyes open, firm surface), vestibular/somatosensory interaction (eyes closed, firm surface), somatosensory/visual interaction (eyes open, dynamic surface), and somatosensory/vestibular interaction (eyes closed, dynamic surface). All values for postural control measures represent deviations from the centre of the platform.

Training Statistics

In addition to outcome measures, training data provided by the BIODEX Gait trainer 3.0 were recorded after each training session. Training metrics consisted of heart rate, treadmill speed, stride length, and cadence. Cadence was measured in gait cycles per minute and was derived from the total amount of steps taken during the 25 minute training session. Cadence (gait cycles per minute)=[(total steps/2)/25]. Heart rate readings from the handles of the Biodex gait trainer 3.0 treadmills were recorded every five minutes then averaged over the training session then converted to a percentage using the standard Karvonen formula (220-age)

Intervention

The study consisted of 3 separate treadmill based exercise interventions that were deemed RATE, MAGNITUDE, and CONTROL. All interventions trained 3 times a week for 6 weeks for a total of 18 sessions. All participants trained on the Biodex gait trainer 3.0 and wore the Biodex overhead harness to allow for the manipulations bodyweight and for safety to be ensured.

Each session consisted of a 5 minute warm up where participants would walk at a self-selected speed, followed by a 25 minute session that varied depending on their group assignment, then an optional 2 minute cool down. Participants were allowed to take breaks at anytime, however, break time was not included in the 25 minute session. If participants reached a heart rate that was above 75% of their Karvonen age related maximum heart rate (AAMHR), they were given a rest, which involved either walking slowly or sitting down until their heart rate dropped to below 70% of their Karvonen AAMHR.

i. "RATE"

Participants in this group were instructed to walk with as fast of a cadence (gait cycles per minute) as possible during their training sessions. Body weight was removed via the Biodex harness to facilitate high cadence walking. The amount of bodyweight removed was determined by the participants' preference. The protocol was based off of a forced exercise (FE) regime that reported improvements in motor function in those that bicycled at a cadence of 85.8(sd=0.8) revolutions per minute (RPM) (Alberts et al, 2011). In an effort to replicate the high cadence, participants were verbally reminded to keep the cadence of their gait as close to the mark of

approximately 85 gait cycles per minute. To facilitate this, most participants in this group used a greater amount of body weight support.

ii. "MAGNITUDE"

Participants wore ankle weights to increase the response from tension sensitive golgi tendon organs (GTO's) during gait that was larger in magnitude. Participants were given the instruction to walk at their preferred pace. Men wore 3lb weights on each ankle and women wore 2 lb weights on each ankle. For the first 3 sessions, the amount on each ankle was one pound less to allow for participants to safely adjust to the ankle weights.

iii. "CONTROL"

In the control condition, participants were still harnessed and the amount of bodyweight removed was determined by the participants' preference. Participants were told to train at their preferred walking pace. Gait cues were given occasionally to promote proper gait.

Statistical Analysis

The data were analyzed with Statistica version 7 (Statsoft). For participant characteristics at pre and training variables, one way ANOVAs were used to examine group differences. Main and secondary outcome measure differences from pre to post were analyzed with a repeated measures 3x2 (group by time) ANOVA. Post hoc analyses were conducted using Fishers LSD. The significance level was set at .05. For certain outcome measures, a post hoc analysis was run despite the absence of a significant interaction between group and time. The use of more liberal statistics in these scenarios is justified by these comparisons being planned and stated in the

hypothesis. Furthermore, the UPDRS-III changes reported were considered to be

moderately clinically meaningful differences (Shulman, 2010).

Table 1: Protocol Summary

	Condition		
	"Rate"	*"Magnitude"*	*"Control"*
Description	• Treadmill walking with the goal of maintaining as fast of a cadence as possible.	• Treadmill walking with ankle weights	• Regular treadmill walking
Body Weight Support (BWS)	• All participants trained at their preferred amount of body weight support.		
	▪ Due to participants training at a high cadence, most participants trained with a considerable amount of BWS.	▪ A varying amount of BWS was used for training sessions to adapt the exercise to the capabilities of the participant.	
Cadence	• All participants were instructed to walk with a step rate that was fast as possible and were given verbal cues if cadence became too slow.	• No cues for cadence were given to participants during training sessions.	
Intensity	• Intensity was based on participants' % of age adjusted maximum heart rate using the *Karvonen formula (AAMHR). • When AAMHR reached became greater than 75% participants were given a rest until heart rate dropped to <70% AAMHR.		

*Karvonen formula for AAMHR=(220-age)
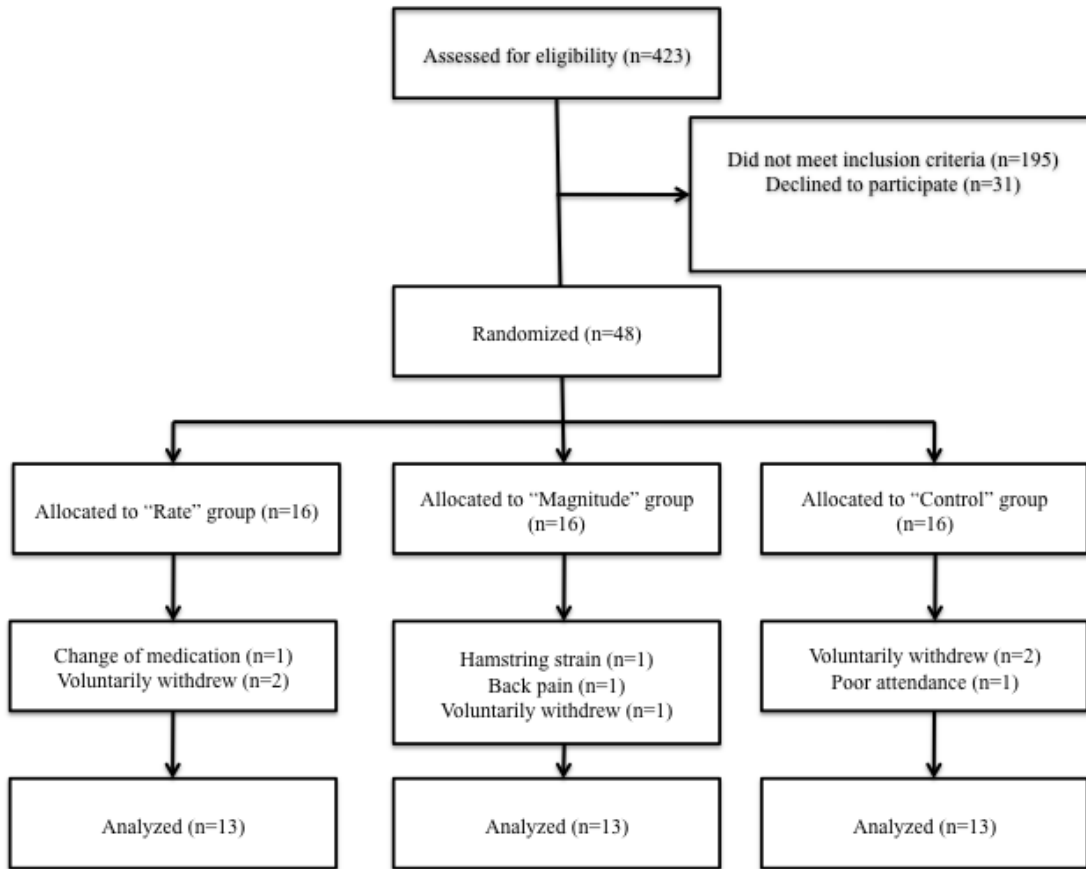
Figure 1: Randomization flow chart

RESULTS

Participants

No significant differences in age, disease severity (UPDRS-III), or walking velocity between groups at PRE were identified (*Table 2*).

