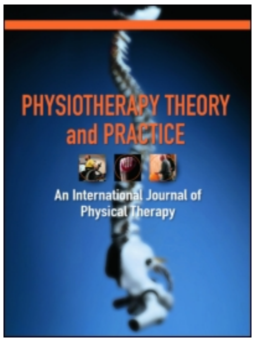

Physiotherapy Theory and Practice
An International Journal of Physical Therapy

ISSN: 0959-3985 (Print) 1532-5040 (Online) Journal homepage: http://www.tandfonline.com/loi/iptp20

Effects of a low-resistance, interval bicycling intervention in Parkinson's Disease

Mehmet Uygur , Maria Bellumori & Christopher A Knight

PHYSIOTHERAPY THEORY AND PRACTICE
https://doi.org/10.1080/09593985.2017.1359868

Taylor & Francis
Taylor & Francis Group

Check for updates

Effects of a low-resistance, interval bicycling intervention in Parkinson's Disease

Mehmet Uygur, PhD [a], Maria Bellumori, PhD[b], and Christopher A Knight, PhD[c]

[a]Department of Health and Exercise Science, Rowan University, Glassboro, NJ, USA; [b]Kinesiology Department, California State University, Monterey Bay, CA, USA; [c]Department of Kinesiology and Applied Physiology, University of Delaware, Newark, DE, USA

ABSTRACT

Previous studies have shown that people with Parkinson's disease (PD) benefit from a variety of exercise modalities with respect to symptom management and function. Among the possible exercise modalities, speedwork has been identified as a promising strategy, with direct implications for the rate and amplitude of nervous system involvement. Considering that previous speed-based exercise for PD has often been equipment, personnel and/or facility dependent, and often time intensive, our purpose was to develop a population-specific exercise program that could be self-administered with equipment that is readily found in fitness centers or perhaps the home. Fourteen individuals with PD (Hoehn-Yahr (H-Y) stage of 3.0 or less) participated in twelve 30-min sessions of low-resistance interval training on a stationary recumbent bicycle. Motor examination section of the Unified Parkinson's Disease Rating Scale (UPDRS), 10-meter walk (10mW), timed-up-and-go (TUG), functional reach, four-square step test (4SST), nine-hole peg test (9HPT) and simple reaction time scores all exhibited significant improvements ($p < 0.05$). These results add further support to the practice of speedwork for people with PD and outline a population-amenable program with high feasibility.

ARTICLE HISTORY
Received 27 May 2016
Revised 6 October 2016
Accepted 22 November 2016

KEYWORDS
Exercise; motor function; neurological diseases; quickness; symptom management mobility

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder and the number of individuals diagnosed with PD is expected to increase by two-fold over the next two decades (Dorsey et al. 2007). The most common motor symptoms of PD include bradykinesia (i.e. reductions in the speed and amplitude of movement), rigidity, postural instability and tremor (Berardelli et al. 2001). Although there is no known cure for PD, pharmaceutical and neurosurgical treatment methods have been used for symptom management. While these methods are beneficial, they are known to lose effectiveness over time and have severe side effects (e.g. Levodopa-induced dyskinesia or impulse control disorder). As an alternative or supplement to medical treatment, exercise has recently been evaluated as a neurorehabilitative tool that could slow down the disease progression and improve PD-related symptoms (Fisher et al. 2004).

Various exercise routines aimed toward improving strength (Corcos et al. 2013; Dibble et al. 2009), aerobic capacity (Bergen et al. 2002), balance (Herman et al. 2007; Li et al. 2012; Rose et al. 2013) and speed (Herman et al. 2007; Rose et al. 2013) have been shown to be effective in the improvement of PD-related symptoms. Among these routines, speed (or quickness) training has recently been identified as a valuable training method addressing bradykinesia. PD patients who accomplished incremental speed-dependent treadmill training showed improvement in gait-related parameters (Cakit et al. 2007; Herman et al. 2007), disease severity (as assessed by the motor section of Unified Parkinson's Disease Rating Scale (UPDRS-III)) (Herman et al. 2007) and postural stability (Cakit et al. 2007). Similarly, both manual dexterity and motor functions were improved in a study involving PD patients pedaling on a tandem bike with an assistant pedaling in front to augment the pedaling rate (Ridgel et al. 2012, 2009).

