Effectiveness of the LSVT BIG™ Exercise Protocol on Measures of Balance, Gait, and Cardiovascular Fitness in Two Persons with Parkinson's Disease

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ABSTRACT

Case Background and Purpose. Parkinson's disease (PD) is a progressive neurological pathology which leads to a decrease in functional capabilities. Non-pharmacologic treatment programs do exist which can enable people to function better while living with this disease. The purpose of this study was to assess the effect of the LSVT BIG™ exercise protocol on measures of balance, gait, and cardiovascular fitness in two subjects with PD.

Case Description. The case study was an A-B design. Two individuals with PD consented to perform the outcome measures weekly for four weeks followed by four weeks of the LSVT BIG™ treatment protocol plus weekly testing. The outcome measures included Multi-directional Reach Test (MDRT), the GAITRite™ gait analysis system, electromyography (EMG), postural stability and limits of stability tests on Biodex™ Balance SD (BBSD), Functional Gait Assessment (FGA), Brief Balance Evaluation Systems Test (Brief BESTest), Five Times Sit to Stand (FTSTS), Six Minute Walk Test (6MWT), heart rate, blood pressure, and pulse oximetry.

Outcome. The two participants demonstrated significant benefits in the outcome measures used. However, the number of changed measures for each subject was not equal, due to differences in PD signs. PD05 was a better candidate as his primary signs were bradykinesia and rigidity.

Conclusion. Results of this study suggest LSVT BIG™ protocol may be used by patients with bradykinesia and rigidity as their primary motor signs of PD to help improve aspects of balance and gait. Further research is needed to solidify the results including more selective sample, larger sample size, and monitoring results of outcome measures post intervention period.

Key words: Parkinson's disease; LSVT BIG™; outcome, cardiovascular, fall risks

INTRODUCTION

Parkinson's disease (PD) is a progressive neurological disorder commonly characterized by symptoms of bradykinesia, rigidity, resting tremor, and postural instability. The cause of this disorder is not well understood but it is speculated to occur due to both genetic and environmental factors[1]. Despite not knowing the initiating factor, the pathogenesis has been observed to be a slow degeneration of dopamine-producing neurons in the substantia nigra pars compacta, located in the basal ganglia. Considering the nuclei of the basal ganglia are involved with regulation of motor function and require dopamine to function normally, loss of these dopaminergic neurons ultimately leads to the movement dysfunction found in people with PD[2,3].

There is no cure for PD, therefore treatment is directed in terms of symptomatic relief[4]. Medical management of PD usually involves the administration of levodopa due to the drug's ability to raise dopamine levels and dramatically reduce PD symptoms[3]. Despite the benefits, levodopa may also result in adverse side effects such as nausea, vomiting, cardiac arrhythmias, dyskinesias, and possible behavioral changes[2]. Also, one of the bigger issues with prolonged use of levodopa is decreased effectiveness over a period of years[2]. Other pharmacological options to manage PD do exist, but like levodopa, these drugs may come with serious side-effects.

Due to the side effects of pharmacologic agents, it is important to also explore non-pharmacologic treatments. Multiple activity-based treatments exist that have demonstrated significant improvement in different factors for people with PD[5,6,7] but still there is no conclusive research stating one treatment is more effective than another. The purpose of this literature review is to examine different treatment techniques to determine how those treatments relate to the possible success of using the LSVT BIG™ protocol as an option for people with PD.

Hackney and Earhart hypothesize that Argentine tango incorporates actions which specifically target PD-related impairments such as initiation of movement, weight shifting, taking steps in different directions, and making turns. Subjects participated in one-hour dance classes twice a week for twenty sessions. The subjects in the dance group show significant improvements in the Berg Balance Scale (BBS), Six-Minute Walk Test (6MWT), and backward stride length[8], suggesting Argentine tango may be a successful rehabilitation technique.

Tai Chi movements are mind-body exercises that incorporate a number of whole-body postures which are linked together in a continuous sequence. These movements emphasize weight shifts and slow, controlled movements of upper and lower extremities[9]. A systematic review examines ten articles to determine the effect Tai Chi has on PD subjects in terms of balance, mobility, functional reach, quality of life, gait quality, and fall risk[10]. Yan et al report a significant improvement in balance and mobility scoring of subjects with PD Tai Chi participation[10]. The researchers conclude that, because it involves joint control and muscle coordination, Tai Chi helps people with PD by promoting postural stability and balance[10].

Other studies have looked into the effect high-intensity exercises have on subjects with PD. Fifteen subjects underwent a sixteen week high-intensity resistance training program, performing exercises while maintaining a heart rate above 50% of their heart rate reserve. The subjects made improvements in strength, balance, neuromuscular control, and cardiorespiratory fitness[11]. In a different study, twelve subjects went through a personalized high intensity exercise program consisting of resistance, cardiovascular, balance, and flexibility training[12]. Results demonstrate significant improvements in activities of daily living, motor performance, and mentation for the subjects in the intervention group[12]. Morberg et al hypothesize one-on-one

training enables subjects to focus intensely on the exercises being performed due to guidance and cueing, allowing each subject to receive the maximum benefit of the exercise regimen[12].

Research suggests a treatment in high amplitude movements might be effective for people with PD. Berardelli et al. proposed bradykinesia is due to lack of recruitment of force during muscle activation, resulting in underscaling of movements[13]. This causes a need to perform multiple attempts to achieve targeted movement[13]. Bradykinesia may be improved upon by amplitude-specific training. Farley and Koshland hypothesize amplitude-specific movements of functional tasks target the pathological mechanisms that underlie bradykinesia in PD by promoting activation of basal ganglia pathways and slowing their decline[14]. Their study observes the effect of amplitude-based exercise and found this type of training results in an increase in speed of upper and lower limb movements. The researchers hypothesize amplitude training increased muscle activation which allowed the subjects to meet the force requirements to reach target distances with upper and lower limbs[14].