Training Characteristics

Training intensity, which was based on a percentage of the Karvonen age adjusted maximum heart rate (AAMHR) did not significantly differ between groups (p=0.18) for total training sessions. Participants in the RATE condition trained at a both faster velocity (p<.01), higher cadence (p<.001), and walked further compared to those in other conditions (p=0.39). Stride length was similar between conditions during training (*Table 3*).

Adverse Events

No major adverse events occurred during the study. 1 participant withdrew due to hamstring pain, and another withdrew as a result of minor back pain (Figure 1).

Primary Outcome Measure

UPDRS-III

A main effect of time for all groups showed improvement on UPDRS-III scores ($F_{(1,36)}$=9.93, p<.01), however, only participants in the RATE condition improved significantly (P<.01). A significant main effect of time was reported across groups in an upper limb subscale (UPDRS-III UL) ($F_{(1,36)}$=9.45, p<.01), again, only

the RATE condition improved significantly in the UPDRS-III UL (p<.01). No significant differences were detected in the posture and gait subscale (p>.05) (*Table 4*). An interaction between group and time was not statistically significant for total UPDRS III F(2, 36)=1.0466, p=0.36, UPDRS III UL F(2,36)=2.39, p=0.11, and UPDRS-III PG F(2,36)=1.26, p=0.30. A post hoc was completed on the UPDRS-III and its subscales because a 4.5 point change in the RATE group is considered to be a moderately clinically meaningful change (Shulman, 2010). Although statistical significance was not reached in the interaction, the clinical importance of this change merited the use of a post hoc test to examine this planned comparison.

Secondary Outcome Measures

Spatiotemporal Aspects of Gait

Self-paced gait

i. Velocity

A main effect of time was found for velocity ($F_{(1,36)}$=9.75, p<.01). Fisher's LSD at post-hoc revealed that only the RATE (P<.01) and CONTROL (P<.05) conditions improved significantly in self paced walking velocity (*Table 5*). A group by time interaction was not significant F(2,36)=2.38, p 0.11.

ii. Stride Length

A main effect of time was reported for stride length ($F_{(1,36)}$=11.83, p<.01). Fisher's LSD post-hoc showed that the RATE and CONTROL conditions improved significantly (P<.05) (*Table 5*). A group by time interaction was not significant F(2,36)=0.53, p=0.59.

iii. Cadence

A main effect of group was detected for cadence ($F_{(2,36)}$=3.65, P<.05). The MAGNITUDE group walked with a significantly lower cadence compared to the RATE and CONTROL groups (*Table 5)*. A group by time interaction was not significant F(2,36)=3.066, p=0.06.

Fast-paced gait

i. Velocity

A main effect of time on velocity was detected ($F_{(1,36)}$=22.56, p<.001). Post-hoc showed that the RATE (P<.01), MAGNITUDE (P<.05) and CONTROL (P<.01) groups increased fast paced walking velocity (*Table 6)*. A group by time interaction was not significant F(2,36)=0.43, p=0.66

ii. Stride Length

A main effect of time was reported for stride length ($F_{(1,36)}$=16.21, p<.001). Fisher's LSD post-hoc showed that the RATE and MAGNITUDE groups increased their stride length during fast paced walking (P<.05) (*Table 6). A group by time interaction was not significant F(2,36)=0.41, p=0.67*

iii. Cadence

No significant differences were detected for cadence during fast paced walking.

Balance and Postural Control

Modified Clinical test of Sensory Integration on Balance (m-CTSIB)

No significant differences were observed in the m-CTSIB *(Table 7).*

Postural Stability Testing (PST)

No significant differences reported in total, anteroposterior, or mediolateral PST

scores (*Table 7).*

Table 2: Participant characteristics at baseline

	Rate	Magnitude	Control	P value
N	13	13	13	n/a
Age	63.77 (7.01)	70.46 (9.52)	66.31 (9.07)	p=.16
UPDRS III "PRE"	23.00 (8.51)	22.96 (6.93)	22.46 (8.64)	p=.98
Gender	m=10, f=3	m=12, f=1	m=12, f=1	n/a
Self paced walking velocity (cm/s)	116.19 (24.09)	122.54 (8.58)	116.21 (30.24)	p=.71

UPDRS-III, Unified Parkinson's Disease Rating Scale (motor subsection). One way ANOVA used to determine differences between groups at PRE. Disease severity (UPDRS-III) and age were comparable at PRE. Bracketed numbers represent standard deviations.

Table 3: Training Statistics

	Rate	Magnitude	Control	Sig
Intensity (% of AAMHR)	67% (3.83%)	68% (3.79%)	64% (5.60%)	p=.18
Velocity (km/h)	**5.63 (0.60)	4.60 (0.97)	4.63 (1.24)	p=.01
Cadence (gait cycles per minute)	**80.21 (1.85)	59.68 (4.12)	59.85 (3.41)	p<.001
Total distance (m)	*2773.31 (310.22)	2318.62 (451.22)	2329.31 (661.29)	p=.039
Stride Length (cm)	151.69 (17.07)	160.00 (21.88)	148.15 (29.21)	p=0.42

AAMHR, Karvonen based age adjusted maximum heart rate (220-age)

*P<.05 difference one way ANOVA between groups

**P<.01 difference one way ANOVA between groups

Table 4: UPDRS-III

	Rate	Magnitude	Control
UPDRS-III			
Pre	23.35 (8.13)	22.96 (6.93)	22.46 (8.64)
Post	**18.81 (7.17)	20.69 (8.39)	20.92 (6.14)
UPDRS-III PG			
Pre	2.92 (2.23)	2.88 (1.40)	4.04 (3.48)
Post	2.42 (1.89)	3.03 (1.81)	3.24 (3.04)
UPDRS-III UL			
Pre	12.00 (5.39)	11.15 (4.14)	10.8 (5.02)
Post	**9.15 (4.14)	10.15 (5.90)	10.27 (4.62)

UPDRS=Unified Parkinson's disease rating scale, PG=Posture and gait subscore (items 27-31 of UPDRS), UL=Upper limb subscore (items 20-25 of UPDRS). Bracketed numbers represent standard deviations.