The high-speed training modes used in the previous research usually required either a clinical setting with a harness system (Cakit et al. 2007; Herman et al. 2007), an able-bodied cycling partner on a tandem bike (Alberts et al. 2016; Beall et al. 2013; Ridgel et al. 2009) or a motorized bicycle (Ridgel et al. 2012). However, these factors affect the cost of and access to this type of exercise and hinder its use in home or in community-based settings. Considering the promising results for "speedwork" in PD, there is a need for speed training that is more accessible and feasible as compared to existing training modalities. Therefore, we designed a high-speed–low-resistance (HS-LR) cycling program that could be self-administered for individuals at Hoehn-Yahr (H-Y) stage three or less (Uygur et al. 2015). An exercise session consists of 30 min of

CONTACT Mehmet Uygur, PhD uygurm@rowan.edu Department of Health and Exercise Science, Rowan University, Glassboro, NJ 08028, USA.

pedaling at a preferred comfortable speed including 20 bouts of 15-s high-speed pedaling, nested within the middle 20 min of exercise. We preferred to use a stationary recumbent bicycle to reduce the risk of falls compared with exercise modes such as treadmill or upright cycle. The resistance of the bike was set at the lowest possible level in order to keep musculoskeletal loading minimal.

The aim of this study was to evaluate the effects of a six-week HS-LR recumbent bicycling on the physical and cognitive functional performance in people with PD. We hypothesized that the disease severity along with mobility and balance-related functions would improve after six weeks of HS-LR training. In addition, since this type of training is expected to elicit neural adaptations through increasing neurotropic proteins and the neurotransmitters (Alberts et al. 2011), we also hypothesized that the improvements would be present in dexterity and cognition-related function.

Methods

Participants

Fourteen people with idiopathic PD were recruited through local PD support groups to participate in the study (Table 1). The whole data collection was completed in 11 months and 16 days. The participants read and signed an institutionally approved informed consent document. A physician's clearance for exercise was provided if participants answered yes to one or more questions in the physical activity readiness questionnaire (Adams 1999), or if they were 75 years old or older. Exclusion criteria included: recent (< 3 months) myocardial infarction; muscle or joint conditions that could be worsened by the exercise or testing; insulin-dependent diabetes; inability to communicate with investigators; and inability to walk without assistance from another person but may use a cane or walker. None of the subjects who participated in the study required any assistance during walking. Subjects were instructed not to change their medications during the study. We valued testing in the "on-meds" condition because it represented the actual conditions under which PD patients would exercise. Participants completed all training sessions and assessments at the same time of the day to minimize the effects of timing of medication on the motor function.

Table 1. Description of study participants.

Descriptive (mean (SD))	
Age (y)	62.64 (8.81)
Gender (men/women)	10/4
Height (cm)	176.9 (12.12)
Weight (kg)	73.73 (14.28)
Disease duration (months)	40.14 (28.91)
Medication (Levodopa equivalent daily dose in mg)	
Mean (SD)	883.71 (645.92)
Range (min - max)	200–2400

Pre- and post-training assessments

Pre- and post-assessments were completed within three days before the start and after completion of six weeks of HS-LR intervention, respectively. In each assessment session, participants were asked to practice the functional tests until they felt comfortable performing the task. The order of functional tests was randomized. Subjects self-reported their "more affected side", which was then tested in unilateral functional tests. Unless otherwise noted, each functional test was performed three times within both sessions and 30-s rest time was allowed between the trials. In all of the functional tests, subjects were instructed to perform at their best or fastest possible level while being safe. Two experienced researchers timed the tests (manually), and the average value of the two researchers was recorded for each trial. Since the subjects were instructed to perform at their maximum ability, we used the trials with the best performance in further analyses. Pre- and post-assessments included a clinical assessment, questionnaires and functional tests.

Clinical assessment

An experienced neurologist conducted the 14-item motor examination of UPDRS (UPDRS-III), and the scores ranged from 0 to 56 (Brusse et al. 2005; Fahn and Elton 1987; Li et al. 2012).

Questionnaires

Participants completed the Activities-specific Balance Confidence (ABC), which has been used as a subjective measure of balance confidence in performing various ambulatory activities (Mak and Pang 2009) and the Short Form-36 Health Survey (SF-36) that assesses a person's perceived status related to physical, social, mental and emotional health (Ware and Sherbourne 1992).

Functional tests

Participants performed the following tests: 10-meter walk test (10mW) measures the time and number of steps (Steps) taken by an individual to walk the middle 6 meters of the 10-meter walk (Lam et al. 2010). Timed-up-and-go test (TUG) measures the time taken by an individual to stand up from a chair, walk a distance of 3 meters, turn, walk back to the chair and sit down (Podsiadlo and

