

The Effects of Dual Task Training on Motor and Non-Motor Function in Individuals with Parkinson's  
Disease

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**Rationale and Impact:** Activities of daily living often require the ability to dual task (DT), or simultaneously perform two attention-demanding motor or cognitive tasks. The ability to perform DT activities, in particular tasks that require a level of postural stability, is a fundamental problem for individuals with Parkinson’s disease (PD).<sup>1-5</sup> Under DT constructs, individuals with PD typically exhibit a “posture second” strategy, where inadequate attention is allocated to gait and postural stability when challenged with a secondary task.<sup>1</sup> In contrast, young and healthy older adults exhibit a “posture first” strategy by prioritizing gait and balance over the cognitive task.<sup>1</sup> The “posture second” prioritization observed in PD may be a result of decreased attentional flexibility; thus when two tasks require concomitant attention, individuals with PD do not have the attentional flexibility to simultaneously attend to both tasks while controlling for motor deficits due to basal ganglia pathology.<sup>2,6,7</sup> Hence, DT situations lead to increased loss of balance and falls in the PD population compared to their age-matched healthy peers.<sup>3</sup> While these DT deficits in individuals with PD have been noted throughout the literature, there is a fundamental gap in understanding if DT deficits can be minimized through a behavioral intervention.

Single task (ST) training, defined as performing a motor or cognitive task in isolation, does not improve DT performance.<sup>8</sup> DT deficits can be minimized in older adults through DT exercise interventions, which range from seated exercises to treadmill training with concurrent cognitive tasks.<sup>8</sup> Several studies noted improvements in gait speed during DT constructs after DT specific training.<sup>9,10</sup> DT training programs have also demonstrated the ability to improve spatiotemporal characteristics of gait, cognitive performance, clinical measures of balance, and quality of life measures in older adults with a history of falls.<sup>11</sup> These DT therapeutic approaches have not been systematically evaluated in PD patients.

Individuals with PD demonstrate deterioration in stride length, step width, step variability, and walking speed in DT situations compared to performing walking alone.<sup>2</sup> Although the literature is sparse, the feasibility of implementing a DT training program has been investigated for individuals with PD, with results indicating efficacy through improvements in gait speed during DT conditions,<sup>12,13</sup> however, changes in non-motor outcomes have not been well documented. Additionally, it is not known how specific cognitive constructs affect gait. Stegemoller and colleagues suggested that cognitive processing speed correlated with stride length and walking speed, executive function correlated with step length variability, and that there were no significant associations with working memory for individuals with PD.<sup>2</sup> However, these individuals performed the gait testing and cognitive testing separately, so it is not known what occurs when these tasks are performed simultaneously.

Biomechanical systems, such as virtual reality (VR) training, used to assess and treat gait deficits and concomitantly provide a secondary motor or cognitive are promising treatment interventions for individuals with PD.<sup>14,15</sup> We propose that VR training may offer insight into the mechanism of DT deficits. Dr. Albert’s lab owns the one of two non-military installation of the Computer Assisted Rehabilitation Environment (CAREN), a VR reality system with a fully integrated 3-D motion capture system, a surround projection screen, dual belt treadmill with 6 degrees of freedom movable platform, two force platforms, a safety harness, and programmable software that can be used to create a variety of interactive modules (Figure 1). The interactive modules create either game-like or real-world environments that allow therapists to challenge the participant by altering either motor demands (e.g. virtual curbs, variations in walking



Figure 1: Module of wooded path on CAREN system. The treadmill (outlined in red) in front of the projection screen allows the individual feel like they are part of the scene.

surface, uneven surfaces) or cognitive demands (e.g. memory, attention, executive function) in a safe environment. The CAREN system is unique from other experimental environments due to the ability to create real-world environments (e.g. street scene with pedestrian and vehicle traffic, trail walking) in which the motor and cognitive aspects of function can be systematically manipulated and measured.

One of the greatest barriers to DT training is the lack of knowledge about effective clinical interventions.<sup>8</sup> The clear benefit to this highly-advanced system is opportunity to investigate mechanisms of dual tasking deficits in a given environment. For example, if participants with PD exhibit increased step variability and decreased stride length during visual memory cognitive tasks that are not seen during verbal memory cognitive tasks, this would provide valuable insight into task selection during a clinical intervention.

