High intensity eccentric resistance training decreases bradykinesia and improves quality of life in persons with Parkinson's disease: A preliminary study

Leland E. Dibblea,*, Tessa F Haleb, Robin L. Marcusa, J. Parry Gerberc, Paul C LaStayoab

aUniversity of Utah, Department of Physical Therapy, 520 Wakara Way, Salt Lake City, UT 84108, USA
bPinnacle Performance 1410 South Edison St Suite A Salt Lake City, UT 84106, USA
cKeller Army Community Hospital, Physical Therapy, West Point, NY 10996, USA

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Abstract
Persons with Parkinson disease (PD) often demonstrate bradykinesia during mobility tasks. Bradykinesia combined with other PD-related movement deficits may contribute to self-reported reductions in quality of life. At this time, no studies have examined the effects of resistance exercise as an intervention to reduce bradykinesia and improve self-reported quality of life. Therefore, we examined changes in muscle force production, clinical measures of bradykinesia, and quality of life following 12 weeks of a high intensity eccentric resistance exercise program in persons with mild to moderate PD. Twenty individuals with idiopathic PD were matched into an experimental or an active control group. All participants were tested prior to and following a 12-week intervention period. The experimental group performed high intensity quadriceps contractions on an eccentric ergometer 3 days a week for 12 weeks. The active control group participated in an evidence based exercise program of PD. The outcome variables were quadriceps muscle force, clinical bradykinesia measures (gait speed, timed up and go) and disease specific quality of life (Parkinson's disease questionnaire-39 [PDQ-39]). Data was analyzed using separate 2 (group) × 2 (time period) ANOVAs. Results demonstrated significant time by group interaction effects for gait speed, timed up and go, and the composite PDQ-39 score (p < 0.05). Muscle force, bradykinesia, and QOL were improved to a greater degree in those that performed high intensity eccentric resistance training compared to an active control group. Additional research is needed to determine if this type of training has long-term impact and if it results in an alteration of the natural history of mobility and QOL decline in persons with PD.

1. Background and introduction
Idiopathic Parkinson’s disease (PD) is one of the most common degenerative neurologic disorders with an estimated prevalence of 128–187 per 100,000 persons and an annual incidence of 20 per 100,000 persons [1,2]. The cardinal motor deficits of the disease (rigidity, akinesia, bradykinesia, tremor, and loss of postural control) contribute to an on-going deterioration of independence in activities of daily living and quality of life (QOL). Given the progressive nature of PD, and the relatively short duration of uncomplicated medication effectiveness, it is critical to identify rehabilitation interventions that minimize disease related impairments while maximizing QOL.

The potential benefits of exercise for persons with PD are now being elucidated, though the efficacy of specific modes of exercise is unclear. [3] A recent research report by Ellis et al. [4] summarized the effect sizes for exercise intervention studies for persons with PD. Generally, these interventions have produced small to moderate effects on mobility related outcome variables. Resistance training is well supported as a beneficial component of an exercise program designed to improve muscular strength and functional capacity in older adults [5], but it is not generally highlighted as a major part of rehabilitative treatment for persons with PD. Recently however, several reports have demonstrated the beneficial effects of resistance training in persons with PD, but few studies have specifically emphasized high intensity means of improving muscle strength [6–9].

Although the physiologic validity of a resistance training program is best determined by changes in muscle strength, the personal relevance of these changes to an individual with PD are best determined by related changes in speed of movement, mobility, and QOL. In order to examine the clinical validity of high intensity resistance
training in persons with PD, we conducted a preliminary study to compare the effects of a chronic, high intensity eccentric intervention with an evidence based exercise program on measures of clinical bradykinesia and QOL in persons with mild to moderate Parkinson's disease. Based on previous resistance training and QOL research we hypothesized that both groups would improve as a result of training but that the experimental group improvements would exceed those of the active control group.