Richardson 1991). Both TUG and 10mW tests are tests of functional mobility. The four-square step test (4SST) is a dynamic balance test that requires participants to rapidly change direction while stepping forward, backward and sideways over a low obstacle (Duncan and Earhart 2013). Functional reach test (FRT) is a static balance test that measures the maximum distance one can reach in the forward direction while his/her base of support remains fixed on the ground (Duncan et al. 1990). The nine-hole peg test (9HPT) is a test of dexterity and upper extremity function in which subjects were required to place and remove nine pegs in a peg board (Earhart et al. 2011). Cognitive function was assessed by using simple (SRT) and choice (CRT) reaction time tests (Kutukcu et al. 1999). In SRT, seated subjects placed the index finger of their more affected side on a sensor on the reaction time board (Lafayette Instrument Co, Lafayette, IN) with an indicator light directly above it. The subjects were asked to remove their index finger as fast as possible from the sensor as soon as the light was lit. The time from the onset of the light to the removal of the finger was recorded as the SRT. For CRT, subjects placed their index and middle fingers of both left and right hands on four sensors. Relative to the midline of the reaction time board, two sensors were located to the left and the other two were located to the right. Each sensor had a corresponding light. Subjects were asked to lift the finger corresponding to the light that was illuminated as fast as possible while keeping the other fingers on the sensors. The time between onset of the light and removal of the finger was recorded. Grip Strength (Grip) was a test of strength that was found to be highly correlated to knee extensor strength (Bohannon et al. 2012) and it was measured as subjects squeezed a handheld dynamometer (Model 78010) as hard as possible.

Exercise intervention

Participants were trained on a stationary recumbent bike under the supervision of an experienced trainer two days a week for six weeks (12 sessions). The time of day was kept the same across the six weeks and training days were separated by at least two days. Each training session lasted 30 min. For the first and last five min of training, participants were instructed to pedal at a preferred rate to warm up and cool down, respectively. Preferred rate was instructed as the rate at which they could pedal for at least an hour without getting tired. After a 5-min warm-up, participants were asked to pedal as fast as possible for the first 15 s and slow down to their preferred rate for the remaining 45 s of every minute for 20 min. Heart rate was monitored throughout the training, and a longer recovery was given between the high-speed bouts if their heart rate reached 80% of their maximum heart rate (maximum HR = 220-age). The resistance of the recumbent bike was set at the lowest possible level at which subjects typically produced less than 100 Watts of power at their fastest pedaling rate. The maximum rate during the 15 s fast pedaling and the average rate during the preferred pedaling were recorded manually and they were averaged in each session to represent fast and preferred rates. A subjective rating of perceived exertion (RPE) was collected by using the BORG scale (Borg 1982).

Statistical analysis

Two-tailed paired sample t-tests were used to compare the measurements taken before and after six weeks of the HS-LR training. Test-retest reliability of each test was quantified by using ICC (2,1). Together with the standard deviation values obtained from the pretesting results, the ICC values were used to calculate the standard error of the measurement (SEM = sd x $\sqrt{(1\text{-ICC})}$). We also calculated the minimum detectable change at the 95% confidence level (MDC_{95}) (MDC_{95} = SEM x 1.96 x $\sqrt{2}$) (Portney and Watkins 2008). To analyze the improvements in pedaling rate, we divided the six-week training (or 12 training sessions) into three blocks of two weeks (or four training sessions). This decision was made *a posteriori* after visually observing the trend obtained from pedaling rate data. Comparisons among blocks were made by using two repeated measures of analysis of variance (ANOVAs) separately for the preferred and fast pedaling rates. All statistical analyses were performed in SPSS (version 22, IBM, SPSS Statistics, Armonk, NY) and the p-value was set at 0.05.

Results

All subjects completed the study with no adverse effects. The average fast pedaling cadence changed across the three blocks ($F (1.24, 12.36) = 12.57$, $p < 0.01$), with a faster pedaling rate in the second and third blocks compared with the first block ($p < 0.05$). Fast pedaling rate in the second and third blocks was not different ($p > 0.05$). There were no differences in the preferred pedaling rate across the three blocks ($F (2, 20) = 0.13$, $p > 0.05$) (Figure 1).

Table 2 compares the assessments completed before and after six weeks of HS-LR training. Compared to pre-assessments, disease severity (i.e. UPDRS-III; $p = 0.001$, UPDRS_Brady; $p < 0.05$), the tests of functional mobility (i.e. 10mW; $p = 0.001$, Steps; $p < 0.001$, and TUG; $p < 0.001$) and balance (i.e. FRT; $p < 0.01$, and 4SST; $p < 0.01$) improved after six weeks of HS-LR training. Similar to improvements in tests of balance, the ABC scores also had a trend toward improvement after training ($t = 1.95$, $p = 0.073$). Regarding the cognitive function measures, SRT showed 13.1% improvement ($p < 0.05$),

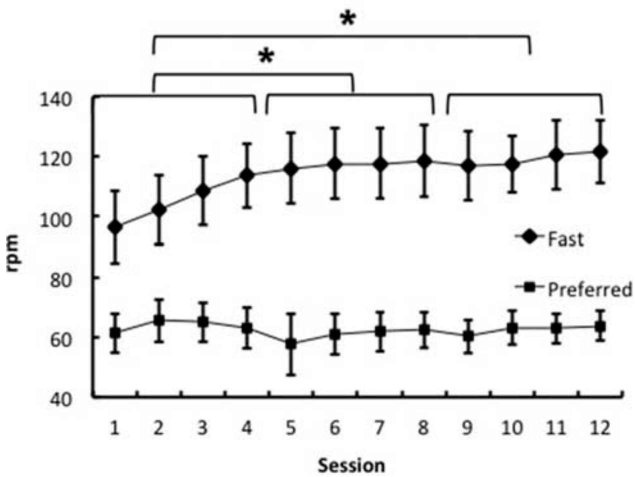

Figure 1. Progression of fast pedaling rate (rpm) from session 1 to session 12. * denotes significant improvements in fast rpm during first 4 sessions ($p < 0.05$).

while there was a nonsignificant trend toward improvement (12.6%) in CRT (t = 2.06, $p = 0.06$).

