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Enhanced Exercise Therapy in Parkinson's disease: A comparative effectiveness trial

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ABSTRACT

Objectives: Exercise can improve motor function in people with Parkinson's disease but depression reduces the motivation to participate in regular exercise. The aim of this study was to develop a novel Enhanced Exercise Therapy program that uses manual-driven guided exercise and peer-facilitated psychoeducation for individuals with Parkinson's disease and depression.
Design: 24 week randomized controlled design.
Methods: Thirty individuals were randomized to Enhanced Exercise Therapy or self-guided therapy, and evaluated at baseline, 12-weeks and at 24-weeks. Enhanced Exercise Therapy included group exercise and group psychoeducation for 12 weeks. Between 13 and 24 weeks, individuals had access to the fitness facility but group sessions were not held. Self-guided therapy included written guidelines for a self-paced exercise program and psychoeducation. Primary outcome measures included the number of exercise sessions and International Physical Activity Questionnaire score. Secondary measures included resting heart rate, supine blood pressure, estimated VO_2max and incidence of orthostatic hypotension.
Results: Twenty four individuals completed the study (80% retention) and both groups attended similar number of exercise sessions. There were no significant changes in cardiovascular fitness measures but there was a significant increase in the amount of physical activity in the Enhanced Exercise Therapy group and a decrease in the self-guided therapy group during the post-intervention period.
Conclusions: Enhanced Exercise Therapy appears to promote engagement in an exercise program and more physical activity, even after group sessions were concluded in individuals with Parkinson's disease and depression.

1. Introduction

Parkinson's disease (PD) is a progressive neurological disease that leads to significant motor deficits (tremor, bradykinesia, rigidity, gait impairments), physical inactivity, and apathy.[1] In addition, depression can promote loss of initiative and can decrease self-esteem and self-efficacy.[2] The incidence of depression in PD (PD-Dep) is estimated to be 30–50%.[3] Regular aerobic exercise improves motor function in PD[4,5] and the effects of exercise on depression are generally positive.[6,7] However, a significant barrier to physical activity is active engagement. Active engagement can be fostered through the integration of peers with PD and caregivers into an exercise program.[8,9] Development of community-based programs, which integrate peer advocates, are likely to empower individuals with PD to overcome physical and emotional barriers[10] to physical activity.[8,11,12]

This Enhanced Exercise Therapy (EXCEED) intervention combines psychoeducation with both peer support and exercise to take advantage of behavioral approaches, the positive effects of exercise on motor function and cognition, and the tremendous potential of individual empowerment to manage illness. Psychoeducation integrates psychotherapeutic and educational interventions to improve self-management and coping skills.[13] Combining psychoeducation with both peer support and exercise may enhance the value of either approach independently.[8] The peer support component was adapted from previous work, using peer educators to assist with health management in serious mental illness and diabetes.[14] The exercise component of EXCEED is unique because it focuses on

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interval high-cadence cycling and resistance training using equipment found in the typical fitness center. Previous studies have shown that high-cadence cycling can improve motor and cognitive function in PD.[15–17]

This study examined the impact of a structured exercise program paired with peer support and targeted psychoeducation on mood, mobility, fitness, physical activity and cognition in individuals with PD-Dep. The effects on mood and cognition will be reported in a separate paper. The goal of this paper is to demonstrate the effectiveness of this program by addressing three major questions: (1) Are individuals adherent with the program?, (2) Do fitness parameters change with this program? and (3) Does physical activity behavior change after the program is completed?

2. Methods

Thirty individuals with PD-Dep were recruited from the neurology practices and community support groups. All participants had (1) a diagnosis of idiopathic PD by UK Brain Bank Criteria, Hoehn and Yahr stage I–III; (2) a diagnosis of unipolar major depression and minimum Montgomery–Åsberg Depression Rating Scale score of ≥14; (3) the ability to walk independently; (4) no changes to current PD medication within the last 2 weeks and within the last 4 weeks for antidepressants. Individuals with MMSE score of <24, unstable cardiovascular disease, high fall risk, or who suffered from uncontrolled chronic conditions that would risk safety were excluded. Medical clearance for exercise was obtained from the primary physician. The study was approved by the Case Western Reserve University IRB and all participants provided written informed consent.