**$P<.01$ using Fisher's LSD post hoc within groups

Table 5: Spatiotemporal aspects of self-paced gait

	Rate	Magnitude	Control
Velocity (cm/s)			
Pre	117.07 (24.09)	122.64 (8.58)	116.2 (30.24)
Post	**129.38 (21.30)	125.56 (20.51)	*124.5 (32.33)
Stride Length (cm)			
Pre	125.46 (26.29)	136.6 (11.87)	122.48 (28.52)
Post	*133.62 (27.04)	140.32 (17.48)	*128.77 (29.53)
Cadence (steps per minute)			
Pre	111.59 (7.36)	107.85 (7.50)	112.97 (9.86)
Post	116.82 (8.88)	105.28 (10.45)	115.44 (10.90)

Bracketed numbers represent standard deviations.

*P<.05 using Fisher's LSD post hoc within groups

**P<.01 using Fisher's LSD post hoc within groups

Table 6: Spatiotemporal aspects of fast paced gait

Outcome Measure	Rate	Magnitude	Control
Velocity (cm/s)			
Pre	156.54 (37.33)	164.83 (22.32)	155.92 (43.98)
Post	**169.12 (26.95)	*176.87 (20.83)	*165.47 (48.02)
Stride Length (cm)			
Pre	143.27 (31.00)	158.69 (37.18)	143.54 (37.18)
Post	*150.31 (28.13)	**166.57 (17.66)	148.02 (35.87)
Cadence (steps per minute)			
Pre	130.06 (10.17)	127.34 (13.90)	130.72 (11.42)
Post	135.75 (12.11)	125.78 (13.06)	132.67 (17.37)

Bracketed Numbers represent standard deviations.

* $P<.05$ with Fisher's LSD post hoc within groups

**$P<.01$ with Fisher's LSD post hoc within groups

Table 7: Measures of balance and postural control

		Rate	Magnitude	Control
m-CTSIB	Full Sensory Availability			
	Pre	0.76 (0.22)	0.78 (0.21)	0.85 (0.31)
	Post	0.80 (0.29)	0.82 (0.29)	0.76 (0.25)
	Somatosensory Dominant			
	Pre	1.26 (0.46)	1.34 (0.33)	1.73 (1.11)
	Post	1.28 (0.50)	1.56 (0.63)	1.62 (0.62)
	Visual Dominant			
	Pre	1.15 (0.30)	1.42 (0.49)	1.32 (0.45)
	Post	1.21 (0.40)	1.43 (0.63)	1.24 (0.48)
	Vestibular Dominant			
	Pre	2.9 (0.77)	3.3 (1.25)	3.24 (1.26)
	Post	2.9 (1.00)	3.15 (1.11)	3.43 (1.85)
Postural Stability Test (PST)	Overall			
	Pre	1.38 (0.29)	1.68 (0.52)	1.85 (0.51)
	Post	1.54 (0.50)	1.78 (0.61)	1.71 (0.77)
	Anteroposterior			
	Pre	0.98 (0.37)	1.25 (0.49)	1.26 (0.51)
	Post	0.97 (0.39)	1.25 (0.56)	1.15 (0.58)
	Mediolateral			
	Pre	0.78 (0.24)	0.88 (0.25)	1.07 (0.34)
	Post	0.96 (0.37)	1.01 (0.32)	1.03 (0.47)

Full sensory availability=eyes open on firm surface, somatosensory dominant=eyes closed on firm surface, visual dominant=eyes open on foam surface, vestibular dominant=eyes closed on foam surface. Values are representative of deviations from the centre of the platform. Bracketed numbers represent standard deviations. m-CTSIB, modified clinical test of sensory integration on balance.
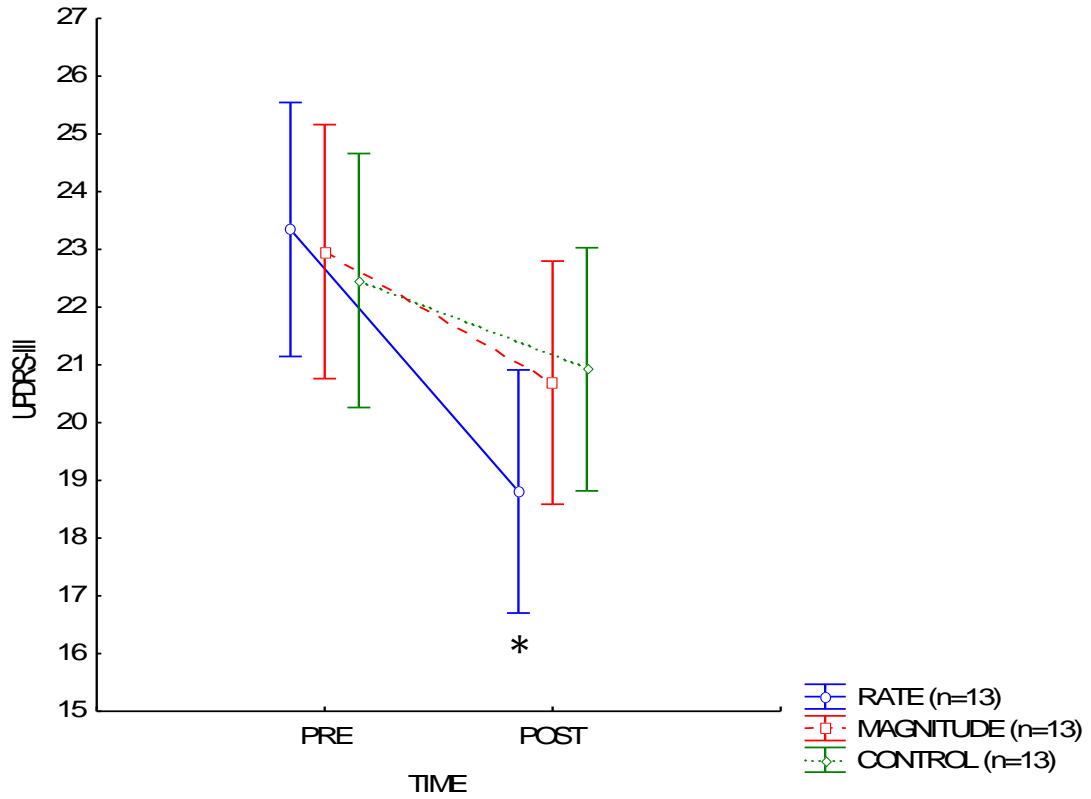
Figure 2: UPDRS III change over time. A main effect of time was reported for all participants. At post hoc, only the RATE group showed significant improvement

*P<.05 Fisher's LSD Post hoc within groups

DISCUSSION

The aim of the current study was to evaluate the influence of different types of afferent feedback elicited from exercise have on the motor symptoms of PD. Results showed that a high sampling rate of afferent feedback was the most therapeutic, as only the RATE group which trained at a high cadence significantly improved their UPDRS-III symptom scores at post. Furthermore, participants in this condition improved on an upper limb subscore of the UPDRS-III. Since treadmill training involves little use of the upper limbs, the improvement in upper limb functioning cannot be explained by practice or motor learning theories, but rather may be indicative of an improvement in BG functioning. Lastly, considering that intensity, type, frequency, and duration of training were matched between all training groups, the type of afferent feedback that exercise generates must be a key consideration for exercise prescription for those with PD, as this study demonstrated that a high rate of afferent feedback is most effective in regards to improving the motor symptoms of PD.