Table 3 presents the SEM, ICC and MDC_{95} for each selected measure. MDC% ranged between 12.92 and 44.65 for functional tests and 11.73 and 50.02 for clinical assessments, while SEM% ranged between 4.66 and 16.11 for functional tests and 4.23 and 18.04 for clinical assessments.

Discussion

This study was designed to evaluate the effects of six weeks of HS-LR recumbent cycling on the disease severity and functional and cognitive performance in people with mild to moderate PD (H-Y scale ≤3). We found that six weeks of HS-LR training was effective in improving physical and cognitive function in people with mild to moderate PD. Specifically, significant decreases were observed in disease severity as well as improvements in the tests that assess mobility, static and dynamic balance, dexterity and cognitive function after completion of “speedwork” training.

The average RPE of 13.72 indicates that the participants found the high-speed interval training to be

Table 2. Effects of high-speed–low-resistance (HS-LR) intervention on clinical and functional tests.

	Pre		Post			Statistics	
	Mean	SD	Mean	SD	% Change	t-Value	pValue
UPDRS-III	17.53	6.43	14.00	5.62	−20.14	4.35	**< 0.001**
UPDRS_Brady	7.19	2.52	6.08	1.77	−15.01	2.19	**0.049**
H&Y Scale	2.54	0.61	2.38	0.63	−6.24	0.77	0.455
ABC	79.95	16.10	88.59	10.80	10.81	−1.95	0.073
SF36	58.15	23.46	62.00	22.09	6.62	−1.55	0.147
10mW (s)	3.42	0.88	2.88	0.66	−15.59	5.51	**< 0.001**
Steps (#)	8.10	1.21	7.08	0.95	−12.59	6.87	**< 0.001**
TUG (s)	7.29	1.60	6.19	1.51	−15.06	6.59	**< 0.001**
FRT (cm)	27.12	4.95	33.28	6.10	22.71	−3.98	**0.002**
4SST (s)	9.11	4.51	7.56	3.08	−17.04	3.07	**0.009**
9HPT (s)	25.38	5.95	23.36	5.98	−7.96	3.61	**0.003**
SRT (s)	0.285	0.077	0.247	0.055	−13.15	2.62	**0.021**
CRT (s)	0.412	0.081	0.360	0.071	−12.55	2.06	0.060
Grip (kg)	32.71	10.3	32.43	9.9	−0.87	0.18	0.872

UPDRS-III: motor section of the Unified Parkinson’s Disease Rating Scale; UPDRS_Brady: UPDRS bradykinesia subsection (total score of the items #23 (finger taps), 24 (hand movements), 25 (rapid alternating movements of hands, 26 (leg agility), and 31 (body bradykinesia and hypokinesia); H&Y: Hoehn-Yarn; ABC: Activities-Specific Balance Confidence; SF36: Short Form-36 Health Survey; 10mW: 10-meter Walk Test; Steps: Steps taken in 10mW; TUG: Timed-Up-and-Go; FRT: Functional Reach Test; 4SST: Four-Square Step Test; 9HPT: Nine-Hole Peg Test; SRT: Simple Reaction Time; CRT: Choice Reaction Time; Grip: Grip Strength

Table 3. Standard error of the measure (SEM), SEM as the percent of pre-intervention (SEM%), intra-class correlation coefficient ($ICC_{(2,1)}$) with 95% confidence interval, minimal detectable change ($MDC_{0.95}$) and minimum detectable change as percentage of pre-intervention condition (MDC%).

Outcome Measure	SEM	SEM %	$ICC_{(2,1)}$	$MDC_{0.95}$	MDC%
UPDRS-III *	1.96	11.16	0.90 (0.69–0.97)	5.42	30.94
UPDRS_Brady *	1.30	18.04	0.65 (0.11–0.88)	3.60	50.02
H&Y Scale	0.11	4.23	0.97 (0.90–0.99)	0.30	11.73
SF36	6.32	10.86	0.92 (0.77–0.98)	17.50	30.10
ABC	11.70	14.63	0.27 (−0.28–0.69)	32.42	40.55
10mW (s) *	0.26	7.50	0.89 (0.70–0.96)	0.71	20.79
Steps (#) *	0.38	4.66	0.88 (0.65–0.96)	1.05	12.92
TUG (s) *	0.44	6.04	0.92 (0.77–0.97)	1.22	16.74
FRT (cm) *	4.02	14.81	0.48 (−0.75–0.81)	11.13	41.05
4SST (s) *	1.34	14.70	0.88 (0.67–0.96)	3.71	40.75
9HPT (s) *	1.49	5.85	0.94 (0.82–0.98)	4.12	16.23
SRT (s) *	0.038	13.29	0.68 (0.26–0.89)	0.10	36.83
CRT (s)	0.066	16.11	0.24 (−0.32–0.67)	0.18	44.65
Grip (kg)	4.19	12.79	0.83 (0.55–0.94)	11.60	35.46

*Denotes outcome measures with significant improvements after intervention.

