Influence of community-based group exercise on fall risk on Parkinson's disease

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10.3 Approach

10.3.1 Feasibility

The PI has in-depth experience researching kinematic outcomes related to falls in both cross-sectional and longitudinal studies of persons with PD and healthy older adults (Aim #1).[16,26,28,29] Our preliminary studies have recently demonstrated improvements in functional mobility in a small sample of persons with mild-to-moderate PD undergoing this intervention (n=5). A statistically significant improvement was found in the Timed Up and Go (TUG) score (a measure of balance and mobility) from baseline to the mid-point assessment (-2.1 seconds, p=.035). Our preliminary data also demonstrate a clinically meaningful effect of the intervention with an effect size of *d*=0.66.[15] Further, our preliminary data also suggests that of these 5 individuals tested thus far, 3 had primary deficits in anticipatory postural control adjustments at baseline according to the miniBEST test.[15] This data will be used to guide our hypothesis-driven Aim #1.

Based on our recent postural control studies following an 18 week rehabilitation program[30] with no participant dropout, no difficulties are expected in recruitment and retention of PD participants for the proposed longitudinal exercise studies.

10.3.2 Health Disparities in PD in Caldwell, Canyon County, ID

Treatment disparities and access to resources for persons with PD are prevalent across healthcare settings.[31] Specifically, resources for exercise and physical therapy are extremely limited in Canyon County due to the general health disparities in this region. We have specifically chosen to host our community-based exercise intervention in Canyon County because of its traditionally sparse access to healthy living resources. The Caldwell, Canyon County YMCA serves all of the western Treasure Valley region, where the average adult is less likely to be physically active than any other region of the valley.[32] Several factors may be involved in these differences, including less access to safe and affordable recreation opportunities such as parks, green spaces, and community recreation centers across the region, less access to healthy foods, and higher rates of poverty in Canyon County as compared to Boise.[33] Our intention is to provide our community-based intervention in this area specifically to increase access to healthy living resources for persons with PD in Caldwell and Canyon County, ID.

10.3.3 Research Design

Participants (aged 50 – 65; either sex, all ethnicities) will be recruited from local hospitals and clinics by various means, including physician referral or by response to flyer advertisements (see section 10.3.5) Potential participants will be screened over the phone regarding their possible inclusion in the study (see inclusion/exclusion criteria below). Among other things, participants will be asked if they have received a medical diagnosis of idiopathic PD from a neurologist, and if they have been medically cleared to participate in exercise by a physician.

On day one, participants will come to the Exercise Science laboratory at Idaho State University in Meridian. The PI will obtain informed consent and will complete patient screening according to our IRB approved research plan. Participants will be verbally asked for demographic information including name, contact information, ethnicity, age, gender, weight, height, and number of falls experienced over the past 3 months. Subjects will also take the Montreal Cognitive Assessment, which is a brief screening tool that provides a quantitative assessment of cognitive impairment.[34] The Hoehn & Yahr scale will be used to identify Parkinson's disease stage.[35] Participants meeting the inclusion criteria will be enrolled in the study and will undergo the baseline outcome assessments, which are described in the Section 10.3.4 below.

The intervention will take place at the Caldwell YMCA and consist of 12 weeks of exercise, guided by four certified personal trainers at the YMCA who are trained to work with individuals with neurologic conditions such as PD. All trainers have been trained to safely and effectively perform the balance activities that will be employed throughout the program. The head trainer has received a specialty certification in the boxing training program utilized in this study. A version of the proposed exercise program has been validated in a group of persons with PD previously.[23] Our incorporation of balance training activities into the program introduces a novel and essential ingredient for fall reduction to the program.

Each session will begin with a 10-minute warm-up of breathing and stretching exercises for major muscle groups in the trunk and extremities. This will be followed by a 45- to 60-minute circuit training regimen of function, balance, and non-contact boxing activities that alternate between 3-minute training bouts and 1-minute rest breaks. The functional training will incorporate activities for whole-body fitness and calisthenics, such as push-ups and reaching tasks that are tailored to each participant's capability, along with boxing ring work, which focuses on footwork and agility drills. The balance training activities will focus on tasks in the following areas: quiet stance, anticipatory postural adjustments, reactive postural adjustments, and dynamic

postural control (Table 1). Participants will be placed into groups for this section of the training so that each individual is assigned to work on activities focused on their area of greatest deficiency in the four balance domains. Each domain will be overseen by a specific trainer to ensure safety and continuity of the balance training within each group. The boxing activities will include punching heavy bags, speed bags, and focus mitts. Participants will not make contact with each other while boxing. Participants can pace themselves during the training sessions and take rest breaks as needed. The exercise sessions will end with a 15- to 20-minute cool-down that will emphasize core stretching and breathing exercises.