The hypothesis that high rates of afferent somatosensory feedback from muscle spindles and golgi tendon organs (GTO's) facilitates the motor symptom relief seen from exercise was initially proposed by Alberts et al. Their high cadence protocol showed a 35% improvement in UPDRS-III scores compared to regular cadence exercise control group. The current study supports the Alberts et al. findings regarding the therapeutic effect of high cadence exercise, but showed a more modest 20% improvement in UPDRS-III. This is likely because the current study included participants that were much less severe and were assessed during the "on" state of

medication, potentially contributing to a ceiling effect. Also, the cadence was slightly slower in the current study (80.21 rpm in current, compared to 85.8 rpm in Alberts et al.). This eludes to the possibility that participants may not have trained with a fast enough cadence to achieve maximal benefits. This was due to the exercise occurring on a treadmill in the current study, and it being more difficult to maintain a fast cadence while walking opposed to bicycling.

Unfortunately, the mechanism explaining why a high rate of somatosensory feedback is therapeutic still remains unknown. However, the high sampling rate of afferent information from muscle spindles and GTOs, which propagates up the dorsal column-medial lemniscus pathway into the thalamus may act as a pacemaker and perturb the abnormal oscillatory rhythms in the beta frequency between the BG and thalamus that have been reported to occur in PD (Brown et al., 2001; Marsden et al., 2001). After multiple sessions of high rate exercise, the abnormal spike in beta band frequencies reported during movement in PD may be attenuated, causing improvements in motor symptoms.

Alongside of changes in UPDRS-III scores, improvements were reported in spatiotemporal aspects of gait. Due to the intervention being treadmill based, improvements in gait were expected across all groups as a result of motor learning. This is congruent with previously completed treadmill studies that have shown improvements in gait (Herman et al., 2007; Fisher et al., 2008; Miyai et al., 2000; Cakit, Saracoglu, Hakan & Erdem, 2007; Pohl, Rockstroh, Ruckriem, Mrass & Merholz, 2003). However, this study was the first treadmill training paradigm to compare varying forms of somatosensory feedback and their therapeutic effects on

gait. During self paced gait, improvements were observed in velocity and stride length, however, only for the RATE and CONTROL conditions (*Table 4*). Although not significant, both stride length and velocity were considerably higher at "pre" for the MAGNITUDE group possibly explaining why this group did not improve after the intervention. During fast paced gait, significant improvements in velocity were observed in all conditions while only the RATE and MAGNITUDE groups increased their stride length (*Table 5*). Typical Parkinsonian gait consists of a slow walking velocity caused by a shorter step length (Morris, Iansek, Matyas & Summers, 1996). Usually, a higher cadence is employed as a compensatory mechanism for a shorter stride length (Morris, Iansek Matyas & Summers, 1994). In the current study, changes in cadence were not significant for self paced or maximal gait speeds in any group, leading us to conclude that treadmill walking improves gait velocity by improving step length, which is the root cause of slow walking in PD. Improvements in gait in the current study are similar to previously completed treadmill programs that are acute (Pohl, 2003) and long term, ranging from moderate (Miyai, 2000) to intense (Herman, 2007; Fisher, 2008) aerobic intensity, the use of body weight support (Miyai, 2000), and speed dependent training (Cakit, 2007). A wide variety of treadmill programs including the current study have demonstrated that treadmill training is a safe and effective therapy for improving gait in PD.

The precise mechanism explaining why treadmill training can improve gait is still unknown. One inherent characteristic of a treadmill is that it moves at a constant speed, and has been demonstrated to promote more rhythmic and uniform gait (Frenkel-Toledo, Giladi & Peretz, 2005; Lim, Van Wegen, de Goede et al., 2005).

Thus, the somatosensory message from receptors in the legs and feet is more rhythmic and may promote neuroplastic changes in the CNS to areas responsible for pace and rhythm of gait at either spinal or supraspinal areas. Interestingly, during fast paced walking, only conditions that received altered somatosensory feedback (RATE, MAGNITUDE) improved their step length. The effectiveness of altered feedback during maximal paced walking may be due to the proprioceptive deficits reported in PD (Rickards & Cody, 1997; Khudados, Cody & O'Boyle, 1999). The altered somatosensory feedback generated from the ankle weights, or the faster sampling of somatosensory information from the high cadence RATE group, may improve how this information is being processed. The improved proprioception may lead to a greater extensor load response in which the afferent feedback causes an increased output from the extensors in the lower leg (Dietz & Duysens, 2000). A greater extensor load response contributes to greater force at toe off, and thus, a greater step length and velocity (Dietz & Colombo, 1998).

Due to treadmill training being based upon walking, it is difficult to determine if improvements are from a practice effect, or an improvement in BG functioning. If a practice effect were to explain the improvements in gait velocity, those in the RATE group would likely have relied on an increased cadence to improve gait velocity. However, this was not the case, as only stride length was increased significantly. Furthermore, since no improvements were detected in any measures of postural control, improvements in gait cannot be attributed to improvements in balance. Since all participants were harnessed during treadmill walking, it is likely that balance was not stressed during the intervention, and thus not improved.

Aside from manipulations in somatosensory feedback between groups, it is important to note that the RATE group also differed in the amount of steps they took, which was a requisite of maintaining a fast cadence and thus a high rate of somatosensory feedback. High cadence walking should be considered more volitionally controlled than self-paced walking because the participant must constantly attend to the maintenance of a fast cadence, which is an unnatural adaptation. This leads to an alternative explanation for motor symptom improvement in the RATE group explained by goal directed exercise. In healthy individuals, motor performance relies on an interaction of volitional and automatic control centers (Mazzoni & Wexler, 2009). As PD progresses, the loss of dopaminergic projections to brain centers responsible for the automatic control of movement force PD patients to rely more heavily on volitional control centers (Redgrave, Rodriguez, Smith et al., 2010). This reliance on volitional control for movements causes those with PD to carry larger cognitive loads to ensure successful motor control, which may lead to difficulties while performing more complex and intricate movements. Therefore, goal directed exercise, which is the practice of certain activities that lead to improved performance, may be able to improve the cognitive aspect of motor output by making actions more learned and automatic (Petzinger, Fisher, McEwen et al., 2013). In the current study, the RATE group was the most goal directed of the conditions, due to participants having to maintain a high cadence during walking. High cadence walking should be considered goal directed exercise because the maintenance of a high cadence is an unnatural movement, and requires constant volitional control.