Individuals were randomized (1:1 ratio) into: (1) EXCEED (Enhanced EXerCisEthErapy) or (2) Self-guided exercise therapy (SGE). Study staff blinded to the group assignment performed the outcome measures. The EXCEED program included three components: Psychoeducation, peer education/support and manualized group exercise. All group meeting and exercise sessions were conducted at a local fitness facility. Study participants were asked to attend three exercise sessions (Monday/Wednesday/Friday) and one psychoeducational session (Friday) per week for 12 weeks and then were given a "continuing exercise manual" for the next 12 weeks. The SGE group was given a written manual of the informational materials delivered in the psychoeducation intervention, a self-guided exercise manual, free fitness center access for 12 weeks and a "continuing exercise manual" for the next 12 weeks. Fitness centers were open to the public so individuals could have contact with members who were not part of the study. Psychoeducation consisted of twelve 60-min group sessions. These sessions were outlined in a manual that emphasized problem-identification and goal-setting (Appendix 1). Sessions were co-lead by a nurse educator with expertise in PD and a trained peer educator with PD-Dep.

Peer-educators were individuals who have successfully managed PD-Dep and the ability to incorporate exercise into their life-style. They were asked to attend two half-day intensive training sessions that included interactive discussion of PD-Dep, as well as discussions regarding supportive listening, group leading, assistance with help-seeking pathways, crisis management and communication skills. After training, peer-educators participated in psychoeducation group sessions as a co-educator, taking an active role in the information-sharing and the question/answer portion.

Individuals in the EXCEED intervention received an exercise manual that outlined both resistance and aerobic training. The exercise sessions were three times a week for 45–60 min and were led by a certified personal trainer (ACE-PT). The program included small-group strength training with resistance tubing and high-cadence interval cycling on a spinning bike. All exercises were designed to minimize fall risk and the amount of time standing. During the high-cadence interval spinning (30 min), trainers started with 5 min of easy spinning and then encouraged the participants to increase their leg cadence up to 80 revolutions per minute (with music) for 1 min bouts, followed by 2–3 min of easy spinning for the next 20 min. Heart rate goals were within the 60–80% HRmax (heart rate maximum).[18] The sessions concluded with a 5 min cool-down of easy spinning. The resistance band program included four upper body exercises (Monday), four lower body exercises (Wednesday) and four combined exercises (Friday, Fig. 1). Spinning and resistance training intensity and difficulty progressed throughout the program. Resistance training progression was: week 1: No band, technique practice, weeks 2–3: 1 set/15 repetitions (reps), weeks 4–6: 2 sets/15 reps, weeks 7–9: 2 sets/12 reps, weeks 10–12: 2 sets/10 reps. If individuals could not complete the sets/reps, then they were instructed to choose an easier band.

The intent of the SGE intervention was to replicate the EXCEED activities in a self-guided format. The SGE intervention consisted of a written manual of the informational materials delivered in the psychoeducation intervention, as well as manualized self-guided exercise and fitness center access. Although this intervention provided flexibility in the timing of exercise, it did not include the group interactions or peer-education component. Individuals were introduced to the exercises by an exercise physiologist (ACSM Health Fitness Specialist). Personal trainers were also available to answer questions. Participants were asked to exercise three times per week and each received weekly phone calls during the first 12 weeks to report activity. The program included machine-based strength training and high cadence cycling on a recumbent exercise bike (Star Trac ERB recumbent). The SGE resistance program exercised the same muscle groups as EXCEED using Nautilus and Lifetime Fitness machines (Fig. 2). For the interval low-resistance cycling component, participants were instructed to warm up (first 5 min) at 50 rpm with low resistance (Level 1 or 2). During the high-cadence spinning (next 20 min), they were instructed to pedal between 80 and 90 rpm. Heart rate goals were 60–80% HRmax. For the cool down (last 5 min), they were instructed to return to 50 rpm. Cycling and resistance training intensity and difficulty progressed throughout the program similar to that describe in the EXCEED group (same sets and reps).

During the second 12 week period, individuals continued to have access to the fitness facility and were given a "continuing exercise manual" that included tips on exercise safety, the importance of continuing to exercise and directions on how to continue the exercise program. It suggested aerobic exercise (20–30 min, 2–3 times weekly, high-cadence stationary cycling), as well as resistance training 2–3 times per week. Both machine-based and resistance band exercise were illustrated in the manual (Figs. 1 and 2). Resistance training guidelines suggested using a weight that would allow for 2–4 sets and 8–12 repetitions for each set, as well as recommendations to increase the weight lifted every 4 weeks.

