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Community-based high-intensity cycling improves disease symptoms in individuals with Parkinson's disease: A six-month pragmatic observational study

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Abstract

Participation in supervised, laboratory-based aerobic exercise protocols holds promise in slowing the progression of Parkinson's disease (PD). Gaps remain regarding exercise adherence and effectiveness of laboratory protocols translated to community-based programs. The aim of the project was to monitor exercise behaviour and evaluate its effect on disease progression over a 6 month period in people with PD participating in a community-based Pedalling for Parkinson's (PFP) cycling program. A pragmatic, observational study design was utilised to monitor exercise behaviour at five community sites. The Movement Disorders Society-Unified Parkinson's disease Rating Scale Motor III (MDS-UPDRS-III) and other motor and non-motor outcomes were gathered at enrollment and following 6 months of exercise. Attendance, heart rate, and cadence data were collected for each exercise session. On average, people with PD (N = 41) attended nearly 65% of the offered PFP classes. Average percent of age-estimated maximum heart rate was 69.3 ± 11.9%; average cadence was 74.9 ± 9.0 rpms. The MDS-UPDRS III significantly decreased over the 6-month exercise period (37.2 ± 11.7 to 33.8 ± 11.7, p = 0.001) and immediate recall significantly improved (42.3 ± 12.4 to 47.1 ± 12.7, p = 0.02). Other motor and non-motor metrics did not exhibit significant improvement. Participants who attended ~74% or more of available PFP classes experienced the greatest improvement in MDS-UPDRS III scores; of those who attended less than 74% of classes, cycling greater than or equal to 76 rpms lead to improvement. Attendance and exercise intensity data indicated that a laboratory-based exercise protocol can be successfully translated to a community setting. Consistent attendance and pedalling at a relatively high cadence may be key variables to PD symptom mitigation. Improvement in clinical ratings coupled with lack of motor and non-motor symptom progression over 6 months provides rationale for further investigation of the real-world, disease-modifying potential of aerobic exercise for people with PD.

KEYWORDS
aerobic exercise, cadence, community-based exercise, cycling, disease progression, heart rate, Parkinson's disease

1 | INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease that results in a degradation of motor and non-motor function. Over a dozen randomised controlled trials have been completed to evaluate the potential of pharmaceutical agents to modify PD progression (Hart et al., 2009); none have demonstrated unequivocal disease-modifying properties. Longitudinal studies demonstrate that individuals who regularly engage in moderate to vigorous exercise in their early adult life have a significantly reduced risk of developing PD (Chen et al., 2005; Thacker et al., 2008), potentially due to an elevation in neurotrophic factors such as glial cell line-derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF) accompanying exercise (Tajiri et al., 2010; Zigmond, 2006; Zigmond et al., 2009). Assuming the physiological mechanism(s) responsible for the protective effects of early adult exercise are at least partially intact in those with PD, it is reasonable to hypothesize that vigorous exercise may trigger a similar, though possibly blunted, neural response and thereby slow disease progression. Animal models support the hypothesis that exercise-induced neurotrophic changes remain intact despite the presence of dopaminergic cell death, as rodents administered the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) or 6-hydroxydopamine (6-OHDA) to induce dopaminergic cell death and subsequent PD symptoms still experienced increased GDNF, BDNF, dopamine, and dopamine transporters within the striatum and basal ganglia following aerobic exercise (Fisher et al., 2004; Petzinger et al., 2006, 2007, 2010; Tajiri et al., 2010; Zigmond, 2006, 2009).

Neuroimaging studies suggest similar activity-dependent neuroplasticity may be present in people with PD (Alberts et al., 2016; Beall et al., 2013; Duchesne et al., 2016; Fisher et al., 2013; Shah et al., 2016). Corroborating results from several clinical trials indicate that regular aerobic exercise over 6 months mitigates PD motor symptoms and potentially alters disease trajectory (Schenkman et al., 2018; van der Kolk et al., 2019). The results of these prescriptive, well-controlled laboratory studies are encouraging; however, the effects of promising exercise interventions are largely untested in real-world settings, resulting in a substantial gap between aerobic exercise delivered in a laboratory setting and the translation and effectiveness of that intervention in the community.

Recognising the potential global benefits of exercise for people with PD, the American College of Sports Medicine (ACSM) and the Parkinson's Foundation created comprehensive PD exercise recommendations (*Parkinson's Foundation. Parkinson's Foundation Exercise Convening Summary Report*. https://www.parkinson.org/expert-care/Professional-Education/Resources/Exercisey, 2021). Regarding aerobic exercise, it was recommended that people with PD participate in a minimum of 90–150 min of moderate to vigorous aerobic exercise per week. Despite the documented benefits of exercise, only 27% of people with PD engage in 150 min of moderate-vigorous physical activity per week (Benka Wallen et al., 2015). Diminished exercise time associated with PD highlights the importance and need to evaluate engaging methods aimed at increasing exercise adherence in people with PD in real-world environments. Common barriers to physical activity in people with PD include low outcome expectation, lack of time and fear of falling (Ellis et al., 2013). Community-based, disease-specific exercise classes address barriers to exercise in people with PD by creating an environment with adaptive equipment and space to meet the physical needs of people with disability, employing exercise instructors with disease-specific knowledge, and allowing a caregiver to accompany the exerciser (Rimmer et al., 2004). Furthermore, being surrounded by individuals with a mutual experience may improve one's ability to cope with the disease (Claesson et al., 2020), heighten motivation to exercise (Tidman & Skotzke, 2020), and increase exercise self-efficacy and mood (Annesi, 2019). Studies have investigated community-based exercise programs (Cash et al., 2018; Duncan & Earhart, 2012; Kwok et al., 2019; Mak & Wong-Yu, 2021; McGough et al., 2016; Tidman & Skotzke, 2020; Volpe et al., 2013); however, the majority have largely been conducted in controlled environments (e.g. supervised by researcher or highly trained medical personnel, conducted in medical or academic settings, prospectively

What is known about this topic

- Regular and long-term engagement in supervised laboratory-based aerobic exercise protocols hold promise in slowing the progression of Parkinson's disease (PD).
- The effectiveness of translating evidence-based exercise programs to community settings to improve or slow PD progression has not been systematically addressed.