Different factors which made multiple PD treatments successful have been incorporated into the LSVT BIG™ protocol, which helps improve limb and trunk movement. The LSVT BIG™ program was developed from LSVT LOUD™, an established treatment to improve the speech motor system in people with PD[14]. The treatment principles of LSVT BIG™ are high intensity/maximum effort, high amplitude, repetition, and complexity with all movements[14]. The hypothesis behind these principles is that specific exercises will enhance function in targeted movements of the subject[15]. The BIG™ protocol, which includes part standardized exercises and part personalized exercises, is delivered by trained clinicians in one-on-one treatment sessions to ensure exercises are performed safely and properly.

The purpose of this study was to investigate the impact of the LSVT BIG™ protocol on two subjects with PD. The outcome measures were used to determine changes in balance, gait quality, and the cardiovascular system. The measures included the Five-Time Sit-to-Stand, Brief BESTest, Biodex™ balance testing, Multidirectional Reach Test, Functional Gait Assessment, electromyography, Six-Minute Walk Test, and vital signs.

METHODS

Participants

Approval was received through the Internal Review Board committee of Angelo State University. Volunteers were recruited at the local PD support group, where the researchers presented an overview of the project and welcomed interested members to participate. Two volunteers committed to the two-month research study and provided informed consent (Table 1). PD04 was an 81 year-old female with a 3.5 year history of diagnosed PD, with initial symptoms beginning approximately 20 years prior to the study. Participant PD04 was not an ideal match for the BIG protocol, as it was designed to address bradykinesia and rigidity while her primary PD sign was tremors. PD04 had the added caution of a history of surgically corrected cardiac valve. PD05 was a 63 year-old male with a 0.5 year history of diagnosed PD, with symptoms beginning approximately 1.0 years prior. Primary PD signs included bradykinesia and cogwheel rigidity, while mild extremity tremors and other secondary symptoms were also present. PD05 also reported cardiac issues of 10% arterial blockage and occasional palpitations with exertion. Cardiovascular objective measures as well as subjective symptom reports from both subjects were monitored throughout the program to ensure subject safety. Both subjects met the inclusion criteria of no fractures or orthopedic surgeries in past year, no history of stroke, and the ability to

understand and follow instructions, ability to walk independently 30 meters with or without an assistive device such as a cane or walker. Exclusion criteria included: deep brain stimulators, severe cardiac or respiratory issues that may limit participation in an exercise protocol, and cognitive impairments that prevent being able to follow commands.

Research Design

The single-subject A-B design study followed two subjects through baseline and intervention phases over the course of two months to assess effectiveness of the LSVT BIG™ exercise protocol on clinical measures of balance, gait, and cardiovascular system in participants with PD.

Outcome Measures

Participants were assessed at 8 time points: weekly baseline measure for 4 weeks prior to the initiation of intervention and weekly measures during the 4 weeks of intervention. Full outcome measure instructions are located in Appendix A.

Five Times Sit-To-Stand. Sit-to-stand is a key functional indicator of balance, more closely tied to the Berg Balance Scale than are muscle strength or exercise endurance via 6MWT.[16] For the Parkinson's population, a completion time greater than 16 seconds indicates fall risk.[17] As further discussed in the Instrumented Sit-to-stand section below, the activity of transferring from sit-to-stand is composed of four distinct kinematic phases requiring vastly different motor recruitment and momentum-transfer strategy to function optimally.[18]

Brief BESTest. This condensed version of the Balance Evaluation Systems Test (BESTest) was developed to maximize results within limited clinic time.[19] Minimally Clinically Important Difference (MCID) scores have not yet been established for this outcome measure, but the cut-

off score to determine fall risk in the PD population is ≤ 11/24[20] or 69%.[21]

Biodex™ Balance SD (Shirley, New York) (BBSD). This system provides both quantitative and qualitative data regarding a subject's ability to maintain their body's center of mass within its base of support.

Postural Stability. Greater amounts of body movement associated with an unstable posture produce a high stability index (SI); a low SI indicates little body movement and is associated with a more stable posture.[22] Postural instability tends to occur in the later stages of PD, so maintaining it through strength and endurance training may lead to increased quality of life and fewer incidences of falls.

Limits of Stability. Limits of stability (LOS) is tested on the BBSD via weight shifting to a visual target in eight different directions while maintaining balance on a platform via integration of sensory and motor control.[23] The BIG™ protocol emphasizes weight shift, so it would be expected to see improvements on this measure following BIG™ training.

Multi-directional Reach Test. Many activities of daily living require reaching in a variety of directions while safely maintaining balance. Safety cut-off scores for community dwelling elderly persons are 8.38 inches (21.29cm) forward, 4.06 inches (10.31cm) backward, 6.12 inches (15.55cm) to the right, and 5.67 inches (14.40cm) to the left.[24]

Functional Gait Assessment. This test measures safety with a variety of gait methods used in daily life. Since patients with PD frequently have difficulty with backward stepping such as when opening doors or avoiding collisions in a crowd, this measure was included in the study. FGA cutoff scores to predict fall risk are ≤ 15/30 in Parkinson's population[21] and ≤ 22/30 in community-dwelling older adults (sensitivity 85%, specificity 86%).[30]

Instrumented Sit-to-Stand, Gait Initiation, and Gait Analysis.

Patients provided informed consent to be video recorded for gait quality analysis.

Sit-to-Stand. The surface EMG electrodes record muscle activation patterns showing force generated and muscle work. The process of transferring from sit to stand may be broken down into four kinematic phases, each requiring recruitment and coordination of distinct muscle groups which were measured via surface electrodes placed on the tibialis anterior and soleus muscles bilaterally: Flexion Momentum, Momentum Transfer, Extension, and Stabilization.[18]

Gait Initiation. To initiate gait, the patient first needs to weight shift onto the intended stance leg. EMG activity is a means of assessing this muscle activation for gait initiation.[25]

Gait. Short shuffling steps and increased double limb stance time are hallmarks of Parkinsonian gait. The GAITRite™ Gait Analysis System measures step length and cadence for comparison over time. Ideally, the focus on large amplitude movements through the BIG™ exercise program would result in improvement in these measures toward normalization.