Primary outcome measures were number of exercise sessions completed and International Physical Activity Questionnaire (IPAQ) scores. Program adherence was determined by recording the number of exercise sessions over the 12 week exercise intervention. A research assistant recorded attendance in the EXCEED group and individuals in the SGE group were called weekly to record number of exercise sessions. Estimates of physical activity were calculated using the short form of the IPAQ[19] score at baseline, after the 12 week intervention and after the 12 week follow-up period (week 24). This questionnaire asked individuals to assess the days and time they spent in the last 7 days in four categories: (1) vigorous activity (heavy lifting, aerobics, fast bicycling), (2) moderate activity (light lifting, moderate bicycling), (3) walking (at least 10 min), (4) sitting (watching TV,

ARM/LEGS/HIPS	
Seated Upright Row Place tubing under your feet. Grasp the handles with an overhand grip and pull upwards until your upper arms are parallel with the floor.	
Seated Leg Extensions Begin by looping the center of the band around the ankle of your exercising leg. Bring the ends of the band underneath the foot of the opposite leg. Slowly extend your leg against the band, pulling forwards.	
Seated Chest Press Wrap the middle of the tubing behind you at shoulder level. Grasp the handles at shoulder-level and push forward, extending your elbows. Hold and slowly return. Keep your head and trunk upright.	
Standing Gluteal Hold onto the back of your chair with one hand. Wrap the band around your foot and hold onto the handles with the opposite hand. Kick your leg backward, keeping your knee straight.	

Fig. 1. EXCEED resistance band exercise manual sample of combined arm and leg exercise day. Bands of varying resistance were provided to the participants and the personal trainer assisted them to choose a band strength that was appropriate for the recommended repetitions and sets.

reading). Total physical activity was calculated as the sum of Walking + Moderate + Vigorous MET-minutes/week scores. The short form IPAQ data shows fair to moderate agreement with accelerometer measures in a large sample of 18–65 year old adults (Spearman correlation coefficients = 0.30) and is repeatable (Spearman correlation coefficients = 0.76).[19] Furthermore, IPAQ validity in adults over 65 is deemed adequate and is a useful tool for assessing physical activity.[20]

Secondary outcome measures were resting heart rate, supine blood pressure, estimated VO_2max (YMCA Submaximal Cycling Protocol),[21] measured prior to and after completing the 12 week exercise intervention, and incidence of orthostatic hypotension. This submaximal cycling protocol has been shown to be significantly correlated with a treadmill-based VO_2max measurements in both males ($r = 0.63$, $p \leq 0.05$) and females ($r = 0.90$, $p \leq 0.05$).[22] Individuals were fit to an upright cycling ergometer (Monark Exercise AB, Sweden) and warmed up for 3 min at 0 W and 50 rpm. During the second 3 min, load was increased to 50 W and heart rate was recorded during the last 15 s. Load for the subsequent two levels was determined based on the YMCA protocol. If the participant was unable to maintain 50 rpm at a given level for 3 min, the test was aborted. Orthostatic hypotension was defined as a systolic blood

ARM/LEGS/HIPS	
Seated Leg Press Lifetime Fitness Machine #34	
Compound Row Lifetime Fitness Machine #22	
Seated Chest Press Lifetime Fitness Machine #20	
Standing Gluteal Lifetime Fitness Machine #30	

Fig. 2. SGE resistance-machine exercise manual sample of combined arm and leg exercise day. Individuals were instructed to complete exercises on four machines in the fitness center. The personal trainer assisted them in learning to use each machine and in selecting the appropriate weight for the initial recommended repetitions and sets.

pressure decrease of at least 20 mmHg or a diastolic blood pressure decrease of at least 10 mmHg within 3 min of standing[23] and was assessed at baseline, after 12 weeks and after week 24.

Baseline demographic and fitness variables, between the two groups, and the number of exercise sessions attended were compared with independent samples *t*-test. Changes in cardiovascular fitness measures from baseline to post-intervention were compared between the two groups using an independent samples *t*-test. Cardiovascular parameters were not measured after the 24 week period. IPAQ scores were analyzed using mixed linear modeling over three time periods (baseline, 12 weeks, 24 weeks) and with participant level random intercepts and serial correlation structure. Inferential focus was given to time by group interaction effects. Results are presented as mean ± SD. All statistical analyses were performed using SPSS (Version 20; IBM, Somers, NY). Significance levels were set at 0.05.