What this paper adds

- A pragmatic, real-world experimental design in the investigation of exercise adherence and intensity provides a realistic expectation of the effectiveness of a community-based exercise program.
- When PD-specific exercise programs are available in the community, people with PD attend on a regular basis and most exercise at moderate to high intensities.
- Regular program attendance and pedalling at a relatively high cadence may be key variables in mitigating PD symptoms.

assigned individuals to interventional groups, etc.). Furthermore, individuals were prescribed a specific amount of exercise (i.e. 1-3x/week), and the intervention occurred over a finite period of time (i.e. 8 weeks, 6 months, etc.). While these controlled community-based research projects have aided in understanding exercise in group settings, they do not represent real-world exercise translation and behaviour in people with PD due to the interaction between study personnel and participants.

Pragmatic studies examine interventions in real-world settings to ultimately inform clinical practice or policy (Ford & Norrie, 2016). Pragmatic trials differ from traditional explanatory trials as pragmatic trials are conducted in routine settings where the intervention is likely to occur (rather than laboratory settings), are implemented by general practitioners (rather than research personnel), include a wider range of participants who are likely to receive the intervention (rather than having extensive and potentially restrictive inclusion/exclusion criteria), and often do not have a placebo or control group (Ford & Norrie, 2016; Macpherson, 2004; Sox & Lewis, 2016). Our previous work with high-intensity cycling (Alberts et al., 2011; Jansen et al., 2021; Miller Koop et al., 2019; Ridgel et al., 2009; Rosenfeldt et al., 2016, 2021) has been successfully adapted and translated to over 150 community-based fitness facilities through the Pedalling for Parkinson's (PFP) program (https://www.pedalingforparkinsons.org), and serves as one of few examples of a successful and widespread translation of a laboratory intervention to a community setting. The PFP program creates an ideal environment to observe exercise adherence and intensity in a true community-based setting.

We previously reported exercise adherence and intensity data from a cohort of 49 individuals with PD participating in the PFP program over a 12-month period (Rosenfeldt et al., 2022). Data indicated that the majority of participants attend an average of 1–2 classes per week and exercise at a mean cadence of approximately 74 rpms. The present manuscript builds upon the exercise adherence results by evaluating the potential effects of community exercise behaviour on disease progression in the same cohort of people with PD participating in a PFP program over a 6-month period. It was hypothesized that people with PD would be compliant with a long-term high intensity exercise protocol and the exercise adherence and intensity would have a positive impact on disease progression. The project was originally planned to include a 12-month data collection point; however, due to the COVID-19 pandemic and associated travel restrictions, the in-person 12-month assessment was unable to be completed.

2 | MATERIALS AND METHODS

A pragmatic, observational study design was implemented at five community exercise facilities (two in northern Washington and three in central Colorado) from 2019–2020. Members of the study team travelled to each site at enrollment and following 6-months of PFP class offerings to gather motor and non-motor outcomes. Between the data collection sessions, the study team had limited interaction with study participants or exercise instructors and did not provide guidance regarding the frequency, duration, or intensity of exercise. During the 6-month exercise period, participants attended PFP classes, led by a group exercise instructor at their facility.

2.1 | Study sites and participants

The five community-based exercise sites were selected based on the stability of their established PFP programs, diverse geographical location (e.g., urban, suburban and rural representation), and site-based accommodation for study activity. Individuals who attended the PFP class at each site were invited to participate in the observational study, regardless of the frequency of class attendance. Consistent with a pragmatic study design, inclusion and exclusion criteria were broad in an effort to reflect individuals who were exercising in the community. Inclusion criteria included diagnosis of idiopathic PD, participation in a PFP program, and ability to provide informed consent. Exclusion criteria included participation in a pharmaceutical or interventional PD-related study, diagnosis of dementia, deep brain stimulation and neurological disease diagnosis other than PD.

Participants completed the informed consent process approved by the Cleveland Clinic Institutional Review Board prior to study activities. Participants were instructed to continue to attend their PFP classes at their typical frequency with no additional exercise attendance or intensity guidance from the study team.

2.2 | Pedalling for Parkinson's exercise protocol

Each of the five PFP sites had established programs that had been in existence from 8 months to 4.5 years. To establish a PFP program, the fitness centres completed a no-cost licensing agreement, which details the requirements for the PFP program. The PFP exercise protocol includes a 5–10 min warm-up, 40 min of high-intensity cycling and a 5–10 min cool-down. During the 40 min of the main exercise set, the exercise parameters include: a target pedalling cadence between 80–90 revolutions per minute (rpm), and an aerobic exercise intensity between 60–80% of individual's age-predicted heart rate (HR) maximum or a rating of perceived exertion (RPE) between 4–7 on a 10-point Borg RPE scale. The PFP protocol provides PD-specific safety guidelines (e.g., mount and dismount a cycle based on physical ability) and a pre-exercise participation medical screen and physician clearance form for participation in exercise. The PFP protocol provides PD-specific information, including typical PD motor impairments, safety recommendations and cueing for cycling instructors. The PFP classes are typically taught by group fitness instructors who do not have PD-specific training.

There is no cost associated with the PFP licence. Each facility that executes the PFP program can elect to monetarily charge the participants at their discretion. The fee associated with the PFP program at these five sites ranged from no-fee to the monthly membership fee for use of the facility and class participation.