6 Minute Walk Test. This test measures overall endurance with gait, as well as cardiac endurance. As the subjects progress through the four weeks of BIG™ training, their distance measured by 6MWT is expected to increase. The MCID for geriatric and stroke population is 50 meters, or 164 feet.[26]

Vital Signs. Cardiovascular dysautonomia and autonomic nervous system dysfunction are common in PD, and roughly 50% of patients with advanced-stage PD have orthostatic hypotension.[27] Heart rate, blood pressure, and digital pulse oximetry were monitored throughout all sessions during the eight-week program to ensure safety during exercise, as well as to assess any changes that may occur to cardiovascular fitness.

Procedures

The data collection phase of study occurred over the span of 2 months which included 4 days of baseline measurements 1 day per week, 4 weeks of 4 days of intervention with 1 day of testing. Testing and interventions were performed at the same time of day across the study in an effort to standardize results across the participants' medication cycle.

Initial evaluations included a signed informed consent, with a copy provided to the participant. A brief medical history, physical, and neurological examination were completed with each participant.

Baseline Testing. 1 day per week for 4 consecutive weeks, participants were tested in the outcome measures described above to determine a consistent baseline level of function as well as determine the rate of change due solely to test-retest participant learning rather than intervention.

BIG intervention phase. A certified LSVT BIG™ therapist supervised trained examiners as they led participants through the program. Participants were scheduled for 4 consecutive days per week for 4 weeks, totaling 16 individualized sessions in one month. 60 minutes per session was allotted for performance of the intervention as well as for rest breaks, subjective reports, and review of daily homework. Each intervention session included all components of the LSVT BIG™ protocol as described on the LSVT site http://www.lsvtglobal.com/big-certification.

During intervention phase. On the fifth day of each intervention week, data collection of all outcome measures took place to determine any physiological and functional changes that may have occurred.

Data Analysis

Due to the single-subject design of the study, the most accurate depiction of significant

change required a change in the mean of two standard deviations. See Results section for further details.

RESULTS

Data for outcome measures are presented in figures. Figures contain baseline data points, during intervention data points, the mean, and two standard deviations. The mean in each figure is denoted by a dotted green line and significance level is represented with a dotted purple line. Notation of (SL; M) in results represents significance level (SL) determined from baseline mean ± 2 standard deviations; maximum change (M) during intervention phase.

PD04 did not demonstrate any conclusive trend in performance of FTSTS. While PD05 showed small improvement in performance of FTSTS (Fig. 1), he performed near age-related normal value throughout all data collection days[31]. Multi-directional reach results for PD04 were inconclusive for all directions (Fig. 2). PD05 showed significant decrease in forward reaching but did demonstrate upward trend in reaching backward (SL 12.08 cm; M 21.10 cm), to the left (SL 18.98 cm; M 21.10 cm), and to the right (SL 18.40 cm; M 22.40 cm). PD04 did not demonstrate significant changes in the Brief BESTest. The results for PD05 of the Brief BESTest show consistent trend during baseline and intervention phases, with results remaining near the ceiling of the test which has a maximum score of 24 (Fig. 3). When testing postural stability on Biodex™ system, there were no significant changes noted for either subjects (Fig. 4A). Limits of stability, which was performed on Biodex™ system, showed an overall increase performance of PD04 (SL 39.6 points on Biodex™ balance index; M 48.0 points on Biodex™ balance index) during intervention period, as compared to baseline, with emphasis on weight shifting backward, to the right, and to the left. The results of PD05 also demonstrated an overall increase in

performance (SL 95.8 points on Biodex™ balance index; M 88 points on Biodex™ balance index) during the intervention period, when testing limits of stability on Biodex™ system. Despite this overall improvement in limits of stability (Fig. 4B), significant improvement was only found when testing limits of stability when weight shifting backwards (SL 91.5 points on Biodex™ balance index; M 96 points on Biodex™ balance index).

The results for PD04 demonstrated a significant increase in performance for the FGA (SL 22.9 numerical total; M 26.0 numerical total) (Fig. 5). PD05 showed no significant change in FGA. The results in examining step length, step width, and velocity, showed no significant difference in either subject. Both PD04 and PD05 showed no significant improvement in muscle activation as evidenced by EMG (data not shown), due to several limitations discussed later in this paper. Both subjects show a positive trend in improvement on the 6MWT (Fig. 6). PD04's results were shown to trend into significance during the intervention period (SL 1264.5 ft; M 1268.0 ft). The results of PD05 were significant throughout the last 3 data points during the intervention period (SL 1840 ft; M 1924 ft).

Vital signs (Table 2) which include pre- and post-session blood pressure, heart rate, and oxygen saturation did not show any significant changes or trends.

DISCUSSION

Participant PD05 showed a positive change on most tests, while PD04 did not. PD04 demonstrated measurable improvements in balance, especially the Limits of Stability and FGA, while PD05 met ceiling effect on FGA due to his high level of function. The MDRT, Biodex™ Limits of Stability, and 6MWT were the most appropriate instruments to demonstrate change following the BIG™ protocol for PD05, whose symptoms more closely matched with the target

audience for BIG™.

Improvements to balance measures were anticipated due to the BIG protocol's emphasis on maximum effort in multidirectional weight shifts. Both subjects reported one fall each within the past year, indicating that while falls are only a mild concern at present, fall prevention training will be important in the near future. FTSTS greater than 16 seconds indicates fall risk in the PD population[17], so PD04 was considered a high risk for falls at baseline and PD05 was not. Also supporting this classification, PD04 began above the mean of 14.8 seconds for an 80-89 year old community-dwelling adult[31], again indicating an increased fall risk. Though performance improved in significance during the intervention period, by both of the clinical standards she remained at high risk following the study. Due to the fact that PD05's baseline scores in FTSTS were near the mean normal for his age group[31], the mild improvement seen is not considered clinically significant. Another fall predictor previously studied in the PD community is the Brief BESTest, which places cutoff score for falls at $\leq$ 11/24 points and mean normative score at 13.2.[20] By this standard, PD04 would not be classified as a fall risk and scored above average for a person with PD. This discrepancy in classification of risk demonstrates the importance of using various balance measures in the clinic. The Brief BESTest is more accurate at identifying non-fallers (sensitivity 76%, specificity 84%)[20] compared to the FTSTS (sensitivity 75%, specificity 68%)[17], as a possible correlation to the variety of balance components it challenges. However, due to the ceiling effect, it was not the most appropriate balance measure to detect change in active patients like PD05.

