THE EFFECTS OF BLOOD FLOW RESTRICTION TRAINING ON FUNCTIONAL IMPROVEMENTS IN AN ACTIVE SINGLE SUBJECT WITH PARKINSON DISEASE

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ABSTRACT

Background: Blood flow restriction (BFR) applied during low intensity exercise produces hypertrophy and strength gains equivalent to traditional training. Previous research has shown the positive effects of BFR on younger and older adults. However, the effectiveness of BFR on subjects with Parkinson Disease (PD) has not been investigated.

Hypotheses/Purpose: The purpose of the study was to determine the effects of BFR on a recreationally active person with PD in regards to functional improvements and safety. The hypothesis was that BFR training will demonstrate improvements in motor function, gait and endurance, while decreasing symptoms associated with Restless Leg Syndrome (RLS) in a subject with PD.

Study Design: A single subject, B-A design was used.

Methods: The subject was an active 65-year-old male recreational boxer diagnosed with PD. Baseline data were measured on day one. The intervention (Phase B) consisted of five, two-minute bouts of walking on treadmill with lower extremity BFR cuffs interspersed with 1 minute rest, three times a week for six weeks, at 0 grade incline, and speed of 50 meters/min. The pressure increased from the initial 120 to 160 mmHg at the end of the phase B as per the subject's tolerance. A four-week baseline phase (A) without the BFR intervention followed phase B. The outcome measures which were measured every two weeks over the 10 weeks included: Timed Up and Go Test, 6-Minute Walk Test, 30-Second Chair Stand Test, and the RLS Questionnaire.

Results: All outcome measures steadily improved every two weeks during the six week intervention phase and steadily declined when the intervention was removed during the second four week baseline phase according to visual inspection of the graphed data points.

Conclusion: The subject enjoyed and tolerated the intervention well without any adverse effects. The results were that BFR training can produce functional improvements, reduce restless leg syndrome symptoms and can be safely utilized with a subject with PD who wishes to maintain his ability to remain recreationally active.

Key words: Blood flow restriction, exercise, single-subject; treadmill, walking.

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INTRODUCTION

Parkinson disease (PD) is a debilitating disease of the central nervous system that affects over one million people, over 65 years old in the United States. PD is a chronic disease and is characterized by progressive degeneration of dopaminergic neurons within the substantia nigra.¹ These motor circuits within the basal ganglia are essential for control and coordination of movement. The degeneration of dopaminergic substantia nigra neurons manifests in rigidity, bradykinesia, resting tremors, and impaired postural reflexes.² These primary features of PD result in an overall decrease in motor function, muscle strength, level of endurance, and gait efficiency. Restless legs syndrome (RLS) is another symptom specific to PD, which has a prevalence of up to 52% in patients with PD.³ RLS is a neurological disorder characterized by throbbing, creeping, and other unpleasant sensations in the legs with an uncontrollable, and sometimes overwhelming urge to move them while attempting to sleep.³

Aerobic and strength training exercise has been shown to facilitate the brain to produce growth factors to protect dopamine-producing neurons, in order to preserve function of those persons with PD.⁴ In the mid-1970's, Yoshiaki Sato created KAATSU training in Japan.^{5,6} KAATSU training is also known as Blood Flow Restriction training (BFR). BFR involves the application of an external constricting device to provide mechanical compression of the underlying vasculature.⁶ BFR applied to an active muscle during low intensity exercise, produces muscular hypertrophy and strength gains equivalent to improvements made from traditional high resistance strength training.⁷ The minimum intensity accepted for weight training in order to see strength gains is 65% of a person's one-repetition maximum (1-RM), for that active muscle group during a particular exercise.⁶ Low intensity exercise is either an aerobic exercise or resistance training at 20-30% of a person's 1-RM.⁸ Low intensity resistance training alone has not been shown to provide strength gains.⁶ The physiological mechanisms behind BFR are attributed to the increase in metabolic stress induced by the diminished blood flow, potentially leading to increased muscle fiber recruitment during exercise. It also elevates systemic hormonal production and enhanced

muscle protein synthesis due to an increase in phosphorylation of proteins in muscle signaling.⁹ Low intensity exercise with BFR produces a metabolic overload, with a depletion of phosphocreatine stores and a decrease in the muscle's pH. This is normally present with higher intensity muscle activation in resistance exercise.¹⁰ BFR has been researched and used on subjects during various forms of exercise including walking and isotonic exercises (grip strength and leg extensions). It may be more beneficial to perform low intensity exercise in older adults because it decreases the stress on joints and musculature.¹¹ Therefore, the purpose of using BFR and low intensity exercise is to lower the adverse ramifications involved with high intensity exercise training.