"somewhat hard". All subjects completed all 12 training sessions and there was no self-reported adverse effect of training. Moreover, subjects improved their fast pedaling cadence within the first two weeks, and maintained their improved fast cadence for the remaining four weeks of the training program (Figure 1). Altogether, these findings indicate that the HS-LR training was well-received by study participants. The brevity and feasibility of the proposed training method suggest the inclusion of this training program into the current standard exercise recommendations that includes cardiorespiratory fitness, flexibility and strength (Carr and Shepherd 1998).

In line with our interest in improving the speed of movement in people with PD through HS-LR training, in all of the selected functional tests, participants were instructed to perform as fast as possible and we reported the best performance. We assessed functional mobility through the standard clinical tests including 10mW and TUG. Regarding the 10mW test, results indicate that both walking speed and step length increased after HS-LR training. Together with improvements observed in the bradykinesia subsection of UPDRS-III, results indicate the efficacy of HS-LR training in counteracting the PD-related decrease in the speed and amplitude of a movement. Similar improvements were also seen in TUG. One should note that, unlike 10mW, TUG consists of three main components that include walking, turning, and standing up and sitting down on a chair (Wall et al. 2000). Although we did not measure the individual times to complete each component within TUG, increased walking speed (i.e. 10mW) and dynamic balance (i.e. 4SST) suggest that the improvement in TUG was mainly due to the improvements in walking and dynamic balance components rather than the strength component. Similar improvements in functional mobility were also reported in the previous research that studied the effects of high-speed gait training on a treadmill in people with PD (Cakit et al. 2007; Herman et al. 2007; Miyai et al. 2000, 2002). Although the treadmill training modalities have shown promising results in PD-related symptoms involving mobility, cautionary remarks have been made about how commonalities among interventions and testing procedures may limit the potential for mechanistic conclusions involving supraspinal centers (Ridgel et al. 2009). While some tests used in our study were not anatomically independent of our HS-LR training, the overall improvements seen in both the upper and lower extremity tests support central adaptations rather than a simple practice effect.

The performance of both static (e.g. FRT) and dynamic balance (i.e. 4SST) improved after the completion of our HS-LR training. Moreover, this improvement was also partly supported by the nonsignificant ($p = 0.07$) positive trend shown in the subjective balance confidence score (i.e. ABC), which is a tool that predicts future falls in PD (Mak and Pang 2009). Overall improvements in balance indicate that HS-LR training could also be an effective strategy for fall prevention in PD. This improvement is quite promising when one considers the high incidence rate (Li et al. 2012) and detrimental consequences of falls in people with PD.

Results of our study indicated that people with PD improved their dexterity and simple reaction time after completing a six-week HS-LR training. Similar to our findings, Ridgel et al. (2009) showed an improvement in manual dexterity in PD patients who are forced assisted by a trainer co-pedaling on a tandem bike to cycle at a rate that is 30% higher than their preferred rate for a period of eight weeks. Although the present reaction time measures do not point specifically to improved executive processing or information-processing rates, they are consistent with the cognitive improvements observed after a single session of high-speed passive cycling (Ridgel et al. 2011). Improvements seen in the dexterity and cognitive functions after completing a lower-extremity training program could indicate the presence of the higher-level neural adaptations following speed-based exercise.

The percent changes of all of the selected outcome measures that improved significantly after the completion of HS-LR training were smaller than the MDC% estimates, but larger than the SEM% estimates (the only exception was UPDRS_Brady: 15.01% improvement, SEM% = 18.04). Therefore, we question the use of MDC% in clinical and rehabilitation research regarding its conservative nature and suggest the use of SEM% as a more accurate estimate of the observed changes that were determined to be significant.