MDRT and Biodex™ Limits of Stability test are parallel fall prediction methods that analyze multidirectional weight shifting, which is an activity emphasized in the BIG™ protocol.

Especially difficult for patients with PD is backward weight shift due to retropulsion, secondary to loss of postural stability. As MDRT and Biodex™ LOS both demonstrate, more significance can be seen in backward weight-shifting scores for both subjects, especially PD05.

The large-amplitude movements and maximum effort of the BIG™ exercise protocol were anticipated to translate into larger, faster, and more efficient muscle activation and subsequent translation into functional movements such as sit-to-stand and gait. Despite EMG data showing inconclusive results, video footage of instrumented gait demonstrated qualitative clinical improvements in gait over the course of the intervention phase. This was especially noted for timing of weight shift and dorsiflexion during swing phase of gait. This may have clinical and functional applications in efficiency of gait and reduced fall risk.

On the 6MWT, PD04 showed a trend toward clinical significance in distance walked throughout entire intervention phase and passed significance on the last data point, though her progress did not meet the established MCID of 164ft for the geriatric population which would demonstrate improvement in gait speed.[26] PD04 exhibited kyphotic posture with possible stabilization via co-contraction to decrease the impact of tremors, which may relate to less improvement in distance walked. PD05's results surpassed both significance of two-standard deviations and clinical significance during intervention period and stabilized at approximately the same level on the last 3 data collection days, pointing to improvement in efficiency with gait. This was seen in PD05's increased trunk rotation, increased rate and amplitude of arm swing, longer step length, and increased cadence during 6MWT throughout the intervention phase.

Prior studies demonstrate that resistance training above 50% of heart rate reserve may lead to positive cardiac adaptation in endurance and efficiency[11], so the researchers hypothesized

that the BIG's™ emphasis on maximum effort may have similar effects. As previously mentioned, roughly 50% of patients with advanced-stage PD have orthostatic hypotension, which can also be worsened by various classes of PD drugs including levodopa carbidopa.[27] One study found an oral dose of 200 mg levodopa/50 mg benserazide to cause decrease in mean arterial pressure, cardiac stroke volume, and measures of cardiac contractility, which may lead to decreased cardiovascular performance.[28] In a systematic review, one study found lower systolic BP during exercise in subjects with PD, but results were not significant.[29] The results of our monitoring of subjects' vitals also did not show significant change with exercise, as both patients' medications included substances known to decrease cardiovascular response.

There were multiple limitations in regards to this study. Due to time constraints, this study was narrowed to an A-B design as opposed to an A-B-A design which monitors effect of BIG™ protocol past intervention phase. Therefore, it is impossible to determine how long positive effects lasted after the intervention phase concluded and if the subjects continued performing their home exercise program like the BIG™ protocol prescribes. Consequently, it cannot be concluded the benefits the subjects received from the BIG™ protocol continued past the conclusion of this study.

The limited number of people with PD willing to participate in four weeks of baseline testing followed by a four week exercise program lead to a convenience sampling of subjects who were not necessarily ideal candidates for the BIG™ protocol. PD04 was able to participate in all activities; however, upper extremity tremor often impeded performance during testing. Intensity of PD04's tremor varied on each testing day, resulting in variance of performance. Moreover, due to the small sample size, firm conclusions cannot be made from the results of the

study. With a bigger sample size of subjects, who exclusively have bradykinesia and rigidity, correlation of cause and effect would be more evident and definitive conclusions could be made with increased certainty.

Sensitivity of equipment was a significant factor affecting multiple outcome measures. Significant upper extremity tremor was a common sign of PD04 which made it difficult to attain accurate vitals. In addition, PD04 had limited circulation to the fingers, making pulse oximetry difficult and limiting its reliability. Also, despite PD05 being a more ideal candidate, slight tremor in multiple muscles of the lower leg caused interference when measuring muscle activation with EMG.

Future research should focus on the effect of balance and gait of people with PD who only present with bradykinesia and rigidity. This will allow for more accurate results from the subjects. Furthermore, the power of the results would also benefit from an increase in sample size. Researchers could then generalize conclusions to the PD population primarily affected by bradykinesia and rigidity. Lastly, focus should be placed on determining how long the effects last for people with PD who undergo the BIG™ protocol.

In conclusion, both subjects demonstrated significant improvement on multiple objective measures of performance following four weeks of LSVT BIG™ exercise training. PD05 proved to be the more appropriate candidate for the LSVT BIG™ due to his primary issues of bradykinesia and rigidity. However, due to limitations of study, conclusions cannot be generalized to PD population without further research.