2. Methods

2.1. Participant selection criteria

Persons with Hoehn and Yahr stages 1–3 PD receiving care for PD through the Movement Disorders Clinics at local hospitals and physician offices were recruited to participate. Utilizing the within group effect size for muscle strength changes in previous research [10], an a priori power analysis suggested that a sample size of 7 participants in each group would result in statistical power greater than 0.80 at an alpha level of 0.05. A target sample size of twenty participants was recruited to participate in order to account for attrition and to control for the risk of type 2 statistical errors.

Participants were included if they had a physician confirmed diagnosis of mild to moderate idiopathic PD (Hoehn and Yahr 1–3) [11], were between 40 and 85 years of age, and were willing and able to comply with a 12-week resistance training program. Potential participants were excluded if they had a history of any neurologic, cardiovascular, hematologic, or orthopedic condition that limited their ability to participate in resistance exercise or tolerate testing or intervention procedures. In addition, potential participants were excluded if they demonstrated unpredictable motor fluctuations or severe dyskinesias.

2.2. Procedures

The purpose and procedures of the study were explained to all participants and an institutional review board approved consent form was signed. Participants were then placed into groups by matching for age, gender, and disease severity (as measured by the Hoehn and Yahr scale). (Fig. 1) Testing and training were performed during participants on medication states. To accomplish this, testing and training were performed 1–1.5 h after taking their PD medications to control for the effects of medication status on functional performance. The following demographic data was collected from participants: age, sex, height, body mass, duration of PD, predominant PD symptoms, most affected side of the body, current medication regimen, and PD severity (Hoehn and Yahr Scale rating).

2.3. Outcome measures

2.3.1. Severity of motor deficits

The motor subsection of the Unified Parkinson's Disease Rating Scale (UPDRS) was used as a measure of the severity of participants' motor deficits. [12] The motor subsection of the UPDRS is comprised of 14 items, each rated on a 5-point ordinal scale (0 = no signs, 4 = severe signs), with a total possible score of 108. Higher scores indicated more severe motor deficits.

2.4. Muscle force

Quadriiceps muscle strength was measured using unilateral maximal voluntary isometric force (MVIC) on a KinCom dynamometer (Chattanooga Inc., Hixon, TN). Subjects were stabilized by chest and thigh straps and asked to hold their arms across their chest while performing these tests. Both lower extremities were tested and these strength measures were assessed prior to and following the training interventions. Participants were seated and their knees were fixed at 60 degrees of flexion. Participants practiced submaximal contractions at 50 and 75% of their perceived maximal effort prior to one practice maximal contraction trial. After a 2 min rest period, three separate maximal contractions were performed. Each maximal contraction was held for 5 s with a 3 min rest between trials. Muscle force was operationally defined as the average peak force of the 3 trials. The order of testing (more affected vs. less affected limb) was randomized among subjects.

2.5. Mobility tests

A battery of two timed movement tasks regularly employed with elderly and exercise limited populations were used to determine any change in movement speed. A measure of the speed a person walks over a 10 m distance (TMW), and the timed up and go (TUG) were used as measures of bradykinesia during gait [13]. For the TMW, participants were asked to start from a stationary standing position and on a “Go” signal to walk forward at their maximal safe speed over a 16 m walk way. Time was recorded for the middle 10 m of the walk to avoid acceleration and deceleration effects. Time was recorded to the nearest 0.01 s from a verbal go signal to final foot crossing of the 10 m mark on the walk way. For the TUG, participants were asked to start from a seated position and rise to stand, walk out 3 m, turn around, and return to sitting as quickly as possible. Time was recorded to the nearest 0.01 s from the time the person’s buttocks left the chair until return contact with the chair. For both tests, the average of 3 trials was used as the outcome variable. Both tests have been reported to be valid, reliable, and sensitive measures of gait function in a variety of neurologically impaired populations including persons with PD. [14,15] All measures were performed by one of two investigators and all participants underwent this series of tests prior to and following training.