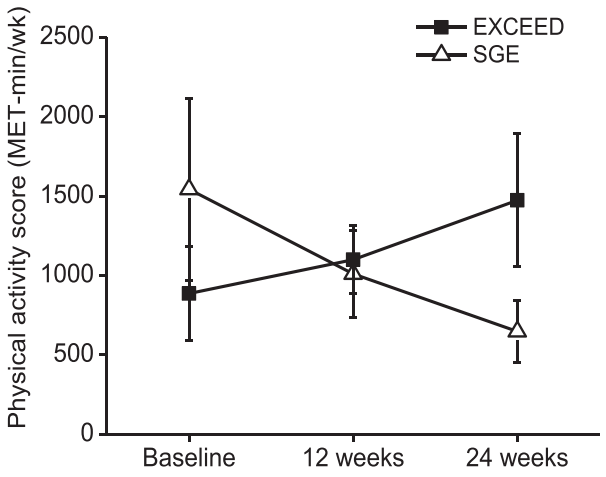

Fig. 3. IPAQ questionnaire. Individuals completed the IPAQ short form at baseline, 12 weeks and 24 weeks. Total physical activity in MET-minutes/week was calculated using the formula outlined in the IPAQ manual. There was a significant interaction between time and group ($p = 0.03$). Interestingly, there was an increase in physical activity in the EXCEED group over the course of the study and a decrease in the SGE group. This suggests that the EXCEED program promotes a continuation of physical activity even after the program was completed (week 24). Error bars – standard error of the mean.

3. Results

Thirty individuals were enrolled in the study ($N = 15$ EXCEED, $N = 15$ SGE; Supplemental Figure). Nineteen participants (63.3%) were male, 29 (96.7%) were Caucasian, and one (3.3%) was African-American. The average age was 70.2 ± 7.9 years (range 53–82). Body mass index (25.7 ± 3.4, range 16.8–31.4) was just above the lowest value for overweight individuals. Baseline resting heart rates (75.5 ± 12.9 bpm) were in the 'average to below average' category[21] and estimated VO_2max values (37.2 ± 15.5 ml/kg) were in the 'good' category for individuals 56–65 years old.[21] There were no significant differences in the age, height, weight, body mass index, resting heart rate, blood pressure or estimated VO_2max between the two groups at baseline (Supplemental Table 1). Levodopa equivalent dosages were significantly higher in the EXCEED group ($p = 0.03$) but UPDRS Motor III baseline values (off medication) were not different between the two groups at baseline.

There were no significant differences in the pre- and post-intervention values of resting heart rate ($p = 0.59$) or estimated VO_2max ($p = 0.86$). Blood pressure showed a decrease in both EXCEED (pre – 144/77; post – 135/71) and SGE (pre – 146/85; post – 136/80), but these differences were not statistically significant. At baseline, 3/12 (25%) of individuals in the EXCEED group showed symptomatic orthostatic hypotension and only 1/12 (8%) continued to have symptoms at the 12 week assessment. Only one person in the SGE group presented with these symptoms, which persisted after the intervention.

There were changes in self-reported total physical activity as reported with the IPAQ. Data from one individual in the SGE group was removed from the analysis due to likely overestimation of baseline physical activity (more than double the next highest value). In the mixed model, which was fit with an autocorrelation structure, there was a significant interaction in total metabolic equivalents between time and group (Fig. 3; $p = 0.03$). Specifically, the EXCEED group showed a 34% increase physical activity from week 12 to week 24 (after the formal intervention was completed) and the SGE groups showed a 32% reduction in activity. The difference in physical activity between the two groups at the end of the study (24 weeks) was 56% (EXCEED-1472.7 MET-min/wk, SGE-646.5 MET-min/wk).

Although the goal of the intervention was 36 sessions over 12 weeks, both groups attended similar number of exercise sessions (EXCEED = 20.7 ± 8.1, SGE = 22 ± 8.0). Missed sessions were not made up. The exercise program was safe and well-tolerated by this population. Three individuals dropped out of EXCEED for reasons unrelated to the exercise program. Two individuals dropped out of SGE due to arthritis pain and a recurrence of lower back pain, and one was removed from the analysis due to signs of dementia (Supplemental Figure). Therefore, overall retention was 80% in both groups.