2.3 | Exercise adherence and intensity monitoring

Exercise time, cadence and heart rate were recorded for all participants during each exercise class. Depending on the facility and internet access at each site, one of the following monitoring systems were utilised for continuous exercise variable monitoring: FitMetrix Indoor Cycling System (Atlanta, GA), Stages Cycling Flight System (Boulder, CO), or the Wahoo Fitness mobile application (Atlanta, GA). FitMetrix and Stages Flight systems were web-based group monitoring systems, while the Wahoo Fitness mobile application operated on each participant's smartphone; each has been described in detail in a previous publication (Rosenfeldt et al., 2022). Each participant was provided a Bluetooth Wahoo Fitness HR and cadence monitor, which was de-identified using a study ID within the monitoring system. Participants were instructed to wear their HR and cadence monitors for the duration of each class. Exercise data were stored on each system's commercial website, labelled under a unique study ID, downloaded or emailed to the study team and stored on a secure server accessible only to the study team. Percent of maximum HR was estimated based on age-predicted maximal heart rate: (220-age) (Fox 3rd & Naughton, 1972) or (164–0.7 × age) for those on beta blockers (Brawner et al., 2004).

2.4 | Outcomes

Primary and secondary outcomes were assessed at enrollment and 6-month follow up. The assessments were completed in the 'off' medication state (minimum of 12 h post antiparkinsonian administration) to gain a more accurate assessment of symptom severity. A board-certified neurologic physical therapist was present during the assessments to ensure safety in the 'off' medication state.

The primary outcome was the change in Movement Disorders Society-Unified Parkinson's disease Rating Scale III motor portion (MDS-UPDRS III) from enrollment to the 6-month exercise time point. The MDS-UPDRS III is a global motor scale of PD symptoms (Goetz et al., 2008). Secondary analyses of MDS-UPDRS III subscores included tremor (items 3.15–3.18), bradykinesia (items 3.4–3.8, 3.14), rigidity (item 3.3), and postural instability and gait dysfunction (PIGD; items 3.9–3.13) were conducted to evaluate potential symptom specific effects of exercise in people with PD. The MDS-UPDRS III was completed by the same administrator at each time point. The administrator was blinded to exercise adherence or intensity data.

Additional outcomes were gathered to estimate changes in aerobic fitness, cognitive function and manual dexterity. The six minute walk test (6MWT) is a submaximal test that measures walking capacity and mobility (Guyatt et al., 1985). The test was completed on either an indoor track, gymnasium, or hallway with at least 20 m of clear space, depending on the layout of the facility. Participants were instructed to cover as much distance as possible while walking for 6 min; the outcome was the number of meters walked over 6 min.

The processing speed test (PST), visual memory test (VMT), manual dexterity test (MDT), and quality of life in neurological disorders (NeuroQoL) were administered on an iPad® (Apple Inc.). Computerised, auditory instructions were uniformly provided through the iPad, allowing the tests to be self-administered (Figure 1).

The PST was created to closely resemble the symbol digit modalities test (Rao et al., 2017); both tests display a symbol/digit key at the top and ask the user to select the appropriate symbol with its corresponding digit (Figure 1a). The primary outcome of the PST is number of correct responses during the two-minute testing period. The PST is a valid measure of processing speed and information processing in individuals who are healthy and with chronic disease (Gorodeski et al., 2019; Rao et al., 2017), and has been effectively integrated into clinical care for individuals with neurological disease (Macaron et al., 2020; Rhodes et al., 2019; Rudick et al., 2014).

The VMT is a test of immediate and delayed visual memory. Seven icons are displayed on a 4 × 6 grid on the iPad (Figure 1b). After studying the grid for 10 s, the icons are removed from the grid and appear at the bottom of the screen. The participant is asked to place the icons back on the grid in the same place they were originally displayed. This process is repeated five times or until the items are correctly placed three times consecutively. The maximum score for each trial is 14—one point is awarded for each correct square that is filled and another point if the correct item is placed in the square. If an individual successfully replicates the display three times in a row, a maximum score is awarded for the remaining trials. The five trials are summed together for the total score (maximum score is 70).

The manual dexterity test (MDT) was used to evaluate upper extremity performance. The manual dexterity test, modelled after the traditional nine-hole peg test (Earhart et al., 2011), utilises the high-resolution, multi-point touch screen on the iPad and a customised overlay fitted to the iPad screen (Figure 1c). The MDT measures dexterity by requiring an individual to grasp, transport, and insert pegs from a home row to a 3 × 3 grid and back to the home row (Macaron et al., 2020; Rhodes et al., 2019; Rudick et al., 2014). The primary outcome is time to completion for each hand. Participants were asked to self-select a more and less PD affected side, which was confirmed by MDS-UPDRS III laterality ratings.

The NeuroQoL is a quality of life metric for adults with neurological disease (Gershon et al., 2012). The following domains were selected and administered as a computerised adaptive test on the iPad (Rhodes et al., 2019): lower extremity, upper extremity, positive affect and well-being, ability to participate in social roles, and fatigue (*Neuro-QoL Technical Report. Neuro-QoL Technical Report*, March, 2015). T-scores are calculated for each domain with a score of 50 representing the mean score of the general population. Higher scores indicated better self-reported health with the exception of fatigue, where a lower score is more desirable.