2.6. Disease specific quality of life

Participants' perceptions of their overall PD specific quality of life were tested through the use of a standardized self-report tool, the Parkinson’s Disease Questionnaire (PDQ-39). The psychometric properties of the PDQ-39 have been established in community dwelling persons with PD. [16–18] Scoring of the PDQ-39 resulted in a composite score as well as subscores that reflected distinct components that contribute to overall QOL. The PDQ-39 sub-scale scores are mobility, activities of daily living, emotions, stigma, social support, cognitions, communication and bodily discomfort. The PDQ-39 is scored on a 0–100% scale, with higher scores indicating greater disability. Although all of the sub-scale scores were calculated, due to the physical nature of our intervention, we hypothesized that any observed changes would be focused on the physical sub scores (ADL, mobility, bodily discomfort). [16–18].

2.7. Participant training

Once participants were recruited, they were allocated to either the experimental or the control group matched for age and sex. The study design utilized “active controls”, i.e., individuals engaged in an evidence based rehabilitation program appropriate for their PD and individual impairments. [3] The standard exercises utilized by all participants included stretching, walking on a treadmill, riding a bicycle ergometer and performing resistance exercise (both machines and free weights) with the upper extremities. Both groups performed their respective exercises 45–60 min, 3 days/week for 12 weeks. The only difference between the groups was the substitution of high-force eccentric training for traditional lower-extremity resistance strength training in the experimental group.

The eccentric group experienced high muscle forces that were generated on an eccentric ergometer. The progression of the eccentric exercise work rate was determined as a function of the perceived exertion (RPE) using a “target” workload on a computer monitor. The progression of training and RPE for the experimental group has been detailed previously [6].

2.8. Statistical methods

Data summary and analysis were performed with SPSS Version 13.0 (SPSS Inc, Chicago, IL). The assumptions of parametric statistical tests were tested via tests of normality and homogeneity of variance. In all cases, the assumptions were met and therefore parametric tests were performed.

In the analyses, we evaluated the training effect on muscle strength, mobility, and QOL. Each dependent variable was analyzed using separate 2 (group) by 2 (time period) analyses of variance (ANOVA). In order to examine the differential response of the groups, our primary interests were the interaction effects. In addition, because both groups exercised, we also hypothesized that there would be an overall time effect for each dependent variable. The magnitudes of effect from pre-intervention to post-intervention tests for each group were estimated using calculations of effect size. The level of significance was set at p < 0.05. Bonferroni corrections to control for increased Type I error risk were conducted on each category of outcome variables [19].

3. Results

Twenty individuals with PD were enrolled in the trial (10 eccentric group participants, 10 controls). One participant from the standard care group did not complete the trial because of unrelated health issues; therefore the results reflect 19 participants. There were no significant differences between the groups on any of the demographic variables or outcome measures at the pre-intervention tests (Table 1).

3.1. Severity of motor deficits

Post test UPDRS data was unable to be gathered on 2 experimental group participants and 1 control group participant, therefore the results reflect 8 participants in each group. There was no significant time by group interaction, group, or time effects for the UPDRS motor score. (Interaction effect p = 0.37; Group effect
Calculation of within group effect sizes demonstrated that the improvements in the UPDRS motor score demonstrated by participants in the experimental group exceeded those demonstrated by the active control group over the course of training (Experimental group: UPDRS motor score ES = 0.32; Active control group: UPDRS motor score ES = 0.17) (Table 2).

3.2. Muscle force

There was no significant time by group interaction effects for either LE (less affected p = 0.38; more affected p = 0.08). However, there were significant time effects noted for both the less affected and the more affected extremities (less affected p = 0.01; more affected p = 0.01). Calculation of within group effect sizes demonstrated that the MVIC increases demonstrated in the experimental group exceeded those in the active control group in both their more affected and less affected extremities over the course of training (Experimental group less affected ES = 0.73; more affected ES = 0.77; Active control group less affected ES = 0.25; more affected ES = 0.06) (Table 2, Fig. 2).