Goal directed movement may lead to neuroplastic changes that revert motor outputs that were volitional movement back to more natural and automatic.

IMPLICATIONS

The current study provides evidence that high rates of somatosensory sampling may be a key attribute of exercise in regards to improvements on motor symptoms of PD. Those prescribing aerobic exercise to PD patients should consider incorporating exercise that is high rate in nature (fast cadence). Future research examining the therapeutic contributions of varying forms of somatosensory feedback should include outcome measures that examine BG functioning directly either by transcranial magnetic stimulation or positron emission tomography. The use of these objective measures will provide more in depth evidence of how altered somatosensory feedback may be improving BG functioning.

LIMITATIONS

Due to the intense nature of the exercise, only those with mild to moderate PD with minimal gait impairment are able to actually perform the exercise properly. Due to time and equipment constraints, the sample was limited to 13 in each group. A potential confounder in the study was that the amount BWS that each participant used over the course of the exercise sessions was not recorded. With varying amounts of BWS, more or less load is experienced by the participant during exercise. The varying amount of load during gait is a concern due to GTO activation (being sensitive to load) was a main manipulation in the study and is an uncontrolled for confounder. Additionally, the average heart rate data was generated using a 220-age

Karvonen formula. An individually generated maximum heart rate for each participant during pre-testing would have been a more accurate method of determining average heart rate. Lastly, the use of beta blocking medication that is common in an older population may have lead to heart rates readings that were not representative of the intensity of exercise that was being performed. Issues with heart rate accuracy lead to the possibility that groups did not train at matched aerobic intensities, introducing a possible confounder explaining differences between groups.

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Appendix A: *Additional Outcome Measures*

The purpose of this additional results section is to provide an objective measure of how upper limb motor performance was affected by the exercise interventions. Since treadmill exercise can be considered mainly lower limb dominant, improvements in upper limb tasks unrelated to the intervention may be representative of overall basal ganglia improvement, as opposed to lower limb improvements that may be explained by practice or the principle of specificity. Although the UPDRS-III has a thorough section devoted to the upper limbs, the subjective nature of the assessment often draws criticism for its lack of sensitivity. To acknowledge this, two objective measures of upper limb function were tested at pre and post.

The first objective measure of upper limb function was performance on a grooved pegboard, which has previously been shown to strongly correlate to overall UPDRS-III scores (Sage, Bryden, Roy & Almeida, 2012). The other objective measure was the Kinesia Homeview® tablet, which emulates the upper limb tasks of the UPDRS-III, but generates scores from an accelerometer on the hand that is being assessed. This device has been previously validated and correlates strongly to clinical tremor (Giuffrida, Riley, Maddux, and Heldman, 2009), and bradykinesia scores (Heldman et al., 2011). Additionally, a Pearson's correlation was used to examine how closely related the grooved pegboard and Kinesia Homeview scores were to the current gold standard of motor symptom severity within PD; the UPDRS-III. All tests were conducted in the week prior to the start of the intervention (Pre), and again during the week following the cessation of the intervention (Post).

Kinesia Homeview Assessment

The Kinesia tablet receives data from an accelerometer placed on the pointer finger of each hand. The accelerometer provides a score from 0-4 on resting tremor, postural tremor, action tremor, rapid alternating movements, finger taps, and bradykinesia (hand grasps). For the movement based tasks separate scores for velocity, rhythm, and amplitude score are provided. All scores were summed for the respective hand (less affected, more affected). More affected side was determined by the higher UPDRS-III score for the right or left hand.

Grooved Pegboard

A 25 peg Lafayette Instruments Grooved Pegboard was used. Participants were timed during both the place and removal phases for each hand for two trials each. Participants were given a maximum time of 5 minutes. The mean times for the two trials were averaged, and divided by the amount of successfully placed or removed pegs to provide a rate (seconds/peg).

Statistical Analysis:

For the Homeview Kinesia and grooved pegboard, a 3X2 repeated measures ANOVA (groups x time) was used. For the correlation, a Pearson's correlation was used. Significance for all tests was set at 0.05.

Results:

Kinesia Homeview® Assessment

1. Affected limb

An interaction between Group and Time ($F_{(2,36)}$=3.69, p<.05) was found for Kinesia Homeview ® symptom score for the more affected limb. Fisher's LSD post hoc analysis showed that only the MAGNITUDE group improved significantly (*Table 8*).

 2. Non-Affected limb

No significant differences were observed in the non-affected limb in the Kinesia Homeview ® assessment (*Table 8*).

Grooved Pegboard

No significant differences were reported in the place or remove phase of the grooved pegboard task (*Table 9*).

Correlational Results

Grooved pegboard "place" with more affected limb correlated to UPDRS-III (r=0.61,p<.05) and UPDRS-III UL (r=0.31, p<.05). Place phase for less affected limb correlated only to total UPDRS-III score (r=0.50, p<.05) (*Table 10*).

Kinesia Homeview tablet with the more affected limb correlated strongly to overall UPDRS-III (r=0.73, p<.05) and UPDRS-III UL (r=0.65, p<.05). Kinesia Homeview score on the less affected limb also correlated significantly to UPDRS-III (r=0.55, p<.05) and UPDRS-III UL (r=0.44, p<.05) (*Table 10*).

Table 8: Kinesia Homeview© assessment

	Rate	Magnitude	Control

More affected limb			
Pre	13.60 (4.32)	14.91 (5.58)	15.58 (4.13)
Post	13.99 (5.03	*12.32 (5.62)	14.2 (3.31)
Less affected limb			
Pre	12.61 (3.90)	11.65 (4.77)	13.17 (3.22)
Post	12.06 (4.15)	11.34 (4.43)	12.07 (2.68)

*P<.05 Fisher's LSD post-hoc within groups.

Table 9: Grooved pegboard performance

	Rate	Magnitude	C
Less Affected "Place"			
Pre	4.4 (1.69)	11.66 (25.54)	8.41
Post	3.97 (1.68)	17.45 (45.50)	5.5
Less Affected "Remove"			
Pre	0.86 (0.17)	0.97 (0.29)	1.1
Post	0.83 (0.19)	0.93 (0.32)	0.9
More Affected "Place"			
Pre	5.33 (4.18)	8.87 (9.53)	9.19
Post	4.53 (1.33)	7.87 (9.16)	6.9
More Affected "Remove"			
Pre	0.88 (0.14)	1.06 (0.26)	1.1
Post	0.86 (0.14)	1.00 (0.30)	1.3

All values are seconds per peg. Bracketed numbers represent standard deviations.