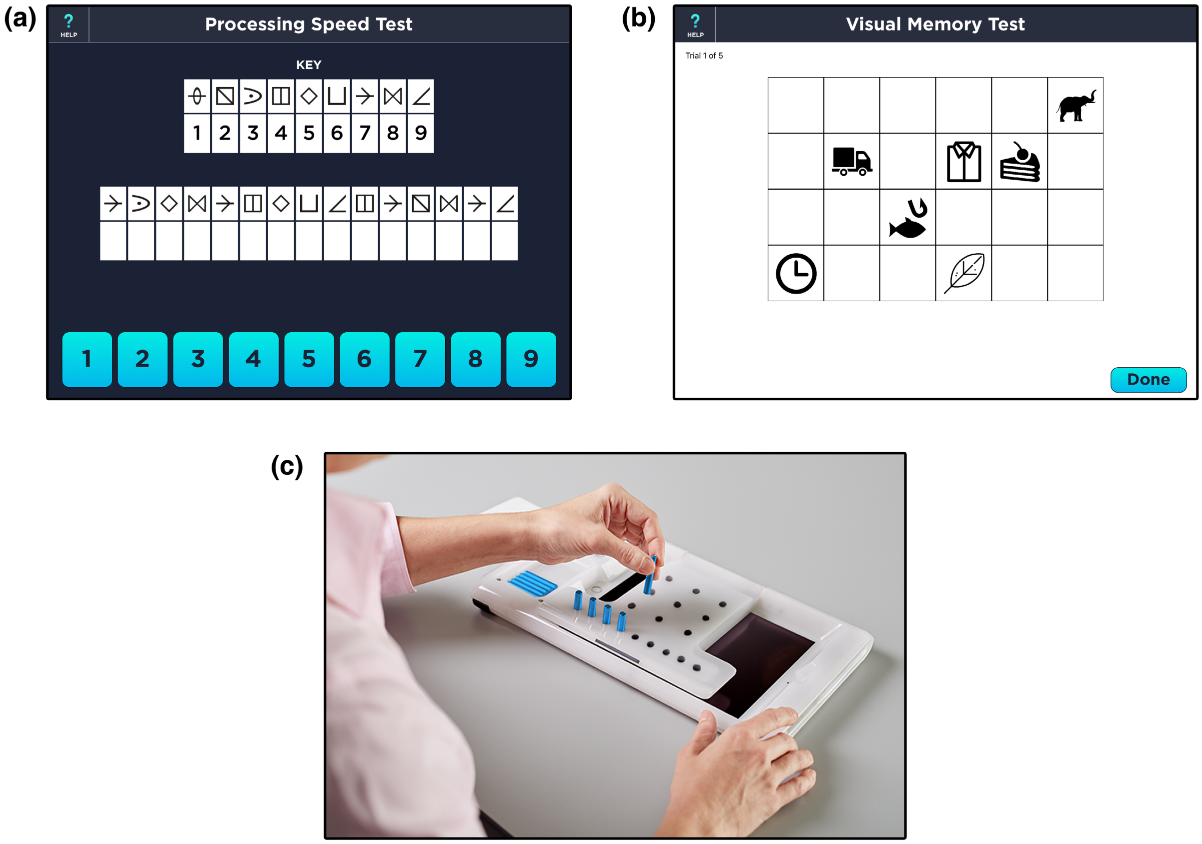

FIGURE 1 Screenshots of the non-motor iPad modules (a, b) and manual dexterity test (c). (a) The processing speed test—a symbol/digit key is displayed at the top of the screen; in the middle row, the user matches the symbol to the corresponding digit by pressing the number button at the bottom of the screen as quickly and accurately as possible. (b) The visual memory test—seven commonly recognised items are randomly placed on a 4×6 grid. After studying the grid for 10 s, the user has up to five attempts to replicate the initial display. (c) the manual dexterity test—similar to the nine-hole peg test, the user is asked to transport the nine pegs (in blue) from a home row, insert them into a 3×3 grid, and remove the pegs and return them to the home row. A plastic overlay covers the iPad while the surface area of the iPad records peg movement.

2.5 | Data analysis

Summary statistics were compiled for demographic information. Attendance, mean cadence, and mean HR data from each cycling session were compiled for each participant. Rarely, technology failure occurred producing outlying data points for the cadence and HR data. As a result, data falling two standard deviations outside of the individual's mean HR and cadence were excluded from analysis (<5 percent of data points for any given participant). Summary metrics for attendance, HR, and cadence were summarised across sites.

The monitoring systems provided an average heart rate per session; heart rate data were averaged for each individual over all attended classes. Exercise intensity was classified using heart rate data and guidelines from the American College of Sports Medicine (American College of Sports Medicine, 2018. Ch. 4). Vigorous intensity was classified as ≥77 percent of HR max; moderate intensity was 64–76 percent of HR max, and low intensity was <64 percent of HR max. Notably, one individual was in chronic atrial fibrillation and HR data were not collected. Cadence data were averaged for each individual over all attended classes. Cadence data were classified as high (≥80 rpms), medium (60–79 rpms), and low (<60 rpms) based on our previous cycling laboratory-based study (Ridgel et al., 2009). Notably, the monitoring systems provided summary metrics for the entire exercise session, which included warm-up and cool-down periods.

Analysis of outcomes proceeded in a two-step process: (1) Were improvements present in primary and secondary outcomes? (2) If significant improvement in the primary outcome was observed (change in MDS-UPDRS III), were any measures of exercise behaviour or demographic variables related to the observed improvement? The presence of changes in primary and secondary outcomes from enrollment to 6 months were assessed using paired one-sided t-tests. Tests were performed to detect an improvement in each of the outcomes of interest, with the null hypothesis stating that the mean participant score did not improve and the alternative hypothesis stating that the mean score did change significantly in a positive direction.

The relationships between improvement in MDS-UPDRS III scores and exercise attendance, intensity (cadence and HR), and demographic variables (i.e. age, sex, years since diagnosis, years participating in a PFP programs, and self-reported fall frequency) were assessed first descriptively using the recursive partitioning program (RPART) (Therneau & Atkinson, 2019) and secondly using regression models. The RPART aimed to divide the data in a manner that maximises the separation of the response (change in MDS-UPDRS III). Exercise attendance, intensity, and demographic factors listed above were considered for the split. Once the split had been identified, the same process continued for each of the subgroups until stopping criteria was met. By default, RPART will not try to split a node of a size less than 20 participants and will not create further subgroups of size less than 7, as smaller splits become arbitrary, noisy, and are no longer insightful.