4. Discussion

This study examined the compliance and effectiveness of an Enhanced Exercise Therapy (EXCEED) program, which combined psychoeducation, peer-education, and progressive exercise for individuals with Parkinson's disease and depression. We were successful in implementing the EXCEED and SGE programs over two six month blocks. The unique aspects of this program were that it was community-based, manual-driven, and supported by peer-educators with PD-Dep. A recent survey suggested that 87% of individuals with PD would likely participate in exercise if they had access to a community-based program (http://www.pdf.org). Community-based participatory research involving individuals with PD,[9] as well as multidisciplinary programs,[11,24] have documented improved physical activity.

A major hurdle to implementing an exercise program is participant engagement and retention. An additional challenge is the lack of motivation and self-efficacy often present in PD-Dep.[12] One of the advantages of EXCEED is the addition of small group training (social support), peer-educators (encouragement, behavior modeling) and manual-based exercises (direction, instruction). A retention rate of 80% suggests that this program provides a solid basis for future development of multidisciplinary interventions for PD-Dep. A limitation of this study, in regard to adherence, was the relatively low attendance rate for both groups (about 20/36 total sessions; 56%). This may be partially responsible for lack of physiological changes in these individuals.

Although there were no significant changes in cardiovascular fitness, it is possible that the YMCA cycling protocol was not ideal for this population. Although the cycling ergometer was appropriately calibrated, some individuals had trouble pushing on the pedals at the higher load levels. This limited our ability to record three levels of intensity. We suspect that the range of estimated VO_2max measures reflect this technical difficulty. However, the same ergometer was used for all measurements. Even though the absolute levels of estimated VO_2max may not have been accurate, the change from pre- to post-intervention is in the expected direction. Furthermore, blunted cardiovascular responses often occur during maximal testing in PD.[25] Future studies should utilize additional measures of cardiovascular fitness, such as the step test or peak VO_2, as well as strength and flexibility assessment.[5] However, there was a decrease in blood pressure over the intervention in both groups, as well as a decrease in the symptoms of orthostatic hypotension in the EXCEED group. Orthostatic hypotension is prevalent in PD (15–58%) due to cardiovascular autonomic dysfunction.[26] This can lead to increased incidence of falls[27] and could be a marker for disease progression and cognitive decline in PD.[28]

Although the levels of physical activity (IPAQ) were similar among the two groups after the 12 week intervention, individuals in EXCEED continued to be physically active after the group sessions were concluded, and participants assigned to the SGE decreased their activity. This finding is important because moderate levels of activity are defined as minimum total physical activity of at least 600 MET-min/wk (www.ipaq.ki.se). After the 24 weeks, the

SGE groups decreased their activity to 646 MET-min/wk, which approaches the 'low' activity category. The most novel aspect of this study is that the EXCEED intervention appears to have motivated individuals with PD-Dep to continue to exercise on their own after the group sessions were completed. This finding differs from recent work that failed to document an increase in physical activity, as measured with the LASA physical activity questionnaire, after a multifaceted behavioral change program (ParkFit[12]). In contrast to ParkFit, which used physiotherapists as motivators for behavioral change, EXCEED used peer-educators. This suggests that PD role models can promote active engagement in persons with PD-Dep.

Limitations to IPAQ results are significant variability among the participants scores and the fact that the IPAQ has been shown to result in over-reporting of physical activity in adults over 65.[29] There is also a possibility of recall bias in the IPAQ, as with any physical activity questionnaire.[30] However, repeated administration of the IPAQ should minimize these limitations.

5. Conclusion

This multidisciplinary intervention, that combines community-based exercise, peer-education and psychoeducation, promotes increases in physical activity in PD-Dep. Future research will refine this intervention so that fitness and improvements to symptoms are maximized.

6. Practical implications

- Enhanced Exercise Therapy (EXCEED), which combines manual-driven guided exercise and peer-facilitated psychoeducation, can be readily implemented in individuals with PD-Dep.
- EXCEED can promote increases in physical activity in PD-Dep.
- Peer-educators with PD can promote active engagement in persons with PD-Dep.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jsams.2015.01.005.

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