Abe et al. investigated the acute and chronic effects of walk training with BFR training on muscle hypertrophy and strength.¹² Eighteen young, healthy men were split into a BFR group and control group. Training was conducted twice a day, six days per week, for three weeks using five sets of 2-minute bouts (treadmill speed at 50 meters/min), with a one-minute rest between bouts. They reported that the combination of lower extremity musculature blood flow restriction, with slow-walk training, produced significant muscle hypertrophy and strength gains.¹² Abe et al. also studied the effects of six weeks of BFR walk training utilizing older adults, aged 60 to 78, and reported significant improvements in the Timed Up and Go Test (TUG) and the 30-Second Chair Stand Test (30-sCST) without any adverse effects to the training.¹³ The safety of utilizing BFR with subjects with pathology was investigated by Mattar et al.⁹ They concluded that BFR training is safe and effective in improving strength, function, muscle mass, and the quality of life for older patients with polymyositis (PM) and dermatomyositis (DM), which helped verify the safe use of BFR with patients with varied neurological disease states. Similar to PD, these are neurodegenerative diseases, which lead to decreased muscle strength and overall weakness.⁹

The purpose of the study was to determine the effects of BFR on a recreationally active person with PD in regards to functional improvements and safety. Previous research has shown the positive effects of BFR therapy during gait training on healthy young

and older adults. However, to the best of the authors' knowledge, there is no research examining the effects of BFR gait training on persons with PD. The hypothesis was that this type of training will demonstrate improvements in strength, motor function, gait and endurance, while decreasing symptoms associated with RLS in a subject with PD.

METHODS

Subject: This study was organized and conducted at the Adele Smither's Parkinson's Disease Treatment Center at W. Kenneth Riland Academic Health Center of the New York Institute of Technology. Inclusion criteria included: (1) a diagnosis of PD by a licensed neurologist (2) a level 2 or 3 on the Hoehn and Yahr scale (3) ability to ambulate on a treadmill (4) overall good health and recreationally active (5) RLS as verified by the RLS Scale (6) score between 1.0 and 1.2 on the Ankle- Brachial Index Scale for peripheral arterial disease. Exclusion criteria included: (1) history of pulmonary disease, heart disease, pneumonia, hypertension, or stroke (2) fall in the prior six months (3) current or former smoker (4) history of deep vein thrombosis, diabetes, intermittent claudication, peripheral vascular disease and peripheral arterial disease. A subject was identified and informed of the procedures of the study and signed a written consent in order to participate in the study. All procedures of the investigation were conducted in accordance with the Helsinki Declaration of 1975. The consent form and the study were approved by the Institutional Review Board of New York Institute of Technology.

The subject in this single-subject design study was a 65-year-old man (height-172.7 cm, weight-78.6 kg, BMI -26.3) who was diagnosed with PD for the past seven years. His United Parkinson's Disease Rating Motor Function Score (MDS-UPDRS III) was a 32, and he was measured as a 2 on the Hoehn and Yahr scale. His Parkinson's medications included artane, azilect, carbidopa/levodopa, rasagiline, and ropinirole. The subject also took a multivitamin daily and CoQ10. He took his medications three times daily and was compliant. The subject's chief symptoms included: shuffling gait pattern, difficulty getting up from a chair, restless leg discomfort, slowness of movement, and difficulty with balance. The subject

was a recreational boxer and his chief complaint was that he could not exercise at the level he would like to, due to the rigidity of his disease and he felt his activity level had decreased. He has a history of a partial tear of the left medial meniscus and partial tear of the right Achilles tendon which he had treated successfully with physical therapy in August of 2015. His previous orthopedic injuries did not interfere with the BFR training. The subject was instructed to continue with his daily functional activities and typical exercise regime during both B and A phases, which included participation in boxing classes, one hour 2-3 x/week and independent static stretching activities.