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TABLES

Table 1. Subject Data

Subject	**PD04**	**PD05**
Sex	F	M
Age	81	63
Length of PD Diagnosis	3.5 years (20 years treated for tremor, which is present at rest and worsens with excitement or anxiety)	0.5 years (1 yr ago first signs)
Primary Symptoms ranked from most to least severe	Tremor Bradykinesia Rigidity	Bradykinesia Rigidity (cogwheel) Tremor
Secondary Symptoms	Right thigh dyskinesia, Difficulty swallowing	Stiffness in back and both hips after prolonged sitting, Dry eye, Double vision with fatigue, Difficulty swallowing, Vocal fatigue and decreased volume, Acting out nightmares, Pill-rolling tremor
PD Medication ● **drug class**	Ropinirole ● dopamine agonist Propranolol ● beta blocker Carbidopa ● DOPA decarboxylase inhibitor Carbidopa/Levodopa ● dopamine precursor	Azilect ● Monoamine oxidase inhibitor [MAOI] Vitamin D ● fat-soluble secosteroid

Table 2. Vital Sign Raw Data

2A. Blood Pressure Pre- and Post-Session

	Pre PD 04	Pre PD 04	Post PD 04	Post PD 04	Pre PD 05	Pre PD 05	Post PD 05	Post PD 05
Baseline/ Intervention	**Systolic**	**Diastolic**	**Sys.**	**Dia.**	**Sys.**	**Dia.**	**Sys.**	**Dia.**
B1	110	75	118	70	140	80	142	82
B2	125	75	138	78	138	85	142	82
B3	121	58	147	65	136	71	131	75
B4	126	75	146	67	130	76	142	73
I1	124	74	144	63	139	75	151	81
I2	141	68	128	58	160	82	156	78
I3	120	58	132	68	111	67	133	77
I4	114	56	126	63	119	68	137	75
	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg

2B. Heart Rate Pre- and Post-Session

Baseline/ Intervention	Pre PD 04	Post PD 04	Pre PD 05	Post PD 05
B1	55	92	48	51
B2	59	57	50	58
B3	60	54	58	64
B4	58	62	58	55
I1	57	63	49	54
I2	65	62	58	70
I3	60	54	61	70
I4	61	58	54	72
	bpm	bpm	bpm	bpm

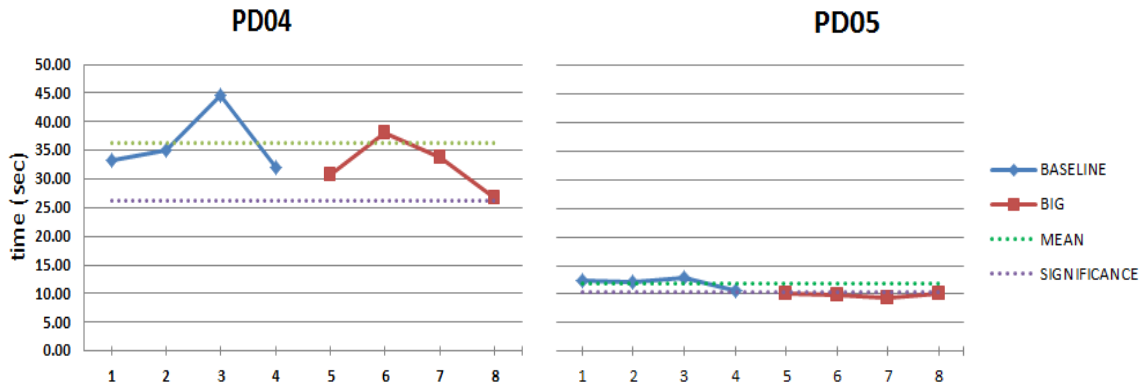
2C. Oxygen Saturation Pre- and Post-Session

Baseline/ Intervention	Pre PD 04	Post PD 04	Pre PD 05	Post PD 05
B1	94		97	98
B2	95	92	95	98
B3	99	99	98	99
B4	90	100	97	98
I1	97	83	99	99
I2	97	99	99	99
I3	98	97	97	98
I4	98	97	97	98
	% O2	% O2	% O2	% O2

FIGURES

The figures showing the data of the study have a consistent format. Unless denoted otherwise in the legend, the initial 4 data points represent baseline period and are noted with blue marker points which are connected with a blue line. The last 4 data points, which were taken during BIG™ intervention, are noted in red and connected with red line. The horizontal green dotted line represents the mean of the data points during the baseline period. The horizontal purple dotted line represents two standard deviations from the horizontal green dotted line and can be considered significant. The purple dotted line will be above or below the green line based on how the test is scored and if an increase or decrease in score demonstrates improvement.

Figure 1.

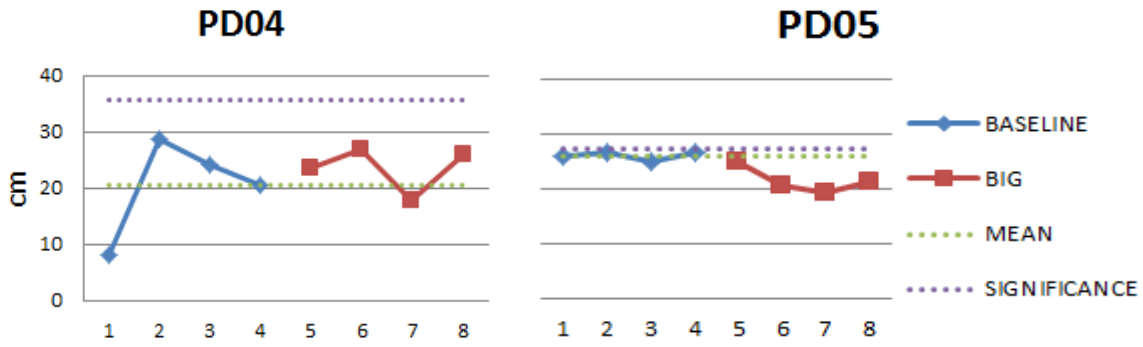


Five Times Sit to Stand

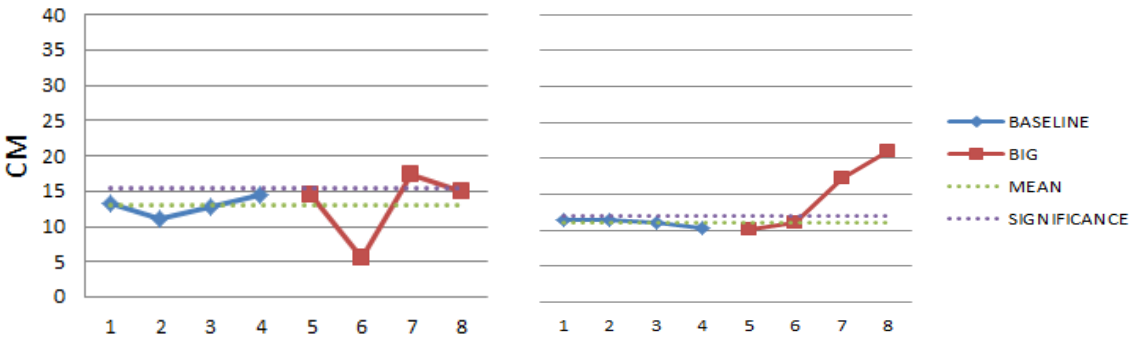
A decrease in time demonstrates improvement in performance with the FTSTS. PD04's performance was variable during baseline phase and during intervention phase. PD05's performance during the BIG phase was below 2 standard deviations of the mean, indicating a significant change.