3.3. Clinical bradykinesia

There was significant time by group interaction effects for both the TMW and TUG tests (TMW p = 0.02; TUG p = 0.03). Calculation of within group effect sizes demonstrated that the improvements in bradykinesia demonstrated by participants in the experimental group exceeded those demonstrated by the active control group.

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Experimental (n = 10)</th>
<th>Control (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean years (SD))</td>
<td>64.3 (9.6)</td>
<td>67.0 (10.2)</td>
</tr>
<tr>
<td>PD duration (mean years (SD))</td>
<td>6.1 (3.9)</td>
<td>6.5 (4.3)</td>
</tr>
<tr>
<td>PD Severity (mean (SD))</td>
<td>2.5 (0.5)</td>
<td>2.5 (0.7)</td>
</tr>
<tr>
<td>Number on dopamine replacement (#/n)</td>
<td>5/10</td>
<td>5/9</td>
</tr>
<tr>
<td>Predominant signs (#/n)</td>
<td>Akinesia (2/10)</td>
<td>Akinesia (1/9)</td>
</tr>
<tr>
<td></td>
<td>Bradykinesia (6/10)</td>
<td>Bradykinesia (6/9)</td>
</tr>
<tr>
<td></td>
<td>Postural Instability (1/10)</td>
<td>Postural Instability (0/9)</td>
</tr>
<tr>
<td></td>
<td>Rigidity (5/10)</td>
<td>Rigidity (4/9)</td>
</tr>
<tr>
<td></td>
<td>Tremor (5/10)</td>
<td>Tremor (4/9)</td>
</tr>
</tbody>
</table>

* PD severity reported on Hoehn and Yahr scale.
for both the TMW and TUG tests over the course of training (Experimental group: TMW ES = 0.68; TUG ES = 0.59; Active control group: TMW ES = 0.12; TUG ES = 0.07) (Table 2, Fig. 3).

3.4. Quality of life

There was a significant time by group interaction effect for the single index score of the PDQ-39. The ADL, Emotional Well Being, Cognitive Impairment, Communication, and Bodily Discomfort subsections of the PDQ-39 all approached significance for the interaction effects ($p < 0.05$ yet $> 0.01$). However with conservative correction to the a priori level of significance, none of these results reached statistical significance. Significant time effects were noted for the single index score, as well as ADL and bodily discomfort subsections ($p < 0.006$) Calculation of within group effect sizes demonstrated that the improvements in quality of life in the experimental group exceeded those demonstrated by the control group for both the single index score over the course of training (Experimental group PDQ-39 SI ES = 0.45; Active control group PDQ-39 SI ES = 0.08) (Table 2, Fig. 4).

4. Discussion

In this preliminary study, our overall hypothesis was that PD-related bradykinesia was in part reversible, and that high intensity loading of the quadriceps associated with our experimental group would result in amplified benefit in terms of increased movement speed and QOL relative to our active control group. Our results demonstrated that a 12-week program of high intensity eccentric resistance training can produce improved muscle force production, reduced bradykinesia, and improved QOL in persons with mild to moderate PD. These results occurred in the absence of significant changes in the UPDRS motor score. To our knowledge, this is the first clinical trial to demonstrate the effects of

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**Table 2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Eccentric ($n = 10$)</th>
<th>Standard care ($n = 9$)</th>
<th>Time × group interaction effects ($p$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS motor subsectiona</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More affected LE</td>
<td>10.75 (5.97)</td>
<td>9.00 (4.60)</td>
<td>16</td>
</tr>
<tr>
<td>Less affected LE</td>
<td>269.10 (85.69)</td>
<td>330.10 (92.54)</td>
<td>18</td>
</tr>
<tr>
<td>10 m walk (m/s)</td>
<td>1.74 (0.33)</td>
<td>1.97 (0.38)</td>
<td>12</td>
</tr>
<tr>
<td>Timed up and Go (s)</td>
<td>7.13 (2.19)</td>
<td>6.09 (1.44)</td>
<td>17</td>
</tr>
</tbody>
</table>

Abbreviations: Comm, Communication; Bod Dis, Bodily discomfort.