Table 10: Correlations of upper limb measures to UPDRS-III

	Grooved Pegboard		Kinesia Tablet	
	More Affected Place	Less Affected Place	More Affected	Less Affected
UPDRS III PRE	*0.61	*0.5	*0.73	*0.55
UPDRS III UL PRE	*0.36	0.29	*0.65	*0.44

Pearson product-moment correlation coefficients

*p<.05

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Chapter 3:

Grand Discussion

The primary objective of this randomized, controlled trial was to understand the therapeutic contributions of somatosensory feedback manipulations during exercise programs for those with PD. The purpose of examining this was to uncover potential mechanisms responsible for improvements in cardinal Parkinsonian motor symptoms from successful exercise interventions. Having a greater understanding of the mechanism underlying therapeutic responses from exercise in PD is necessary, as it facilitates the development of more effective exercise prescription, and ideally establish exercise as a primary adjunct treatment for those with PD.

The greatest challenge with understanding the mechanism(s) responsible for the therapeutic effects of exercise is that the modalities reported to be successful in improving the motor symptoms of the disease have been diverse in nature. Thus, elucidating which components of exercise (type, frequency, duration, intensity) that possess therapeutic potential is difficult, as they range from aerobic interventions ranging from moderate (Miyai et al. 2000; Ridgel et al., 2009) to intense (Fisher et al., 2008; Herman, Giladi, Gruendlinger & Hausdorff, 2007), to strength training (Corcos et al., 2013), and body awareness based exercises (Li et al., 2012; Sage & Almeida, 2009; Sage & Almeida 2010). One trait or component of exercise that appears to be common among all programs is that they are long term studies with repeated bouts of exercise. Studies that have reported UPDRS-III improvement as a result of exercise have been longitudinal designs with a minimum duration of 4 weeks (Miyai, 2000), with most others ranging from 8-12 weeks (Herman, 2007; Sage, 2009; Sage 2010; Ridgel, 2009). In regards to intensity, average heart rate data is not

provided in most studies, making it difficult to provide a threshold value that is necessary to maintain in order to obtain therapeutic benefits. This was addressed in the current study by ensuring all exercise groups trained at a matched age adjusted heart rate which ranged from 64% to 68% of a Karvonen based AAMHR. A major finding in the current study was that improvements in UPDRS-III were different between groups despite all groups exercising at a matched AAMHR. This led us to conclude that not all aerobic exercise has the same therapeutic potential, and that the somatosensory feedback generated from exercise is an important trait of exercise to consider.

Due to the wide array of exercise modalities shown to be successful in improving the motor symptoms of PD, skeptics would argue that practically any and all exercise possesses therapeutic possibility for those with PD. To an extent, this argument is valid. However, recent evidence stemming from more carefully designed studies employing blinded assessors, randomization, and the inclusion of suitable control groups have shown that only specific types of exercise have the ability to improve the motor symptoms of PD. In particular, Ridgel, Vitek & Alberts (2009) examined two bicycle based aerobic interventions that were matched in intensity (age adjusted maximum heart rate), duration, and frequency, while manipulating pedaling cadence between the groups. Despite the aforementioned exercise traits being similar, only the group which pedaled at a fast cadence reported improved motor symptoms. This was a critical finding because it was the first study to demonstrate that not all aerobic exercise possesses the same therapeutic potency. Although the sample was limited, the drastic improvements reported in the high

cadence group merited further investigation as to why high cadence exercise was therapeutic.

In the current study, we attempted to conduct a randomized, controlled trial including three aerobic treadmill programs that were also comparable in regards to intensity, duration, and frequency. The main manipulation between groups was the somatosensory feedback that each of the different treadmill conditions elicited. Randomization was successful, as groups at pre-test were matched for symptom severity (UPDRS-III), age, and self-paced walking velocity. Furthermore, intensity of exercise (age adjusted maximum heart rate) was successfully matched between treadmill interventions. This was a crucial component of the study to ensure that differing levels of aerobic intensity during exercise would not be a confounder between groups. In the current study, the RATE and MAGNITUDE conditions were considered to be the experimental conditions hypothesized to lead to motor symptom improvements (UPDRS-III), whereas the CONTROL group was meant to serve as the active comparator. The inclusion of an active comparator control group was another key aspect of the study, as a non-exercising control group is often used in PD exercise based studies. While still better than no control group, a non-exercising control may not adequately account for potential bias from the placebo of being involved in a study and receiving care, which can be particularly powerful in a Parkinsonian population (Lidstone, 2014).

The primary finding was that the RATE condition was the only group to significantly improve their UPDRS-III scores. Furthermore, when all groups were collapsed together, UPDRS-III scores improved as a main effect of time. This led to

the conclusion that although all types of treadmill training in the current study should be considered successful, high cadence exercise (RATE group) was the most effective in reducing the motor symptoms of PD. The success of the RATE condition supports another high cadence exercise program that was successful, albeit on treadmill rather than bicycle (Ridgel et al., 2009). Ridgel also reported an improvement on an upper limb task unrelated to the exercise intervention, which was proposed to be an indicator of overall basal ganglia functioning. Similarly, in the current study, an upper limb subscore of the UPDRS-III improved in only the RATE group. Since treadmill walking minimally involves the upper limbs, the transfer of motor symptom improvement to the upper limbs may be indicative of improvements in basal ganglia functioning resulting from exercise. It is proposed that the rapid and rhythmic pulses of somatosensory feedback generated from high cadence exercise may be interacting with the basal ganglia, and recovering its ability to control motor output.

The exact mechanism explaining how a high rate of somatosensory feedback improves the motor symptoms of PD remains unclear. However, the high frequency of rhythmic afferent feedback generated from high cadence exercise may act as a pacemaker and perturb the abnormal rhythms that have been reported to occur within the Parkinsonian basal ganglia (Brown et al., 2001; Marsden, Limousin-Dowsey, Ashby, Pollak & Brown, 2001). These abnormal oscillatory rhythms recorded from the subthalamic nucleus are prominent in the 20 Hz range, or the "beta band" (Brown, 2001). This spike in beta band frequency is not present in healthy subjects, is attenuated by dopaminergic medication and deep brain stimulation, and lastly correlates to bradykinesia and rigidity based motor symptoms (Kuhn et al., 2006;

Kuhn et al., 2008; Kuhn et al., 2009). This pacemaker effect is plausible because input from the mechanoreceptors propagates up the medial lemniscus pathway which interacts with the thalamus; the relay centre for the basal ganglia. After repeated high cadence exercise sessions, the abnormal spike in beta band frequencies that occur during movement in PD may be altered by the fast rate of somatosensory feedback that high cadence exercise generates. Although further research would be needed to confirm this hypothesis, it is proposed that the somatosensory feedback generated from high cadence exercise may adjust the abnormal oscillatory rhythms within the basal ganglia in a manner similar to dopaminergic medication and deep brain stimulation, provoking long lasting therapeutic effects as a result.