Figure 2.

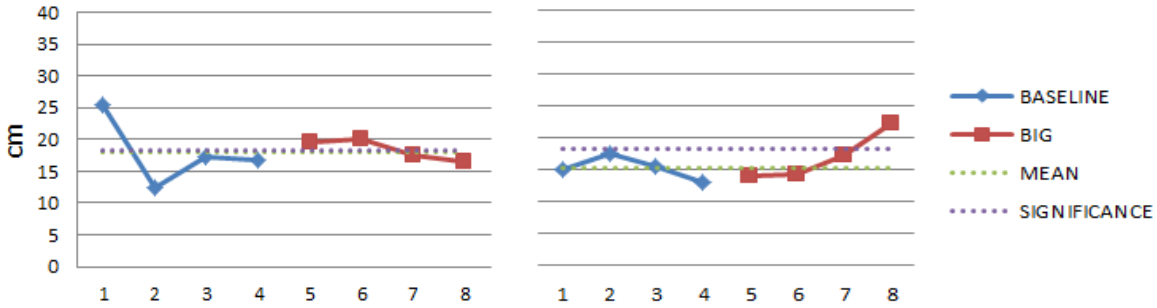
A. Forward



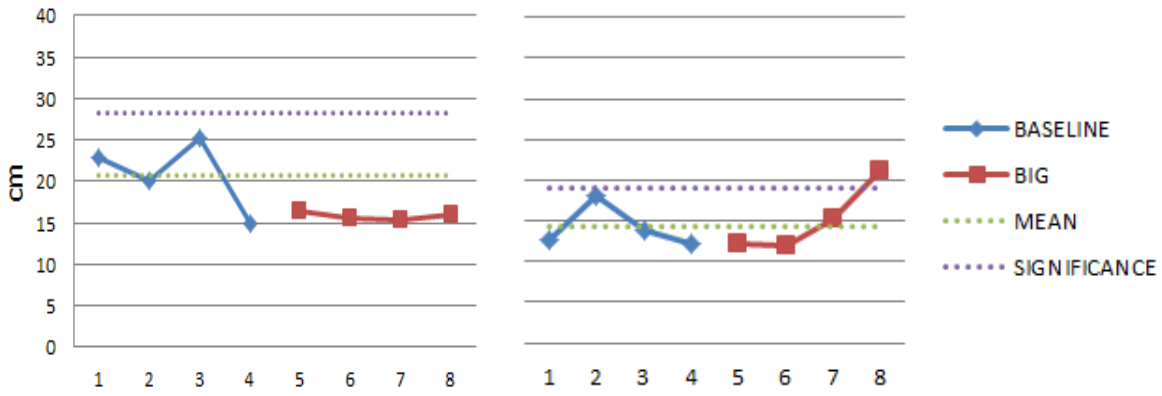
B. Backward



C. Right



D. Left

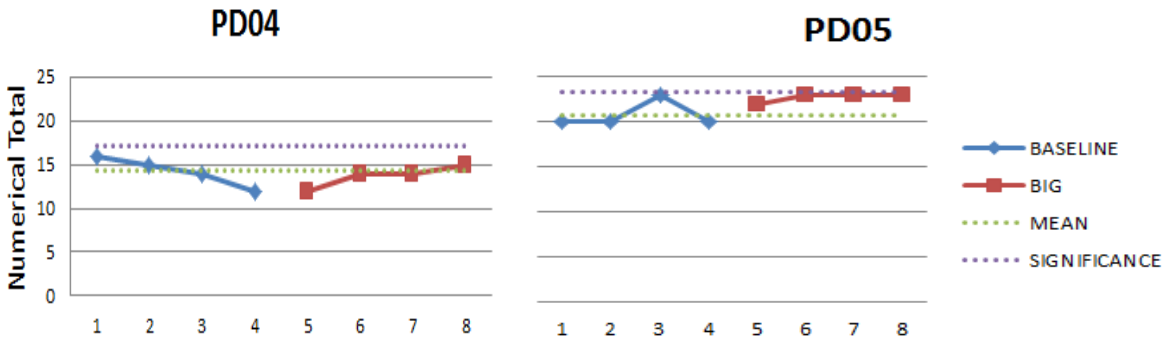


Multidirectional Reach Test

PD04: Overall the performance of PD04 during the MDRT was not constant during the baseline period. During the intervention phase, the distance reached to the right and left stabilized and did not change significantly from the baseline mean.

PD05: In contrast to the performance of PD04, PD05 was much more consistent in reach distances during the baseline phase. During the intervention, PD05 exhibited a significant loss of forward reach. However, the subject's performance in the other directions increased over the 4 weeks of intervention. Backward reach was found to cross significance threshold in data collection day 7 and continued to trend upward on data collection day 8. Right and left reach performance met significance level on data collection day 8.

Figure 3.