Study Design: The study research design was a single subject B-A design, due to subject's time constraints and eagerness to begin the study, the original A-B-A design was changed into a B-A design. The original baseline phase consisted of one session and was concluded after the following outcome measures which reflect functional mobility, gait speed and quality of life were tested. They included the Timed Up and Go Test (TUG), 6-Minute Walk Test (6MWT), RLS Questionnaire, and the 30-Second Chair Stand Test (30-sCST). The B phase included six weeks of intervention and the A phase followed by four weeks of no intervention. The subject was familiarized with the treadmill parameters and the lower extremity BFR cuffs prior to the study. The subject was supervised while walking on an H/P/Cosmos® treadmill (H/P Cosmos Sports & Medical GMBH, Nussdorf, Germany) at his regular duration and intensity, while vital signs and Borg Scale of Perceived Exertion (RPE) were assessed. After the baseline phase, the subject engaged in lower extremity BFR gait training following Abe's protocol for KAATSU Walk Training, for the six-week intervention phase (phase B).^{12,13} The subject engaged in BFR training three times a week in the morning hours on nonconsecutive days, under the supervision of the research group. Vital signs and Rating of Perceived Exertion (RPE) measurements were taken pre-, during, and post intervention. Heart rate was taken manually pre- and post-intervention using the dorsalis pedis pulse, while the subject was seated five minutes before intervention and five minutes after intervention. During the intervention, heart

rate was assessed using the radial pulse with a GARMIN fitness tracker watch (Garmin Ltd., Olathe, KS) on the subject's right wrist, and at the subject's sub-sternal region with a Polar heart rate sensor (Polar Electro Inc., Lake Success, NY). Blood pressure (BP) was taken manually on the subject's left arm. These measurements were taken during a one-minute rest period between each of the two-minute exercise bouts, where the BFR cuffs were deflated and the subject stopped walking. During the study, the subject's vital signs were monitored, as well as episodes of nausea, shortness of breath, or any other signs of discomfort.

Outcome Measures: During the intervention (phase B), the outcomes measures were taken at Day one, and at the end of weeks two, four, and six. The outcome measures were taken again at the end of weeks eight and 10 of the baseline phase (phase A). The TUG measures the time it takes for the subject to stand from a chair without the use of his/her arms, walk three meters, turn around, walk back to the chair and return to the seated position.¹³ The 30-sCST requires the subject to stand and sit from a chair as many times as possible in 30 seconds.¹³ Abe et al. utilized the TUG and 30-sCST as measures of functional abilities.¹³ The 6MWT measures the distance the subject can walk over a total of six minutes on a hard, flat surface. The goal for the subject was to walk as far as possible in six minutes. The subject was allowed to self-pace and rest as needed as they traverse back and forth along a marked walkway.¹⁴ The RLS Rating Scale consists of 10 questions that assist in measuring the effects of restless leg syndrome on the subject's quality of life and has been validated by Walters et al.¹⁵

Intervention: The intervention (phase B) followed Abe's BFR walk-training protocol, which consisted of five, two-minute bouts of treadmill walking with a one minute rest between each trial.^{12,13} The subject walked on the treadmill at zero grade incline and a speed of 50 meters/min throughout the intervention. The subject warmed-up each session by walking for two minutes on the treadmill without BFR. The lower extremity thigh blood pressure cuffs (Hokanson, Bellevue, WA) for the BFR training were introduced and placed on each upper thigh after the warm-up period and pumped to the designated pressure each

time. The intervention phase began with the lower extremity blood pressure cuff pumped to a pressure of 120 mmHg. This pressure was chosen because it was the participant's systolic blood pressure, which is in alignment with the guidelines in Abe et al.¹² The cuff pressure was incrementally increased by 20 mmHg every two weeks, as per the subject's tolerance level. As this intervention is the first of its kind for the Parkinson's population, associated impairments of PD were highly considered when determining the appropriate starting pressure of the cuff. The final pressure reached 160 mmHg by the end of week six. The same outcome measures that were used during the intervention (phase B), were measured throughout the post-intervention (phase A). Post-intervention data collection took place over four weeks after the intervention was concluded. The study was completed at week 10.