The MAGNITUDE group was included in the study in an effort to examine the therapeutic effects of another variant of somatosensory feedback during treadmill walking. However, instead of altering the rate at which the somatosensory feedback is being generated, the ankle weights were intended to elicit a response greater in magnitude from tension sensitive golgi tendon organs in the lower limbs of the participant. The rationale for including this somatosensory feedback manipulation was to emulate the feedback that exercise interventions such as strength training, Tai Chi, and PD SAFEx generate. The aforementioned exercises involve aspects of slow, load bearing movements (a lunge in PD SAFEx or Tai Chi, and resistance training in general). Although these exercises differ from each other, they all generate a similar type of somatosensory feedback which is greater in magnitude, particularly from tension sensitive GTO's. Although the exact mechanism leading to the therapeutic benefit of these body awareness exercises is unknown, the feedback from tension

sensitive GTO's may aid in the participant's ability to properly attend to their movements, as the increased output of afferent signaling may help overcome the proprioceptive deficits reported in PD (Khudados, Cody & O'Boyle, 2009; Rickards & Cody, 2007). Thus, the hypothesis was that if a greater afferent signal from somatosensory receptors into the central nervous system contributes to the therapeutic effects reported from these types of exercises, then the MAGNITUDE condition would show improvements in the UPDRS-III in the current study. However, in the current study UPDRS-III scores for the MAGNITUDE group did not significantly improve at post-test, implying that a greater magnitude of somatosensory feedback may not be as therapeutic as a high rate of feedback. Furthermore, the therapeutic benefits generated from slower, load bearing exercise interventions may not be reliant on the magnitude of somatosensory feedback they generate, but rather other factors. For instance, in resistance based exercise, repetitive training sessions have been reported to increase cortical excitability in healthy controls (Kidgell, Stokes, Castricum & Pearce, 2010), a measure that has been reported to be worse in a Parkinsonian population and in part responsible for the pathology of the disease (Valls-Sole, Pascual-Leone, Brasil-Neto, Cammarota, McShane & Hallett, 1994). Improvements in postural control and gait from Tai Chi have been attributed to improvements in muscular strength of the lower limbs, while mechanisms responsible for upper limb motor symptom relief in these studies still remain unclear (Li et al., 2012). Further research is needed to understand the mechanism responsible for improvements in motor symptoms of PD reported in body awareness based exercises.

Body weight support during treadmill training

The use of body weight support (BWS) during treadmill originally arose from gait training studies in stroke populations whose motor impairments were too severe to walk without the aid of an assistive device. Their application was then adapted for use in the Parkinsonian population, who similarly may have motor disabilities preventing them from achieving and maintaining an intensity of exercise necessary for motor symptom improvement. Miyai et al. (2000) were the first to employ the use of BWS in a Parkinsonian population. Their 6 week program yielded a significant 3.2 point improvement in UPDRS-III. Their study did not report cadence or average speed at which the participants trained at, but did mention that the maximum training speed was 3.0 km/h. The greater 4.5 point improvement in UPDRS-III that the RATE group reported in the current study reported program was likely due to the participants walking at a faster velocity (5.63 km/h in the RATE group) and more importantly, with a more rapid cadence which generates a higher rate of somatosensory feedback. Interestingly, in the current study, the MAGNITUDE and CONTROL conditions were fairly similar to the Miyai intervention which reported significant improvements in UPDRS-III. However, an important difference between ours and Miyai's study was that UPDRS-III assessments in the Miyai study were performed by an assessor who was not blinded to group assignment. Lastly, in the Miyai study, the standard deviations about the means at pre and post were considerably smaller than in the current study ($\pm$1.2 in Miyai compared to $\pm$6.93 in MAGNITUDE and $\pm$8.64 in CONTROL). Less interindividual variability may have facilitated the finding of a statistical difference between pre and post tests.

The use of BWS in the current study was employed to have the ability to adapt treadmill exercise to a wider spectrum of locomotor and balance disability. This was especially important for the high cadence RATE group, as it is difficult to maintain a high cadence for an extended period of time without the aid of an assistive device, such as a harness. Although it is beneficial to be able to adapt exercise to a wide variety of participants, the use of BWS may have been the reason for why there were no improvements reported in any of the balance measures. It is proposed that the use of BWS minimizes the dynamic challenges faced by the participant to maintain balance during gait, explaining why no improvements in balance were reported. It is proposed that future studies employing treadmill training within PD or other disabled populations still take advantage of BWS to adapt the exercise to the ability of the participant. However, the minimum amount of BWS required to achieve and maintain a proper gait pattern should be used to still allow the balance and postural control of the participant to be challenged.

Additional Outcome Measures

Additional measures that examined upper limb motor function were included within the assessment battery in an effort to examine if treadmill exercise, which is predominantly lower limb based, could lead to upper limb symptom improvement. Improvement in tasks completely unrelated to the exercise intervention may be indicative of a change in basal ganglia functioning compared to outcome measures similar to treadmill walking, such as spatiotemporal aspects of gait. The UPDRS-III has a thorough upper limb section and is considered the gold standard for assessment of the motor symptoms of PD. However, due to its subjective nature, has drawn

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criticism for accuracy and validity. Due to this, objective measures to compliment the UPDRS-III are a valuable addition to the test battery.

The Kinesia Homeview assessment mimics upper limb tasks from the UPDRS-III, but captures movement data from an accelerometer placed on the index finger of the participant. The results from the Kinesia Homeview showed a group by time interaction revealing an upper limb improvement in the MAGNITUDE group for the participants more affected limb, while RATE and CONTROL groups did not differ significantly. This finding was surprising as it was in direct opposition to the results found from the upper limb sub score of the UPDRS-III, which showed improvement for the RATE group only. This conflicting result may in part be explained by the MAGNITUDE group having a higher score at pre in the Kinesia (14.91, compared to 13.6 in the RATE group), while having a more closely matched UPDRS-UL score. Although the objective nature of the Kinesia is appealing, research regarding its validity is still limited. Existing research shows that the Kinesia system can accurately assess tremor (Giuffrida, Riley, Maddux & Heldman, 2009) and bradykinesia (Heldman et al., 2011), however, its ability to emulate the other upper limb measures on the UPDRS-III is questionable. For this reason, it is recommended to employ objective upper limb measures alongside of the Homeview system.