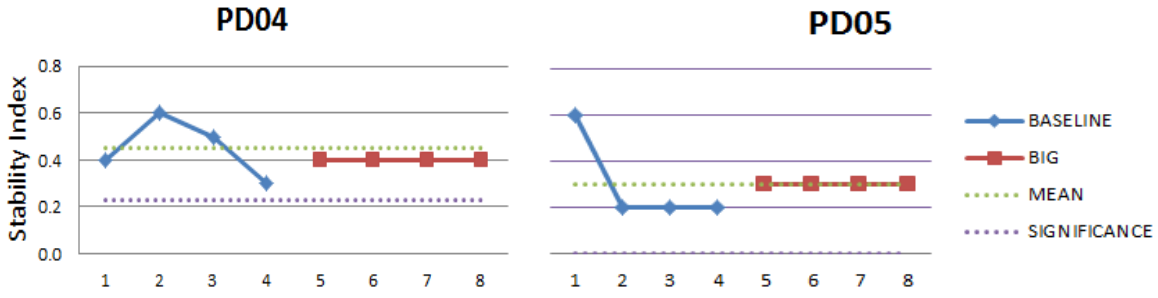


Brief BESTest

PD04 demonstrated trend toward significance during intervention period, however her results did not cross significant threshold at any time. PD05 initially demonstrated a positive trend toward significance but results did not vary throughout the last three data points during the intervention period due to subject reaching ceiling of this outcome measure.

Figure 4.

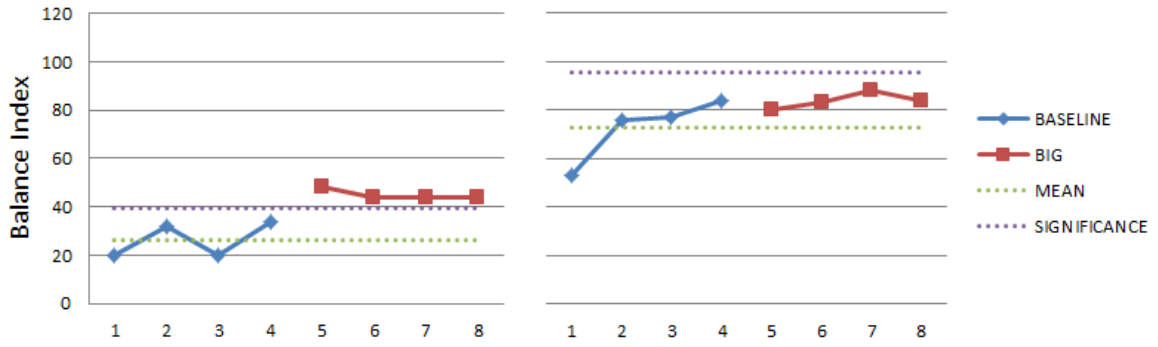
A. Postural Stability



Biodex™ Testing

This measure is used to determine static standing balance utilizing the Biodex™ balance system. A lower score on the balance index indicates improved balance while standing on a static surface. PD04 and PD05 demonstrated little change during the intervention period as compared to the mean of the baseline period. Also, no trends in a positive or negative direction can be noted.

B. Limits of Stability

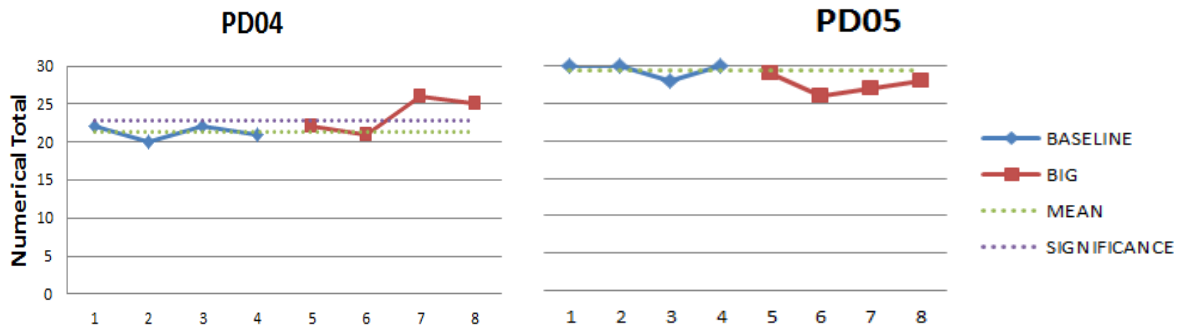


Biodex™ Testing

This measure is utilized to determine standing balance during weight shifts utilizing the Biodex™ balance system. A higher score signifies being able to maintain balance while weight

shifting in a given direction. All results for PD04 were found to be significant during the intervention period. The results for PD05 during the intervention period were not found to be significant but did demonstrate a positive trend toward significance.

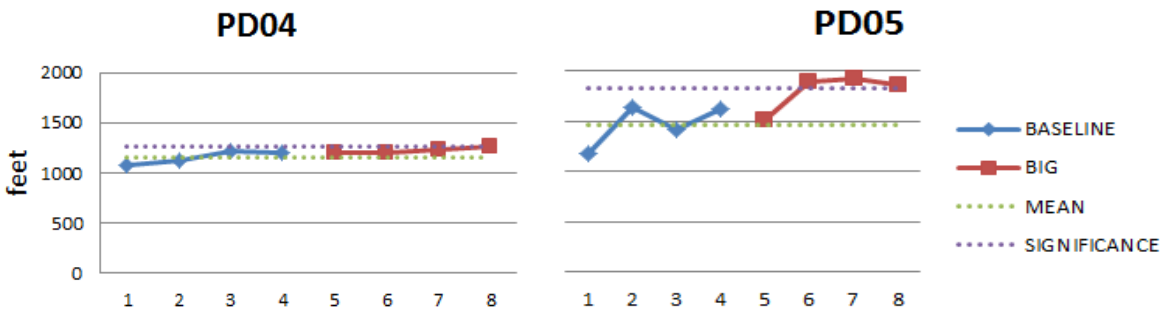
Figure 5.



Functional Gait Assessment

PD04 demonstrated a trend toward significance in the intervention period compared to baseline, and results were considered significant in the last two data points. PD05 demonstrated a decline in results without any perceivable trend. Due to ceiling effect, it would be impossible for PD05 to reach significant results since the FGA has a top score of 30 points and significance level is set above 30 points.

Figure 6.