Although the exact mechanisms responsible for improved disease severity and physical and cognitive function after completing the HS-LR training are unknown, we would like to speculate on several neural factors that could explain improvements in those functions. It has been demonstrated that PD patients have impaired peripheral afferent feedback (Abbruzzese and Berardelli 2003; Klockgether et al. 1995), which affects corticomotor excitability (Coxon et al. 2005). The repetitive nature of our HS-LR training might have resulted in an increase either in the activity of proprioceptors or in the efficiency of utilizing the feedback information from those proprioceptors. This increase in afferent information could, in turn, improve the corticomotor excitability in PD (Christensen et al. 2000; Fisher et al. 2008). Recent findings also suggest increased activation within the cortical areas of PD patients after completing one session of "forced-exercise" during which voluntary cycling cadence of PD patients was augmented by an abled body on a tandem bicycle (Alberts et al. 2011, 2016; Beall et al. 2013). This facilitation could be amplified even more with the interval nature of our training program, which required switching the pedaling pace between high and low rates (Armstrong 1988). Finally, animal models of PD have shown that high-intensity exercise facilitates neuroplasticity through increasing the synaptic availability of dopamine (Petzinger et al. 2007) and improving the dopamine receptor activity within the basal ganglia (Vuckovic et al. 2010). Those improvements would elicit a higher efficiency in neurotransmission and, therefore, improve motor function (Petzinger et al. 2010).

Study limitations

There are few limitations to consider: (1) the results of this study could only be generalized to people with PD who are at the H-Y stage of 3.0 or less; (2) we did not include a time control since previous research has shown stable motor function within similar intervention periods (Lauhoff et al. 2013; Rose et al. 2013) and across a two-week period within our own laboratory (Uygur et al. 2015); moreover, given the progressive nature of the disease, the PD-related symptoms could only get worse without any intervention; (3) although most of the improvements after six weeks of HS-LR training were substantial, we do not know how long these improvements would last since we did not have a follow-up assessment; however, considering the progressive nature of PD and what is known about aging and inactivity, one could assume that people with PD would not continue to improve or maintain function without adherence to favorable activity and exercise behaviors; (4) one can claim that the improvements in the functional tasks could be attributed to the mere exposure to functional tests; however, prior work from our laboratory has shown that the performance of the PD patients for the assessed functional tasks did not change over the course of three different days (Uygur et al. 2015); and (5) finally, one can argue that the improvements seen after completing HS-LR training could be due to a placebo effect of training. Therefore, there is a need for a study that compares HS-LR training to a more traditional cycling training (e.g. moderate intensity, continuous cycling) to distinguish the effect of HS-LR training from the placebo effect of any type of training.

Conclusion

The results of the present study suggest that HS-LR recumbent cycling is a useful training modality to improve disease severity, functional mobility, balance, cognitive and upper extremity function in people with mild to moderate PD. Future neurophysiological studies are needed to understand the neural adaptations associated with HS-LR training. There is also a need for future studies that could be designed to assess the minimum required dose of HS-LR. This could be important when one considers the time requirements of a comprehensive exercise program that includes strength, endurance, balance and flexibility.

Acknowledgment

The authors acknowledge Dr. S. Radosavljevic Jaric for clinical evaluation of PD patients.

Funding

This project was supported by the Delaware INBRE program, with a grant from the National Institute of General Medical Sciences - NIGMS (8 P20 GM103446-13) from the National Institutes of Health and financial support from Shake It Off, Inc. (West Chester, PA).

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

ORCID

Mehmet Uygur http://orcid.org/0000-0001-6152-6995

References

Abbruzzese G, Berardelli A. 2003. Sensorimotor integration in movement disorders. Move Disord. 18:231–40. doi:10.1002/(ISSN)1531-8257.

Adams R. 1999. Revised physical activity readiness questionnaire. Can Fam Physician. 45:1004–05.

Alberts JL, Linder SM, Penko AL, Lowe MJ, Phillips M. 2011. It is not about the bike, it is about the pedaling: Forced exercise and Parkinson's disease. Exerc Sport Sci Rev. 39:177–86.

Alberts JL, Phillips M, Lowe MJ, Frankemolle A, Thota A, Beall EB, Feldman M, Ahmed A, Ridgel AL. 2016. Cortical and motor responses to acute forced exercise in Parkinson's disease. Parkinsonism Relat Disord. 24:56–62. doi:10.1016/j.parkreldis.2016.01.015.

Armstrong DM. 1988. The supraspinal control of mammalian locomotion. J Physiol. 405:1–37. doi:10.1113/jphysiol.1988.sp017319.

Beall EB, Lowe MJ, Alberts JL, Frankemolle AM, Thota AK, Shah C, Phillips MD. 2013. The effect of forced-exercise therapy for Parkinson's disease on motor cortex functional connectivity. Brain Connect. 3:190–98. doi:10.1089/brain.2012.0104.

Berardelli A, Rothwell JC, Thompson PD, Hallet M. 2001. Pathophysiology of bradykinesia in Parkinson's disease. Brain. 124:2131–46. doi:10.1093/brain/124.11.2131.

Bergen JL, Toole T, Elliott RG, Wallace B, Robinson K, Maitland CG. 2002. Aerobic exercise intervention improves aerobic capacity and movement initiation in Parkinson's disease patients. NeuroRehabilitation. 17:161–68.

Bohannon RW, Magasi SR, Bubela DJ, Wang YC, Gershon RC. 2012. Grip and knee extension muscle strength reflect a common construct among adults. Muscle and Nerve. 46:555–58. doi:10.1002/mus.23350.