Regression modelling was conducted using best subset selection. All factors considered for use in the decision tree were also considered for the regression models; additionally, interaction terms were considered, using the results of any interaction from the decision tree. Best subset selection considered models of all possible combinations of predictor variables and then the ideal model was selected based on a scoring function, in this case the Bayesian Information Criterion (BIC). The BIC is a measure of the fit of a model, calculated using the likelihood of a model, given the data, and a penalty term that increases with each added predictor, as to avoid overfitting the data. Given a best model, the significance of the model and the relationship with outcome and predictor variables were observed. All statistical analyses were computed using RStudio 2021.9.1.372, R version 4.1.2.

TABLE 1 Participant demographics and baseline characteristics

Factor	$N = 41$
Age (years)	69.3 ± 6.2
Male	25 (61%)
Race	
White	39 (95%)
2 or more	2 (5%)
Ethnicity	
Hispanic or Latino	1 (2%)
Not Hispanic or Latino	40 (98%)
Years of education	17.0 ± 2.7
Employment status	
Employed full-time	2 (5%)
Employed part-time	3 (7%)
Retired due to PD	10 (24%)
Retired by choice	26 (63%)
Hoehn and Yahr stage	
I	2 (5%)
II	30 (73%)
III	9 (22%)
Disease duration (years)	4.9 ± 4.4
MDS-UPDRS III Score (off medication)	37.2 ± 11.7
Levodopa equivalent dose (LED, mg)	584 ± 397
Self-reported 6-month fall frequency	1.17 (1.88)
Beta Blocker	6 (15%)

Abbreviation: MDS-UPDRS III, Movement Disorders Society Unified Parkinson's disease Rating Scale Motor Exam.

Note: Summary statistics presented as mean ± standard deviation or *N* (%) for categorical data.

3 | RESULTS

3.1 | Study participants

A total of 50 individuals participated in the 6-month pragmatic, observational study. Nine individuals were unable to complete the 6-month evaluation due to being unavailable (out of town ($n = 4$), medical reason ($n = 2$), unable to make appointment ($n = 3$)) on the date of the 6-month site visit; therefore, a total sample size of 41 was used in the final analysis. For the secondary outcomes, technological and connectivity issues resulted in no more than 5 missing data sets for each outcome metric. Demographic variables for those who attended the enrollment and 6-month assessment are provided in Table 1.

3.2 | Exercise performance

Each site offered, on average, 65 classes over the 6 month period. Class cancellations were rare; when cancelled, common reasons included holidays, gym closures, and instructors being unavailable. Heart rate and cadence data over the 6-month observational period from a representative participant is displayed in Figure 2.

Overall, average attendance rate for all participants was 65% with an average of 42.2 ± 11.6 sessions attended out of 65 sessions offered. Further analysis indicated that 20 out of 41 (49%) of the participants attended, on average, ≥2 sessions per week while 19 out of 41 (46%) participants attended 1–1.9 sessions per week. The remaining two participants (5%) attended <1 exercise session per week.

When examining exercise intensity based on average HR during all attended exercise sessions, 9 out of 40 (22.5%) participants exercised at a vigorous intensity, 18 out of 40 (45%) exercised at a moderate intensity, and the remaining 13 (32.5%) exercised at a low intensity. Average percent of age-estimated maximum heart rate for the cohort was 69.3 ± 11.9%.

When examining intensity based on cadence during all attended exercise sessions, 12 of the 41 (29%) participants cycled at high cadence, 25 (61%) at moderate cadence, and 4 (10%) at low cadence. Average cadence for the group was 74.9 ± 9.0 rpms.

Average weekly attendance, HR, and cadence were calculated for each participant and are provided in Figure 3.

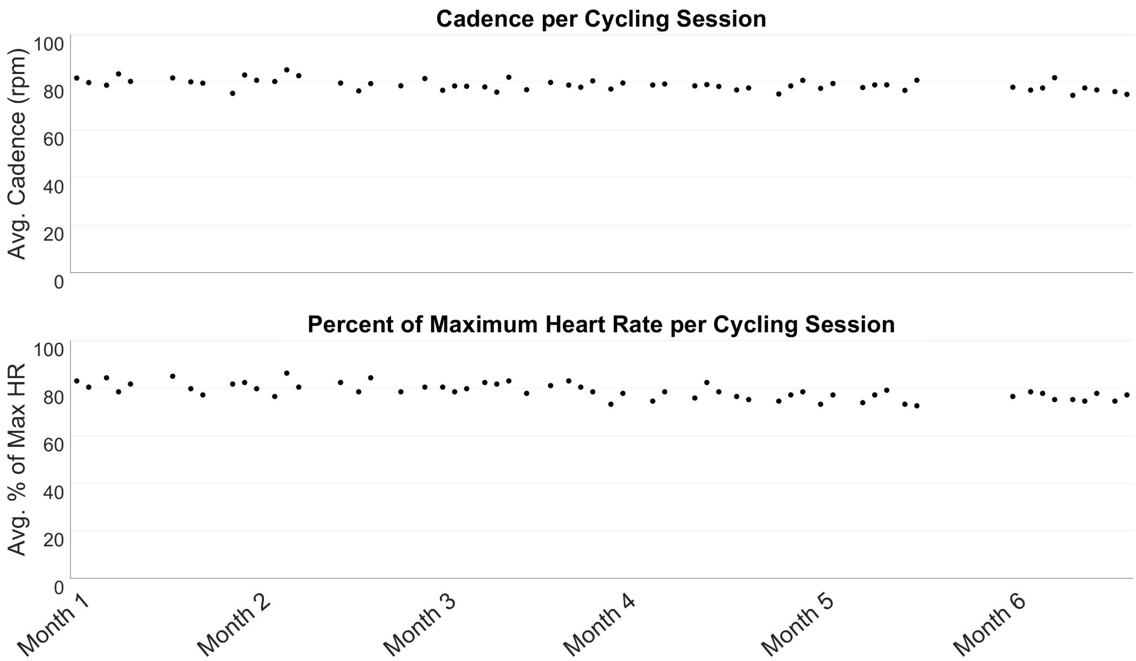

FIGURE 2 Representative data from a single participant. Over the 6 month observational period, the participant attended 58 out of a potential 65 classes. Average cadence was 78.9 ± 2.1 rpms, classifying them in the moderate cadence range. Average percent of HR maximum was 78.5 ± 3.2 percent, which was classified as vigorous intensity. Reflecting the pragmatic design, between months 5 and 6, the individual was out of town and did not attend the local PFP classes.