Statistical Analysis: Visual analysis was utilized to analyze the data because is used most often and is intuitively meaningful according to Portney et al.¹⁶ Comparisons were made between the two adjacent phases based on these three characteristics of the data: level, trend, and slope.¹⁶

RESULTS

Table 1 summarizes all the outcome measure scores from week zero to the end of week 10. Table 2 contains weekly values of average heart rate (HR), peak blood pressure (BP), and peak RPE from the beginning of the study, to the end of phase B, the intervention phase during week six. Figures 1 through 4 illustrate the results of the outcome measures from the beginning of the study to the end at week 10. Figure 1 demonstrates the changes in TUG scores. The level, trend, and slope of Figure 1 is decelerating in phase B representing an improvement in the TUG time while phase A illustrates an accelerating level, trend and slope showing a gradual increase in the TUG time. Figure 1 also displays the fastest time of six seconds, observed after weeks four, six, and eight. Figure 2 presents the changes in 6MWT distance. The level, trend, and slope of Figure 2 is accelerating in phase B representing an improvement in the 6MWT distance time while phase A depicts an decelerating level, trend and slope showing a gradual decrease in the 6MWT distance.

Table 1. Outcome measure scores for baseline, B, and A phase.

Outcome Measure	Week 0	B-Week 2	B-Week 4	B-Week 6	A-Week 8	A- Week 10
30-sCST (repetitions)	14	17	19	20	20	17
6MWT (feet)	1372.45	1771.2	1899.76	1838.96	1636.51	1574.80
TUG (seconds)	9	7	6	6	6	8
RLS	15 moderate	8 mild	8 mild	6 mild	6 mild	10 mild
BFR Pressure	Baseline	Intervention (120 mmHg)	Intervention (140 mmHg)	End of Intervention (160 mmHg)	Post Intervention	Post Intervention

30-sCST= 30-Second Chair Stand Test; 6MWT= 6-Minute Walk Test; TUG= Timed Up and Go Test; RLS= Restless Leg Syndrome Questionnaire; BFR= Blood Flow Restriction.

Table 2. Weekly values for average HR, peak BP and peak RPE.

	HR (Mean $\pm$ SD)	Peak Weekly BP	Peak RPE
Week 1	68.47 $\pm$ 1.71	158/90mmHg	9
Week 2	67.23 $\pm$ 1.71	148/78mmHg	7
Week 3	72.99 $\pm$ 1.71	142/72mmHg	11
Week 4	69.65 $\pm$ 1.71	146/78mmHg	11
Week 5	76.64 $\pm$ 1.71	128/74mmHg	10
Week 6	73.27 $\pm$ 1.71	150/74mmHg	9

HR, Heart Rate; BP, Blood Pressure; RPE, Rating of Perceived Exertion.

Figure 1. Timed Up and Go Test during each phase. First data point represents baseline score.

Figure 2 also demonstrates the furthest distance walked was 1899.76 feet, observed after week four. Figure 3 summarizes the 30-sCST results. The level, trend, and slope of Figure 3 is accelerating in phase B representing an improvement in the 30-sCST results while phase A depicts a decelerating level, trend and slope showing a gradual decrease in the 30-sCST results. Figure 3 also displays the highest score of 20 repetitions observed after week six and eight. Figure 4 represents the changes in the RLS questionnaire. The level, trend, and slope of Figure 4 is decelerating in phase B depicting an improvement in the RLS symptoms while phase A illustrates an accelerating level, trend and slope representing

a gradual increase in the RLS symptoms. Figure 4 also displays the lowest score of 6 (mild symptoms), which was measured after weeks six and eight.

DISCUSSION

The purpose of this study was to investigate the effects and safety of lower extremity BFR training on a recreationally active person with PD. BFR training during treadmill walking has previously demonstrated to improve muscle strength and functional abilities in healthy older adults.¹³ This was the

Figure 2. 6- Minute Walk Test during each phase. First data point represents baseline distance.

Figure 4. Restless Leg Syndrome (RLS) Questionnaire scores during each phase. First data point representing baseline value.

Figure 3. 30-Second Chair Stand Test during each phase. First data point represents baseline value.

first study to investigate the safety of utilizing BFR training on a recreationally active person with PD according to a thorough review of the literature. The subject did not experience any adverse effects and he repeatedly stated he enjoyed the training. This is in agreement with Abe et al.¹³ and Matter et al.⁹ who also did not experience any adverse effects with healthy older adults and subjects with a pathology

during BFR training respectively. Visual analysis of the data demonstrated that the subject's scores on all outcome measures improved throughout the six-week intervention phase (B) and regressed after four weeks of the post-intervention phase (A).