Borg G. 1982. Ratings of perceived exertion and heart-rates during short-term cycle exercise and their use in a new cycling strength test. Int J Sports Med. 3:153–58. doi:10.1055/s-2008-1026080.

Brusse KJ, Zimdars S, Zalewski KR, Steffen TM. 2005. Testing functional performance in people with Parkinson disease. Phys Ther. 85:134–41.

Cakit BD, Saracoglu M, Genc H, Erdem HR, Inan L. 2007. The effects of incremental speed-dependent treadmill training on postural instability and fear of failing in Parkinson's disease. Clin Rehabil. 21:698–705. doi:10.1177/0269215507077269.

Carr JH, Shepherd RB. 1998. Neurological Rehabilitation: optimizing Motor Performance. Oxford: Butterworth-Heinemann.

Christensen LO, Johannsen P, Sinkjaer T, Petersen N, Pyndt HS, Nielsen JB. 2000. Cerebral activation during bicycle movements in man. Exp Brain Res. 135:66–72. doi:10.1007/s002210000493.

Corcos DM, Robichaud JA, David FJ, Leurgans SE, Vaillancourt DE, Poon C, Rafferty MR, Kohrt WM, Comella CL. 2013. A two-year randomized controlled trial of progressive resistance exercise for Parkinson's disease. Move Disord. 28:1230–40. doi:10.1002/mds.v28.9.

Coxon JP, Stinear JW, Byblow WD. 2005. Amplitude of muscle stretch modulates corticomotor gain during passive movement. Brain Res. 1031:109–17. doi:10.1016/j.brainres.2004.10.062.

Dibble LE, Hale TF, Marcus RL, Gerber JP, LaStayo PC. 2009. High intensity eccentric resistance training decreases bradykinesia and improves quality of life in persons with Parkinson's disease: A preliminary study. Parkinsonism Relat Disord. 15:752–57. doi:10.1016/j.parkreldis.2009.04.009.

Dorsey E, Constantinescu R, Thompson JP, Biglan KM, Holloway RG, Kieburtz K, Marshall FJ, Ravina BM, Schifitto G, Siderowf A, et al. 2007. Projected number of people with Parkinson's disease in the most populous nations, 2005-2030. Neurology. 68:384–86. doi:10.1212/01.wnl.0000247740.47667.03.

Duncan PW, Weiner DK, Chandler J, Studenski S. 1990. Functional reach: A new clinical measure of balance. J Gerontol. 45:M192–M197. doi:10.1093/geronj/45.6.M192.

Duncan RP, Earhart GM. 2013. Four Square step test performance in people with Parkinson disease. J Neurol Phys Ther. 37:2–8. doi:10.1097/NPT.0b013e31827f0d7a.

Earhart GM, Cavanaugh JT, Ellis T, Ford MP, Foreman KB, Dibble L. 2011. The 9-hole peg test of upper extremity function: Average values, test-retest reliability, and factors contributing to performance in people with Parkinson disease. J Neurol Phys Ther. 35:157–63. doi:10.1097/NPT.0b013e318235da08.

Fahn S, Elton RL, UPDRS-Development-Committee. 1987. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Calne DB, Goldstein M, eds. Recent developments in Parkinson's disease. Vol. 2. Florham Park, NJ: Macmillan Health Care. 153–64.

Fisher BE, Petzinger GM, Nixon K, Hogg E, Bremmer S, Meshul CK, Jakowec MW. 2004. Exercise-induced behavioral recovery and neuroplasticity in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine- lesioned mouse basal ganglia. J Neurosci Res. 77:378–90. doi:10.1002/(ISSN)1097-4547.

Fisher BE, Wu AD, Salem GJ, Song J, Lin CH, Yip J, Cen S, Gordon J, Jakowec M, Petzinger G. 2008. The effect of exercise training in improving motor performance and corticomotor excitability in people with early Parkinson's disease. Arch Phys Med Rehabil. 89:1221–29. doi:10.1016/j.apmr.2008.01.013.

Herman T, Giladi N, Gruendlinger L, Hausdorff JM. 2007. Six weeks of intensive treadmill training improves gait and quality of life in patients with Parkinson's disease: A pilot study. Arch Phys Med Rehabil. 88:1154–58. doi:10.1016/j.apmr.2007.05.015.

Klockgether T, Borutta M, Rapp H, Spieker S, Dichgans J. 1995. A defect of kinesthesia in Parkinson's disease. Move Disord. 10:460–65. doi:10.1002/(ISSN)1531-8257.

Kutukcu Y, Marks WJ, Goodin DS, Aminoff MJ. 1999. Simple and choice reaction time in Parkinson's disease. Brain Res. 815:367–72. doi:10.1016/S0006-8993(98)01060-9.