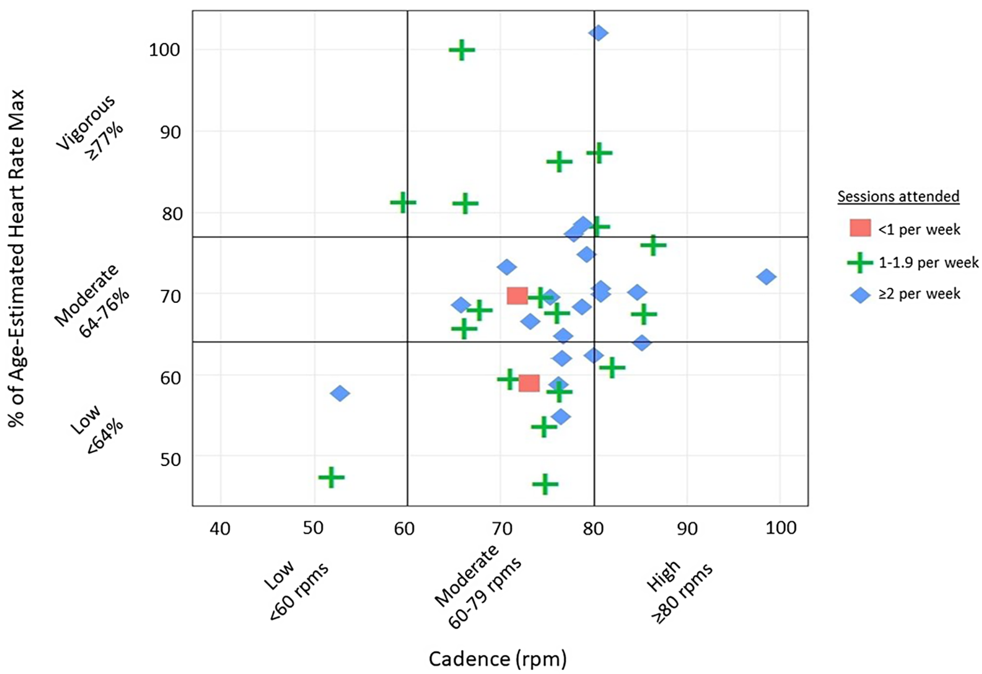

FIGURE 3 Scatterplot of mean percent of age-estimated maximum heart rate, cadence and weekly attendance over the course of 6 months. The majority of participants were able to exercise at moderate-vigorous intensity measured by cadence and/or heart rate. One individual did not wear a heart rate monitor due to chronic atrial fibrillation and is not included in the figure (N = 40).

3.3 | Aerobic exercise improved MDS-UPDRS III outcomes at 6-month follow-up

Overall, MDS-UPDRS III scores improved from 37.2 ± 11.7 to 33.8 ± 11.7 from enrollment to 6-month follow up (p = 0.001). Table 2 displays scores for the subscales of the MDS-UPDRS III. The overall improvement was driven primarily by improvements in the rigidity and bradykinesia subscores.

3.4 | Exercise maintains cardiovascular, upper extremity, and non-motor function

Results of motor and non-motor outcomes are provided in Table 3. Immediate recall in the VMT increased significantly from a mean score of 42.3 ± 12.4 to 47.1 ± 12.7 responses (p = 0.02). No other motor or non-motor secondary outcome improved statistically from enrollment to 6-months.

3.5 | Exercise adherence and intensity influenced 6-month outcomes

The mean improvement in MDS-UPDRS III score was 3.4 points. A post-hoc analysis revealed several factors influenced improvements in PD symptoms. The decision tree in Figure 4 indicates attendance and mean cadence were influential factors in MDS-UPDRS III improvement. Those who attended ≥48 classes (74% of available classes) over the 6 month period on average experienced the greatest improvement in MDS-UPDRS III scores (6.2 points). Of those who attended less than 48 classes, those who cycled ≥76 rpms experienced an average 4.5 point improvement in MDS-UPDRS III score, while those who cycled slower than 76 rpms experienced an average 0.5 point improvement.

TABLE 2 MDS-UPDRS III results

	Baseline	6-month	p-value
MDS-UPDRS III Total score	37.2 ± 11.7	33.8 ± 11.7	0.001*
MDS-UPDRS III Rigidity score	5.8 ± 3.1	4.8 ± 3.0	0.006*
MDS-UPDRS III Bradykinesia score	17.5 ± 5.6	16.1 ± 6.1	0.012*
MDS-UPDRS III Tremor score	6.6 ± 5.6	6.0 ± 4.9	0.17
MDS-UPDRS III PIGD score	4.5 ± 2.6	4.3 ± 3.0	0.31

Abbreviations: MDS-UPDRS III, Movement Disorders Society Unified Parkinson's disease Scale; PIGD, postural instability and gait dysfunction.

Note: Summary statistics presented as mean ± standard deviation.

*$p < 0.05$.

The regression model, using best subset selection, included three terms as predictor variables: attendance, mean cadence and the interaction between attendance and mean cadence (p = 0.016). Further, all predictor variables in the model were significant ($p < 0.01$), indicating that attendance and cadence contributed to the model. The overall R-squared for the model was 0.24.

4 | DISCUSSION

The results of this pragmatic study indicate that when a PFP program is accessible to the community, people with PD attend approximately 65% of available classes over a 6 month period and the majority exercise at a moderate to vigorous level based on average heart rate and/or cadence. Moreover, people with PD who participated in the PFP program had an overall decrease in PD motor symptoms and an improvement in immediate visual memory recall. Other motor and non-motor outcomes remained relatively stable over the 6-month period. Overall, our results support the PFP program as a successful translation from a laboratory-based protocol to a community pillar for people with PD to achieve or approach the recommended aerobic exercise frequency and intensity recommended by ACSM and the Parkinson's Foundation to aid in the mitigation of PD symptoms.