The improvement in the subject's RLS from moderate to mild was a significant finding, which demonstrated that the subject experienced some relief from those symptoms due to BFR training. RLS was one of his major complaints, interfering with his quality of sleep and life as verified by the RLS questionnaire. He had been taking ropinirole for the relief of his RLS. His score at baseline was a 15 (moderate symptoms), which according to Klingehoefer et al. is the score that requires pharmacological treatment.¹⁷ Following six weeks of BFR his score decreased to a 6 (mild symptoms), while his score did increase up to an 8 (mild symptoms) after the BFR phase. The addition of the BFR with ropinirole appears to be effective with reducing his RLS symptoms. The subject was very pleased with the improvement with his RLS symptoms. Massaging or rubbing of the affected limbs and physical exercise may benefit RLS according to Klingehoefer et al.¹⁷ Since he was physically active and maintained his usual exercise activities besides the pharmacological treatment of ropinirole, the addition of the BFR may have contributed to the

reduction in his symptoms. The physiological mechanism behind providing relief of his RLS symptoms may have been the pressure on the affected limbs provided by the BFR training. Further research into this phenomenon is warranted. Although the subject stated his legs were fatigued from the intervention, it did not have any impact on his boxing routine. The subject reported that he felt his performance improved in boxing.

The improvements in the TUG and 30-sCST were similar to the results of Abe et al.¹³ These results suggest that BFR training generates beneficial outcomes in the areas tested with a positive retention period of approximately two weeks. The TUG is highly correlated with functional mobility, gait speed and falls in older adults and has high test-retest reliability in the PD population.¹⁸ His TUG time decreased from 9.0 seconds to 6.0 seconds following BFR training. Both times were below the 11.5 cut off score for to discriminate between patients with PD who have fallen and not fallen.¹⁸ His improvement of three seconds in the TUG was close to the minimal detectable change of 3.5 seconds for people with PD as reported by Huang et al.¹⁹ The 30-sCST is useful for detecting changes in functional gait and mobility in PD patients according to Petersen et al.²⁰ His 30-sCST improved from a 14 to a high of 20 repetitions after six weeks of BFR training and declined to 17 after the intervention was stopped. His initial score of 14 was within the norm and his improvement to 20 surpassed the minimal detectable difference of 3.3 repetitions as reported by Petersen et al.²⁰ The 6MWT provides a measure of walking capacity in PD patients.¹⁴ Our subject improved from an initial distance of 1372.45 ft. to 1899.76 ft. after four weeks of BFR training before decreasing to 1574.80 ft. four weeks after the intervention ended. His initial distance was below the mean of 1790.03 ft. for a PD patient with a Hoehn and Yahr score of 2 as reported by Shenkman et al.²¹

Resistance training and endurance training have been shown to improve neuromuscular function, bradykinesia, and postural instability in patients with PD.⁹ The improvements in cardiorespiratory capacity and endurance is observed to enhance the efficacy of levodopa, which improves gait abnormalities and motor control as seen with persons with

PD.^{22,23} Archer et al.²⁴ have shown that moderate to high-intensity training (65-80% of 1-RM) results in greater quality of life, less fatigue and disorder severity in patients with PD. The results of this study may add BFR training to the available exercise options for the PD population.

The strengths of the study include: subject compliance, consistency of the intervention schedule per week, and the functional outcome measures tested are widely used by rehabilitation specialists for people with PD. The study had several limitations: which include the inherent flaw of the single subject design of its limited external validity or lack of generalizability.¹⁶ The other limitations include the one day of baseline data because the subject wanted to start the intervention phase as soon as possible because of his time constraints and his eagerness to start the intervention which changed the design from a A-B-A to a B-A design. The length of the phases did not allow for sufficient data points to calculate a correlation line, utilize the two standard deviation band method or the C-statistic.¹⁶ Despite these limitations, the positive results on the effects of BFR training with a subject with PD support the need for continued research for this type of exercise. Future studies should replicate this single subject design study with longer phases that would allow for more data points. The use of randomized clinical trials is also warranted that will provide the strongest evidence for the effectiveness of BFR training with the PD population.

CONCLUSIONS

This was the first study to observe the effects of BFR walk training as an effective and safe intervention for a recreationally active person with PD. BFR treadmill training, as a low-intensity intervention, was tolerated well and without any adverse effects. The subject demonstrated improvements in the TUG, 6MWT, RLS, and the 30sCST over the six-week intervention phase with regression noted four weeks after the intervention concluded. BFR treadmill training can be safely added to the exercise regime for a recreationally active person with PD who wishes to maintain his ability to remain recreationally active. Future research is warranted on the use of BFR training as an effective intervention to reduce the debilitating effects of PD.

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