All data reported as mean (standard deviation). Reductions in PDQ scores reflect improvement (i.e., less disability)

*Note: Sample size for UPDRS, n = 8 per group due to missing data.*

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**Fig. 2.** Muscle force changes. Graphs of mean (SD) for both the more affected and less affected lower extremities. The experimental group (blue bars) demonstrated an 18% increase in the more affected extremity and a 13% improvement in the less affected extremity. The active control group (red bars) demonstrated a 4% increase in the more affected extremity and a 9% improvement in the less affected extremity.
high intensity resistance training on bradykinesia and quality of life in persons with PD.

Our muscle force results, although underpowered, corroborate previously published reports of high intensity resistance training in healthy elderly individuals and persons with PD [7–9]. All of these studies demonstrated what appear to be clinically significant improvements in muscle force production in persons with PD. The results presented here extend the results of previous research in that they demonstrate additional functional benefits of resistance training to clinical tests of their speed of movement (direct measurement of gait speed and ability to perform timed up and go) as well as self-reported QOL.

While improvements in force production and mobility measures provide evidence of the physiologic efficacy of resistance training, such results are of little relevance if they do not produce concurrent, clinically meaningful QOL benefits. The change in the overall PDQ-39 score induced by high intensity resistance training appears to have been driven in part by significant changes in the physical subsections (activities of daily living, bodily discomfort). These results are consistent with those studies that report improvements in disease specific QOL outcomes using other exercise modes [20–24]. While these outcomes appear to be clinically significant, their magnitude does not reach that reported as a result of surgical interventions such as deep brain stimulation. [25] Future research should examine the combined benefit of exercise and a medical or surgical intervention to determine if exercise complements and amplifies the benefit of these other interventions.

Although participants improved in some aspects of function and QOL, this change occurred in the absence of significant changes in the severity of motor deficits as measured by the UPDRS motor score. While the UPDRS changes observed in the experimental group exceeded those in the control group, these results lacked statistical power. Several previous exercise studies in persons with PD have reported smaller changes in the UPDRS motor scores than in other outcomes focused on mobility or QOL [5,21,23]. Considered in the context of these previous findings, the small within group effect sizes observed here for the UPDRS motor score suggest that it may be a less sensitive outcome measure for quantifying exercise mediated effects than walking tests such as the 6 min walk or the TUG. Future research should continue to utilize a spectrum of outcome measures that reflect disease severity, mobility, as well as QOL.

Our results add to a growing body of literature that suggests that persons with varied CNS pathologies (PD, CVA, MS) can experience strength, mobility and QOL improvements in response to exercise training [26–28]. The time and interaction effects of our interventions on both the physical subsections of the PDQ-39 and other psychosocial related subsections (Emotional Well Being, Cognitive Impairment, and Communication) suggests that aspects of the program besides exercise mode are important to participants’ QOL ratings. These results agree with recent reports in the literature regarding the positive effects of interventions such as counseling, support groups, and patient education and certainly argue for attention to the types of interactions the supervisors of any exercise program have with participants. [24–29] To our knowledge, there are no reports in the literature that examine combined resistance exercise and psychosocial interventions in persons with PD.

In conclusion, when taken together with previous resistance training studies in PD and our previous reports of safety and skeletal muscle adaptation, [6,30] the results of this preliminary study supports the inclusion of high intensity resistance training as a critical component of exercise interventions for persons with PD. In addition to studying larger samples with a broader range of disease severity, future studies should utilize random assignment to groups and employ well-validated measures of disease severity, mobility, and QOL. In addition, future studies...
should continue to follow participants after the intervention period to determine if continued adherence to a resistance exercise program is necessary to sustain any acute post-intervention benefits.

Acknowledgements

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References