TABLE 3 Secondary motor and non-motor outcomes

	Enrollment	6-month	p-value
Motor outcomes			
Six minute walk test (6MWT; m)	514.5 ± 104.2	501.3 ± 110	0.94
Manual dexterity test (MDT; sec)			
More affected side	30.3 ± 6.1	30.1 ± 6.5	0.39
Less affected side	29.6 ± 6.0	29.0 ± 6.6	0.25
Non-motor outcome			
Processing speed test (PST; number correct)	39.7 ± 8.9	40.4 ± 10.3	0.17
Visual memory test (VMT)			
Immediate recall, number correct	42.3 ± 12.4	47.1 ± 12.7	0.02*
Delayed recall, number correct	9.9 ± 3.3	10.6 ± 3.5	0.13
Quality of Life in Neurological Disorders (NeuroQoL;)			
Upper extremity	38.9 ± 6.2	38.8 ± 6.4	0.55
Lower extremity	46.0 ± 5.9	46.3 ± 6.7	0.27
Fatigue	46.6 ± 5.1	46.6 ± 5.3	0.53
Positive affect and well-being	53.1 ± 5.5	53.4 ± 6.1	0.31
Ability to participate social roles & activities	49.2 ± 6.5	49.1 ± 6.9	0.57

Note: Summary statistics presented as mean ± standard deviation.

*$p < 0.05$.

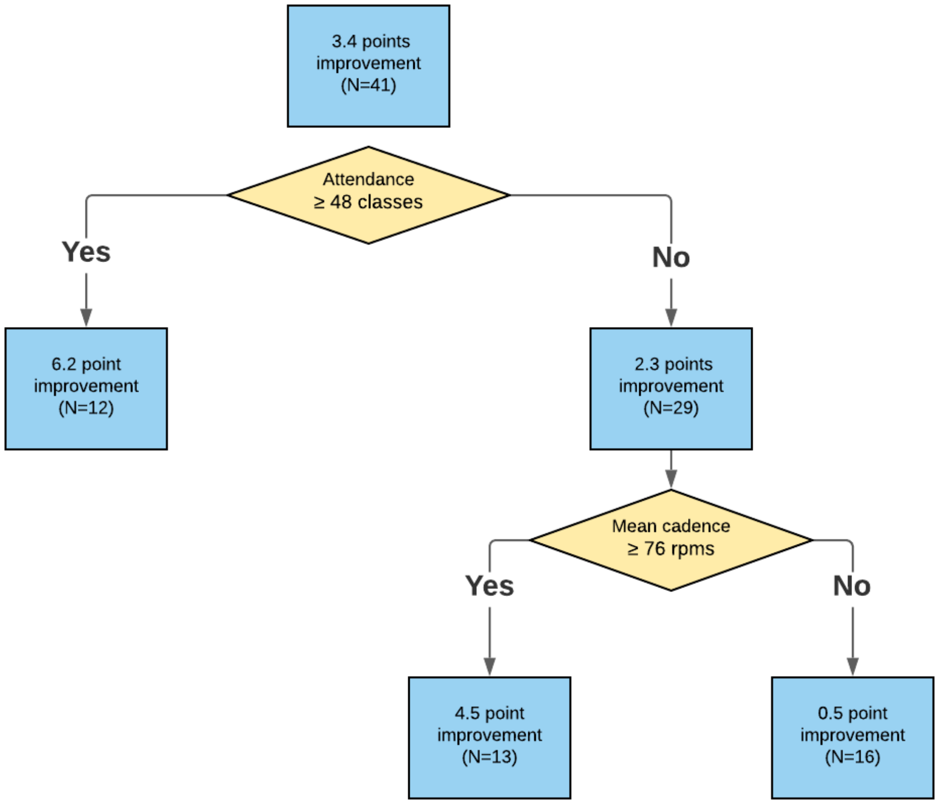

FIGURE 4 MDS-UPDRS III decision tree. Participants who attended ≥48 classes (approximately 74% of the available PFP classes) experienced the greatest improvement in MDS-UPDRS III scores. Of those who attended less than 74% of classes, a cycling cadence of 76 or greater was associated with greater improvements in MDS-UPDRS III than those who cycled at a slower cadence.

This was a pragmatic study without a control group. Previous studies report an increase, or worsening, in UPDRS III scores over a 6 month period ranging from 1.1 (Ellis et al., 2016) to 5.6 points in those who did not perform aerobic exercise (van der Kolk et al., 2019). In individuals with PD who self-reported a minimum of 60 min of exercise per week, Miller and colleagues reported a relative stability in motor and non-motor symptoms, including the UPDRS and 6MWT with no outcome exhibiting greater than 1.2% decline over the 12 month period (Miller et al., 2019). Together, the results of our study and others demonstrate the promise of exercise for mitigating disease symptoms and justify the need for larger, randomised controlled trials examining the long-term effects of community-based aerobic exercise programs on PD progression.

The primary analysis indicated that the sample, on average, exhibited an improvement in clinical symptoms based on a reduction in MDS-UPDRS III scores over the 6-month observational period. Initial decision tree and regression modelling analyses suggest attendance and pedalling cadence may be important variables contributing to an improvement in PD clinical symptoms. These initial analyses provide the cornerstone for future analyses in a larger group of PD patients engaging in long-term aerobic exercise. It is acknowledged that the clinical response to exercise is likely multi-factorial and complicated; data from a longitudinal study that includes a larger and more diverse PD cohort (ethnic, disease state, exercise performance, etc.) will provide the necessary data to create a definitive exercise prescription.