In addition to the Homeview system, a 25 peg Lafayette instruments grooved pegboard (GP) was used as an additional outcome measure. Previous work has shown that the "place" phase of the task correlates strongly with overall UPDRS-III motor scores (Sage, Bryden, Roy & Almeida, 2002). In the current study, no

differences in any measures of the GP were reported as a result of the exercise program. This is likely due to the high standard deviations around the mean values reported in the GP scores. High standard deviations arise from this task because participants with severe tremor are often severely challenged compared to those who are akinetic-rigid dominant. Despite converting values to a seconds per peg rate, the large variance of the data made it very difficult to discover an effect. Although the test does correlate well to overall UPDRS-III scores, it is likely that it is not sensitive enough to detect changes in motor symptoms as a result of exercise. Furthermore, issues with vision as well as arthritis in the hands may skew the results of this outcome measure, as it is influenced by non Parkinsonian ailments.

Adverse Events

There were no major adverse events as a result of the current exercise program. Participants were required to return a PARmed-X with a physician's approval which had an accurate description of the requirements of the program. There were 2 minor injuries as a result of the program, both of which occurred in the MAGNITUDE group. One participant complained of slight hamstring stiffness, and the other developed minor back pain. Since both incidents occurred in the MAGNITUDE group, the ankle weights that this group wore may have contributed to their injuries. No adverse cardiovascular events occurred as a result of the exercise program, likely due to the stringent exclusion criteria. However, in future studies, it is recommended that participants perform a stress test in addition to a PARmed-x form to ensure that they are capable of tolerating aerobic exercise.

Although not considered to be an adverse event, some participants complained about chronic fatigue towards the end of the program as a result of exercise. An inherent difficulty with exercise studies is that participants may feel obliged to complete the program despite feeling fatigued. In future studies, it is recommended that the lead researcher include a section in the informed consent emphasizing that rest days can be taken if needed.

Since no major adverse events occurred as a result of the exercise program, the improvements in UPDRS-III scores and spatiotemporal aspects of gait were worth the risk of participating in the study. Of the 48 people that were initially enrolled in the program, only 2 experienced an adverse outcome.

Limitations

Developing a suitable and effective exercise program for a PD population was a difficult endeavor to undertake. A main issue that arose during the design of the study was the requisite to tailor and adapt this program to make it accessible for as wide of a disease spectrum as possible. Unfortunately, due to the intense nature of the intervention, stringent exclusion criterion had to be applied to ensure that those in the program would be capable of performing the exercise properly, and more importantly, to ensure that no harm would arise from exercising intensely. In general, the sample in the current study included those with mild to moderate PD with little to no gait impairments. This greatly limits the Parkinsonian population that was represented within this sample and suitable for this type of exercise. Although BWS can be used to some extent to accommodate the program to those who are more

severe, most participants still found it very difficult to maintain a high cadence during gait. In future, it is recommended that high cadence exercise (RATE condition) be performed on a bicycle, as there are currently mechanical devices that aid in the maintenance of high cadence pedaling, thus making it less effortful to maintain.

Another limitation was that the amount of BWS that each participant received per session was not recorded. This leads to the possibility that the use of BWS in the current study was not equal between groups. Although the data is not available, the RATE group anecdotally used a much greater amount of BWS than the other conditions in an effort to facilitate the maintenance of high cadence walking for an extended period of time. However, since aerobic intensity was very closely matched between groups, it is still likely that groups performed a comparable amount of work. The main concern regarding a mismatch of BWS between groups has to do with the amount of load that is experienced during gait. Since the magnitude of tension sensitive golgi tendon response was a main manipulation of the study, the varying amount of load that would be experienced is a possible confounder. However, reporting the amount of BWS is a difficult task, as the amount is constantly changing due to the slippage of the harnessing system. Constant, systematic adjustments would be required in order to report it accurately, as there is no recorded mean value available from the device.

Another possible limitation has to do with the average heart rate data recorded during the training sessions. Initially, it was proposed that all participants would wear a Polar® heart rate strap for the collection of average heart rate data. Unfortunately, the harness that all participants wore made it impossible for the strap

to stay in place comfortably while providing accurate readings. In substitution for the Polar® heart rate straps, the pulse sensitive handles of the treadmill were used. Unfortunately, there have been no studies published that have examined the accuracy of the heart rate monitors on the Biodex® Gait Trainer treadmill. A separate issue regarding the average heart rate statistic is the use of beta blocking medication that is common in this population. The use of this medication stunts the response of heart rate from exercise, making it challenging to receive accurate heart rate readings. Furthermore, autonomic system dysfunction particularly in the sympathetic division is common in PD populations and may contribute to inaccurate heart rate readings (Micieli, Tosi, Marcheselli & Cavallini, 2003). In future, to ensure that groups are appropriately matched, it is recommended that a measure of how much work is performed is recorded alongside of heart rate. Additionally, a measure of perceived exertion may be another valuable metric, as it can be indicative of heart rate as well as blood lactate levels. (Borg, Hassmen & Lagerstrom, 1987). Alternatively, the generation of an individualized maximum heart rate from a maximal exercise test prior to training would allow for an accurate average heart rate. However, this test requires an extended bout of maximal exercise which is likely not feasible in this population. Issues with heart rate accuracy lead to the possibility that groups did not train at matched aerobic intensities, introducing a possible confounder explaining differences between groups.

Lastly, it is questionable whether or not the somatosensory feedback generated in the MAGNITUDE group was truly representative of the feedback that is generated in the exercise programs that it was meant to emulate. The additional

muscle tension from the ankle weights would only elicit a greater golgi tendon response from the extensors at the hip and knee. The limited stretch response may not have been widespread enough to accurately represent the kind of somatosensory feedback generated by Tai Chi, PD SAFEx and strength training. These types of exercises, especially Tai Chi and PD SAFEx, receive increased somatosensory input from the legs, trunk, and arms. The gap in somatosensory feedback generated in the MAGNITUDE group compared to that of the exercises it was meant to emulate may be a reason why the group did not improve UPDRS-III scores significantly. A possible method to make the somatosensory feedback more widespread would have been to apply weights to the wrists of the participants in the MAGNITUDE group.

Conclusion

Despite the limitations of the study, valuable findings in regards to somatosensory feedback and its therapeutic contributions to exercise were discovered. The high cadence RATE group proved to be the most effective for motor symptom improvement, leading to the conclusion that exercise that generates a high rate of somatosensory feedback likely has a greater therapeutic potential. This finding stresses the importance of considering the somatosensory feedback that exercise generates when developing exercise programs for those with PD. Specifically, those incorporating aerobic exercise into their routines should focus on maintaining a high cadence, whether the exercise is being performed on a bicycle or treadmill. High cadence exercise can easily be adapted on a bicycle by using a lower gear with

minimal resistance, or on treadmill by using BWS. In regards to the actual aerobic

intensity, a Karvonen based MHR (220-age) should be around 60-70%. This is

supported by the current study, as well as the Ridgel et al. forced exercise programs

that this study was inspired by.

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