Lam HS, Lau FW, Chan GK, Sykes K. 2010. The validity and reliability of a 6-Metre Timed Walk for the functional assessment of patients with stroke. Physiother Theory Pract. 26:251–55. doi:10.3109/09593980903015235.

Lauhoff P, Murphy N, Doherty C, Horgan NF. 2013. A controlled clinical trial investigating the effects of cycle ergometry training on exercise tolerance, balance and quality of life in patients with Parkinson's disease. Disabil Rehabil. 35:382–87. doi:10.3109/09638288.2012.694962.

Li FZ, Harmer P, Fitzgerald K, Eckstrom E, Stock R, Galver J, Maddalozzo G, Batya SS. 2012. Tai Chi and postural stability in patients with Parkinson's disease. New England J Med. 366:511–19. doi:10.1056/NEJMoa1107911.

Mak MK, Pang MY. 2009. Fear of falling is independently associated with recurrent falls in patients with Parkinson's disease: A 1-year prospective study. J Neurol. 256:1689–95. doi:10.1007/s00415-009-5184-5.

Miyai I, Fujimoto Y, Ueda Y, Yamamoto H, Nozaki S, Saito T, Kang J. 2000. Treadmill training with body weight support: its effect on Parkinson's disease. Arch Phys Med Rehabil. 81:849–52. doi:10.1053/apmr.2000.4439.

Miyai I, Fujimoto Y, Yamamoto H, Ueda Y, Saito T, Nozaki S, Kang J. 2002. Long-term effect of body weight-supported treadmill training in Parkinson's disease: A randomized controlled trial. Arch Phys Med Rehabil. 83:1370–73. doi:10.1053/apmr.2002.34603.

Petzinger GM, Fisher BE, Van Leeuwen JE, Vukovic M, Akopian G, Meshul CK, Holschneider DP, Nacca A, Walsh JP, Jakowec MW. 2010. Enhancing neuroplasticity in the basal ganglia: The role of exercise in Parkinson's disease. Move Disord. 25:S141–S145. doi:10.1002/mds.22782.

Petzinger GM, Walsh JP, Akopian G, Hogg E, Abernathy A, Arevalo P, Turnquist P, Vuckovic M, Fisher BE, Togasaki DM, et al. 2007. Effects of treadmill exercise on dopaminergic transmission in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-lesioned mouse model of basal ganglia injury. J Neurosci. 27:5291–300. doi:10.1523/JNEUROSCI.1069-07.2007.

Podsiadlo D, Richardson S. 1991. The Timed up and Go: A test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 39:142–48. doi:10.1111/j.1532-5415.1991.tb01616.x.

Portney LG, Watkins MP. 2008. Foundations of clinical research: Applications to Practice. 3rd ed. Upper Saddle River, NJ: Prentice Hall.

Ridgel AL, Kim CH, Fickes EJ, Muller MD, Alberts JL. 2011. Changes in executive function after acute bouts of passive cycling in Parkinson's disease. J Aging Phys Act. 19:87–98. doi:10.1123/japa.19.2.87.

Ridgel AL, Peacock CA, Fickes EJ, Kim CH. 2012. Active-assisted cycling improves tremor and bradykinesia in Parkinson's disease. Arch Phys Med Rehabil. 93:2049–54. doi:10.1016/j.apmr.2012.05.015.

Ridgel AL, Vitek JL, Alberts JL. 2009. Forced, not voluntary, exercise improves motor function in Parkinson's disease patients. Neurorehabil Neural Repair. 23:600–08. doi:10.1177/1545968308328726.

Rose MH, Lokkegaard A, Sonne-Holm S, Jensen BR. 2013. Improved clinical status, quality of life, and walking capacity in Parkinson's disease after body weight-supported high-intensity locomotor training. Arch Phys Med Rehabil. 94:687–92. doi:10.1016/j.apmr.2012.11.025.

Uygur M, Bellumori M, LeNoir K, Poole K, Pretzer-Aboff I, Knight CA. 2015. Immediate effects of high-speed cycling intervals on bradykinesia in Parkinson's disease. Physiother Theory Pract. 31:77–82. doi:10.3109/09593985.2014.972530.

Vuckovic MG, Li QZ, Fisher B, Nacca A, Leahy RM, Walsh JP, Mukherjee J, Williams C, Jakowec MW, Petzinger GM. 2010. Exercise elevates dopamine d2 receptor in a mouse model of Parkinson's disease: in vivo imaging with [F-18] Fallypride. Move Disord. 25:2777–84. doi:10.1002/mds.23407.

Wall JC, Bell C, Campbell S, Davis J. 2000. The timed get-up-and-go test revisited: Measurement of the component tasks. J Rehabil Res Dev. 37:109–13.

Ware JE, Sherbourne CD. 1992. The MOS 36-Item Short-Form Health Survey (SF-36) .1. Conceptual-framework and item selection. Med Care. 30:473–83. doi:10.1097/00005650-199206000-00002.