Six Minute Walk Test

The results for PD04 showed a trend toward significance throughout the entire intervention phase and passed significance on the last data point. PD05's results surpassed significance during intervention period and stabilized at approximately the same level on the last 3 data collection days.

Appendix A – Outcome Measure Instructions

Five Times Sit-to-Stand (FTSTS). Participant was seated in an armless chair with a seat approximately 43 cm from the ground. Participant was instructed to cross their arms over their chest and sit with their back against the back of the chair. An investigator demonstrated the correct technique of task performance, including coming to a full stand with upright trunk and knees extended followed by sitting down with back making contact with chair back. Timing of the participant began when an investigator said 'go' and stopped when the participant's back reached the chair back after the fifth stand.[17]

6-Minute Walk Test (6MWT). One hundred feet of level tile floor was marked off by a cone at each end. Participants were given the following instructions: "When I say 'go', I want you to walk around the two cones. Keep walking until I say 'stop' or until you are too tired to go any further. If you need to rest, you can stop until you are ready to go again. I am interested in how far you can walk. You can begin when I say 'go.'" The following encouragements were provided:

1. After one minute "You are doing well. You have 5 minutes to go."
2. At two minutes "Keep up the good work. You have 4 minutes to go."
3. At 4 minutes "Keep up the good work. You have two minutes left."
4. At 5 minutes "You are doing well. You have only one minute to go."

Fifteen seconds prior to completion the participants were informed that time would stop shortly, and the test was stopped at six minutes. Total distance walked was measured. Throughout the test, notation was made about any rests and walking difficulties.

Functional Gait Assessment (FGA). The FGA consists of ten activities following standardized instructions and scoring by Wrisley and Kumar[30]. The ten activities are: Gait on a level surface, Change in gait speed, Gait with horizontal head turns, Gait with vertical head turns, Gait and pivot turns, Step over obstacle, Gait with narrow base of support, Gait with eyes closed, Ambulating backwards, and Steps. The standard distance is 20 feet for all activities except gait with a narrow base of support (12 feet) and stairs.

Multi-Directional Reach Test (MDRT). This test measures limits of stability in four directions was a clinical measure that approximates the Limits of Stability Test on the Biodex™ Balance SD described below. The participant stood with feet shoulder width apart and one arm raised to 90 degrees of shoulder flexion with the hand in a fist adjacent to (but not touching) the chalkboard. The body was aligned perpendicular to the chalkboard and the arm parallel. The investigator placed a mark on the chalkboard at the level of the third metacarpal joint, using a triangle ruler for accuracy. The participant was instructed to reach as far forward as he/she could while maintaining his/her balance and not moving his/her feet or taking a step. The investigator then made a second mark at the level of the third metacarpal's new position. Next the participant was asked to lean backwards as far as he/she could without losing balance or moving feet, and a third mark will be made at metacarpal level. The participant was then instructed to turn with his/her back parallel to the chalkboard and raise the right arm to the side at shoulder level. The investigator made a mark as described above. The participant was asked to reach to the right as far as possible without moving feet or taking a step. The investigator made another mark, and the process was then repeated with the left arm. The investigator recorded the distances reached and the preferred arm for forward and backward reach.

Brief BESTest. This test consists of 6 varying components of balance: Biomechanical constraints, Stability limits, Transitions-anticipatory postural adjustments, Reactive postural response, Sensory orientation, and Stability in gait. The standardized instructions and scoring by Padgett et al were used.[19]

Biodex™ Balance SD. This equipment system has a platform with sensors underneath to detect the changes in a person's center of gravity. The platform was stabilized (immobile) for the two tests. A monitor providing visual cues during the test was placed at eye level. Participants were permitted to use the hand rails when transitioning on or off the platform and at any time they felt unsteady. Prior to the testing, the participant's feet were placed in the standardized position (shoulder width apart with the anterior ankle centered anteriorly/posteriorly on the frontal axis of the platform). The first time on the platform, the participant's feet placement was traced onto a sheet of paper labelled with the participant's identification code to ensure consistency for all data collection sessions on the Balance SD.

a) *Postural stability*. This test examined the participant's ability to maintain center of balance. The participant was instructed to watch the monitor and try to keep the dot indicating center of balance aligned in the cross-hairs. The dot moved in response to the participant's postural sway upon the platform. The Balance SD recorded the amount of sway in all directions to compare the amount of sway to norms by age of participant.

b) *Limits of Stability*. This test challenged the participant's ability to move and control his/her center of gravity, a measure of dynamic balance. The participant aligned their center of mass by moving shifting on the platform to align the cursor on the screen with the center dot. One of

eight outer dots blinked, and the participant was instructed to move the cursor to the blinking dot by shifting his/her weight in that direction.

Instrumented Sit-to-stand, Gait initiation, and Gait

Common equipment for all three activities was electromyography (EMG) surface electrodes superficial to the gastrocnemius and anterior tibialis muscles bilaterally. Signals were sent to the computer via telemetry, and videos were taken during testing to enhance analysis. Once gait was initiated, the participant continued walking forward across the GAITRite™ mat. This rubberized surface had been embedded pressure sensors to track the interaction of the feet with the surface to provide information such as step length, step width, and gait speed.

a) *Sit-to-stand.* The participant began the test seated in the the standard chair used in the FTSTS and was given the instructions "Ready. Set. Stand."

b) *Gait Initiation.* From the standing position, the participant was given the instructions "Ready. Set. Walk."

c) *Gait from Seated Position.* From the seated position in the standard chair, the participant was given the instructions "Ready. Set. Stand and walk."

Cardiopulmonary. During each intervention day, the participant was asked to wear a Polaris heart rate monitor when performing BIG™ exercises to determine if their heart rate was within the training window for cardiac conditioning. Beginning and ending heart rate, as well as blood pressure via Dynamap or manual sphygmomanometer and oxygen saturation via fingertip pulse oximeter were recorded each intervention day. These vital signs were also monitored and recorded at various points throughout each exercise session to ensure subject safety.