Table 1. Sample balance training activities focused on domains of balance dysfunction

Domain 1 (trainer #1): Quiet Stance	*Domain 2 (trainer #2):* Reactive Postural Adjustments	*Domain 3 (trainer #3):* Anticipatory Postural Adjustmts	*Domain 4 (trainer #4/head):* Dynamic Postural Control
Quiet stance w/ eyes open or eyes closed	Lean and release	Lower extremity reach (cone) training	Step initiation with light tracking resistance
Weight shifting	Pull test training	Standing and reaching	Ascending/Descending stairs
Sitting on stability ball w/rhythmic stabilization	Perturbation training in dual/single limb support	Gait initiation with resisted progression	Gait training with resisted progression

10.3.4 Outcome Measures

Outcome assessments will take place at baseline (i.e., approximately 1 week before the beginning of the training program (T0)), at 6 weeks (T6), and 1 week after the completion of the 12 week training program (T12), as well as 3 months after the training program. All of the outcome assessments up to T12 will be performed by the PI at the Exercise Science Lab while the participants are on their standard course of medication. Motor dysfunction will be assessed at baseline using the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS). The functional balance outcomes include: the mini BEST test (results of which will be shared with trainers at the YMCA for group assignment), the Activities-Specific Balance Confidence (ABC) scale, the Berg Balance Scale (BBS), the Timed Up and Go (TUG), and the Functional Reach Test (FRT). The kinematic outcomes from the hips, knees, and ankles of both limbs will be gathered using the VSTBalance during a straight line gait assessment at a self-selected pace. The infrared camera will identify the length of each lower-extremity segment (femur, tibia, foot) to derive the precise angular displacement (range of motion) occurring at the hip, knee, an ankle joints of each limb.[36]

For Aim #1 we will be assessing the relationship between modifiable factors and outcomes on mobility assessments. We will compare individual characteristics as follows to identify if they are related to the balance outcomes in our model: gait characteristics (stride length, step length etc), motor dysfunction on UPDRS, lower-extremity joint kinematic range of motion, and balance domain dysfunction at baseline. For Aim #2 we will be asking individuals at baseline to self-report the number of falls they have had during the previous 3 months. We will send a prepaid postcard in the mail 3 months after the completion of the training intervention, asking participants to report the number of falls they have experienced since the training ended.

10.3.5 Participants

Individuals with mild to moderate idiopathic PD will be recruited through various mechanisms including, PD support groups throughout the Treasure Valley (see support letter), the Movement Disorders Clinic at St. Luke's Medical Center (see support letter), the Neurology clinic at St. Alphonsus hospital, the VA Medical center, and through word of mouth from current participants already enrolled in the exercise program.

Inclusion Criteria: A diagnosis of idiopathic PD; Male or female ages 50-65, 30 years or older at time of PD diagnosis; Hoehn & Yahr (H&Y) stages 1.0-3.0; Ability to provide informed consent in accordance with Good Clinical Practice (GCP) and local regulations. Exclusion Criteria: Idiopathic PD H&Y stage 4-5, in order to constrain motor dysfunctions to mild-to-moderate PD; Confirmed or suspected atypical parkinsonian syndromes due to drugs, metabolic disorders, encephalitis, or degenerative diseases; Presence of definite dementia by Montreal Cognitive Assessment (MoCA <21); Central or peripheral nervous system disorders (other than PD); Myopathic disease (e.g. focal myopathy) that affects skeletal muscle structure/function; Severe cardiovascular disease that limits exercise abilities.

10.3.6 Sample size and Statistical analysis

Aim# 1 is the primary aim and based on our preliminary data with alpha=.05, a sample size of 20 will give 84% power to detect a relationship with an effect size of r=.60. The prevalence of PD in industrialized countries is estimated to be about 0.3%.[37] Using this estimation, we anticipate there to be approximately 2,129 persons in the Boise area with PD. Based on these factors we anticipate fully meeting our recruitment needs.