Nevertheless, as anticipated, regular attendance was a key variable to improving motor functioning, as those who regularly attended PFP classes (~74% or more of the available classes) experienced the greatest benefit in motor symptoms. The positive relationship between attendance and enhanced motor function reinforces the importance of consistent exercise behaviour in people with PD and is consistent with our previous 8-week cycling study which demonstrated that improvements in UPDRS III scores diminished following 4 weeks of inactivity (Ridgel et al., 2009). For those who did not attend 74% of classes, a cadence ≥76 rpms was key to symptom attenuation, while those who pedaled less than 76 rpms experienced little change in PD symptomology. This potential differentiation related to cadence suggests exercise intensity, measured by cadence, may be a key variable in facilitating the central nervous system (CNS) response to exercise. Previous data in healthy cyclists indicated that high cadence cycling resulted in a greater functional response of the cortical regions (Ludyga et al., 2016) and that patterns of cortical activity were modifiable following 4 weeks of high cadence compared to low cadence cycle training (Ludyga et al., 2017). Similarly, we have demonstrated in PD participants that a faster pedalling rate was associated with an increase in functional connectivity between the more affected motor cortex to the ipsilateral thalamus during task performance following a stationary cycling intervention (Shah et al., 2016). The observed effects of enhanced cortical activation associated with relatively high pedalling rates, in healthy adults and individuals with PD, support the concept that high cadence training may facilitate neural efficiency (Neubauer & Fink, 2009). It is proposed that neural efficiency may be underlying the observed improvements in information processing reported previously in PD (Rosenfeldt et al., 2021) and improvements in immediate recall demonstrated in this cohort of exercisers. Current studies are in progress to evaluate the hypothesis that high cadence compared to low cadence cycling facilitates neural efficiency and is contributing to changes in cognitive and dual-task performance.

Non-motor and quality of life aspects of PD have largely been ignored in the majority of surgical, pharmacological and behavioural clinical studies in favour of motor outcomes, despite non-motor symptoms consistently being reported among the most bothersome symptom in people with PD (Politis et al., 2010). In this project, immediate visual memory performance significantly improved over time, while information processing, delayed visual memory, and quality of life remained relatively stable over the 6-month observational period. The lack of decline is notable, as PD-associated cognitive declines are present in approximately 25–50 percent of people with PD (Aarsland et al., 2003, 2010; Hobson & Meara, 2015; Mamikonyan et al., 2009; Riedel et al., 2008), and a majority of people with PD will develop dementia over time (Aarsland et al., 2003; Hely et al., 2008). Rate of cognitive decline in people with PD is variable, but may decline at approximately 3 percent annually (Aarsland et al., 2004). Preliminary data indicate short-term bouts of aerobic exercise may improve or preserve various aspects of cognition in people with PD (Altmann et al., 2016; Rosenfeldt et al., 2021; Silveira et al., 2018); however, the long-term effects of high-intensity aerobic exercise on cognition in PD have not been systematically evaluated. The improvement and stability of the cognitive performance in this study over a range of cognitive domains (immediate and delayed memory and information processing) provides rationale to investigate cognitive performance in future long-term aerobic exercise studies.

Notably, the project was originally designed as a 12-month pragmatic observational study. Exercise attendance and performance data over 12-months indicated participants, in general, maintained their consistent attendance and exercise intensity (Rosenfeldt et al., 2022). Unfortunately, the COVID-19 pandemic travel restrictions during the spring of 2020 prevented the collection of 12-month clinical data. Nevertheless, 6-month clinical outcomes provide a viable and reasonable end point to provide insight into the real-world effects of consistent aerobic exercise in people with PD and highlight that community-based programs are key to exercise consistency. Future work can build upon this observational study with the addition of a control group to strengthen the level of evidence supporting aerobic exercise as a disease modifying therapy.

We acknowledge a potential selection bias in our sample. Individuals in the study were already exercising, the results may not be generalizable to an exercise naïve population. The sites were selected based on geographic diversity and administrative willingness to participate and may not be representative of all 150 PFP sites. The majority of the population were white (95%) and highly educated (17.0 ± 2.7 years); it is unknown if this was due to site selection bias or if the racial and educational profile is representative of those who attend community-based exercise classes. The PFP licence is free; however, it is up to the discretion of the exercise facility to set the fee schedule. Several of the sites in this study offer free classes to the participants, while others charge a monthly membership fee to the facility. Notably, there was no difference in attendance or exercise performance across sites (Rosenfeldt et al., 2022), suggesting fee structure in this study population did not serve as a barrier or facilitator to exercise adherence. Further work should be conducted to minimise socioeconomic and racial disparities in community-based care to better understand factors associated with community-based exercise program utilization and adherence.

5 | CONCLUSION

Adherence data support the feasibility of translating a successful laboratory exercise protocol for people with PD to a community setting. Most people with PD are able to achieve and sustain moderate to high intensity exercise in a community-based setting without oversight from a research team or medical professional. The greatest change in MDS-UPDRS III scores were experienced by individuals who regularly attended the class and by those who exercised at a relatively high cadence, stressing the importance of consistent, high-intensity aerobic exercise in people with PD. The lack of motor and non-motor symptom progression over the 6-month observational period supports further investigation of the effectiveness of community-based cycling programs to slow the progression of PD.

AUTHOR CONTRIBUTIONS

ABR contributed to the funding acquisition, study design conceptualization, study methodology, data collection, data analysis and manuscript writing; MMK contributed to the data collection and data curation. ALP contributed to the data collection and manuscript editing. KH contributed to the data curation. EZ performed the statistical analyses. DS contributed to data collection. JLA contributed to the study design conceptualization, study methodology, data collection, data analysis and manuscript editing.

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CONFLICT OF INTEREST

ABR serves as an unpaid member of the Davis Phinney Foundation Scientific Advisory Board. JLA has authored intellectual property associated with the iPad cognitive assessment applications. The remaining authors report no conflicts of interests.

DATA AVAILABILITY STATEMENT

Data available upon request.

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