For Aim #1, the goal is to explore the relationship between modifiable factors and outcomes. Initially because of the exploratory nature of these explorations, change scores for the outcome measures will be

constructed. Bi-variate correlations, parametric and non-parametric as appropriate, will be used to access the strength of the relationship between individual outcome change scores and the modifiable factors. These results may be confounded by the progression of the disease, especially at the later measurement. Change in disease state will be introduced as a possible influence in partial correlations between modifiable factors and outcomes. Effect sizes will be calculate using Cohen's *d*.

For Aim #2 the interest is in the reduction of falls among this patient population. Initially to examine the changes in the number of falls a non-parametric McNemar test of change will be used. To examine other factors outside of the intervention that could influence the outcome will follow-up the analyses with McNemar test stratified by possible confounders (i.e. progression of the disease, continuation of the exercise regimen).

10.3.7 Expected Outcomes

At the completion of this investigation we expect to find that improvements in functional mobility following community-based exercise will be driven by stage of motor dysfunction, peak lower-extremity joint angular displacement, and balance domain dysfunction at baseline **(Aim #1)** (Table 2). These findings will enable a revolutionary approach to rehabilitation for persons with PD, by targeting rehabilitation techniques focused on each individual's modifiable risk factor(s). Finally, we expect to find that by focusing our intervention on the domain of balance dysfunction that is most impaired in individual participants, we will reduce fall incidence **(Aim #2)**. This will be a hallmark finding for the treatment of PD, as therapies thus far have been refractory to fall reduction.[7]

Table 2. Predictors of improvements in functional mobility

Predictors	Modifying factor	Interpretation
Motor dysfunction	Higher UPDRS scores (more advanced PD)	We expect that mobility improvements will be greatest in individuals with more advanced UPDRS stages.[4] This may be due to decreased economy of movement in persons with more advanced PD.[38]
Balance domain dysfunction at baseline	Domain 3: Anticipatory postural control	Based on our preliminary data[15] we expect that individuals with anticipatory postural control deficits will see the greatest improvements in function
Knee and ankle joint angular displacement during gait	Peak joint angular displacement (range of motion)	Increases in peak knee and ankle angular displacement after exercise suggest that individuals with PD may move with greater flexibility and confidence[16,17]

10.4 Potential Problems & Alternative Approaches

One potential problem with this clinical trial is that dropouts may occur. Our prior experience with longitudinal exercise studies suggests that we can expect a dropout rate between 5-20%. We have anticipated a very conservative 20% rate, and will recruit 4 additional participants over our sample size of 20. This will ensure an appropriate number of subjects completing the study to maintain the desired statistical power.

While we are attempting to limit the variability in participant outcomes by constraining inclusion criteria to persons with mild to moderate PD, this also poses a challenge in that many participants who volunteer for exercise studies are likely to be physically active individuals, which has the potential to dilute our treatment effect. This recruitment bias may also mean that few of these individuals will have experienced falls at baseline. In the event that non-statistically significant results appear, we have planned our analysis such that we can utilize clinically significant outcomes (eg., effect sizes) to overcome any potential recruitment bias and demonstrate the clinical impact of the intervention.

10.5 Future Directions

The proposed study will be the first to systematically examine the effect of an exercise program focused on non-contact boxing that is tailored to the domains of balance dysfunction on fall incidence in persons with PD. The accomplishment of these specific aims will lay the foundation for a subsequent NIH R01 application to the National Institute of Neurological Disorders and Stroke (NINDS), using a randomized controlled trial comparing the effectiveness of our exercise therapy versus traditional non-contact boxing on functional mobility and fall reduction in persons with PD. We anticipate submitting this application early in the second year after the conclusion of this study.

10.6 Timeline, Milestones, and Project Deliverables

Proposed timeline of 12 month investigation													
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**Yr.2**
Recruitment & Enrollment													
Intervention & Data Collection									(falls)	(falls)	(falls)		
Process & Analyze Data													
Project Deliverables and Future Grants													
Abstract & Manuscript Submission													
Write & Submit R01													

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