**The primary aim of the proposed project is to characterize DT deficits to improve motor, cognitive, and quality of life outcomes in individuals with PD.** A single center study is outlined in Figure 2. Phase 1 of the intervention will involve an in-depth gait analysis on 15 individuals with PD. The purpose of Phase 1 is to generalize characteristics of gait and postural control during specific DT conditions, as in the example provided above. Phase 2 (N=20) involves the clinical translation of these findings. This phase will involve creating a clinical intervention based on the objective information gathered from the CAREN system. Researchers will use the biomechanical data gathered from the CAREN system to prioritize interventions based on given gait and postural control deviations during DT interventions. To continue with the above example, if we find that visual memory tasks lead to decreased stride length, then the therapeutic intervention would be a task such as targeted stepping during gait (e.g. placing stickers slightly wider than normal step length on a treadmill) while performing various visual memory tasks. The intervention will take place 3x/week for a total of 8 weeks. Interventional groups will include: 1) DT clinical group (N=10) and 2) Single task group (N=10). ST training will serve as a control group.<sup>8</sup>

### **Specific Aims:**

#### **Aim 1: To categorize gait and balance deficits during DT constructs in individuals with PD.**

A three-dimensional (3-D) gait analysis using the CAREN system will be used during ST (walking alone) and DT conditions which consist of walking and completing tasks in the following cognitive domains: processing speed, visual memory, verbal memory, executive function, and attention (See Table 1 for cognitive tasks). Specifically, the CAREN gait analysis will examine spatiotemporal parameters of gait along with gait variability and joint angles. Additionally, a limit of stability (LOS) test will be conducted during ST and DT conditions.

*Hypothesis:* Gait parameters and LOS will be impaired under DT conditions compared to ST.

#### **Aim 2: To create and pilot a DT clinical intervention based on biomechanical analysis from the CAREN system that improves motor and non-motor function of individuals with PD.**

Primary motor outcome will include a 3-D gait analysis using the same parameters as stated in Aim 1. Secondary clinical motor outcome include distance walked during the 2 Minute Walk Test (2MWT) under ST and DT conditions. The Quality of Life in Neurological Disorders (Neuro-QOL) questionnaire will be administered as a quality of life measure. Fall risk will be assessed through the Activities-specific Balance Confidence (ABC) Scale. Cognitive measures, motor, and non-motor tests are described in Table 1.

*Hypothesis:* The DT clinical group will demonstrate the greater improvements in motor and non-motor function compared to the ST groups.

**Research Plan:** A total of 15 individuals diagnosed with idiopathic PD will be included in the initial gait analysis to categorize gait and postural control deficits associated with DT constructs (Figure 2). During Phase 1, all interventions will be carefully documented in order to attribute changes in gait parameters of postural stability with a domain of cognitive function. Phase 2 of the study (N=20) will randomize participants into two groups: 1) DT clinical and 2) ST (Figure 2). *Both groups will receive a time-matched intervention, 3x/week for a total of 8 weeks.* If an individual misses a session, he/she will be required to make it up on a different day of the same week or at the end in order for all 24 sessions to be complete. The entire intervention must be completed within a 10 week period. Intervention sessions for all groups will be completed under the guidance of a physical or occupational therapist who specializes in neurological rehabilitation. Outcome measures for Phase 2 will be administered at baseline, end of treatment (EOT), and EOT+4 weeks (EOT+4) by a blinded evaluator. The purpose of the EOT+4 testing is to gauge the permanence of the training intervention. All participants will be asked to wear a wrist-worn activity monitor that will measure steps/day throughout the duration of Phase 2 participation (baseline through EOT+4).

Motor, cognitive, and quality of life measures selected are described in Table 1. The Movement Disorder Society - Unified Parkinson's disease Rating Scale (MDS - UPDRS) will be taken at the beginning of both Phase 1 and 2 for demographic data. **Notably, cognitive tasks that are used for baseline and EOT evaluation will NOT be used during the intervention to ensure that a learning effect is not present.** Participants will take their PD medication as prescribed for all testing and interventions. If a participant has a life event (vacation, doctor's appointment, etc.) where they must miss a session, they will be permitted to make up the session. The total intervention duration cannot exceed 12 weeks from the date of the first intervention session.

**Dual Tasking Clinical (DT clinical):** Upon completion of Phase 1 of the study, a protocol for DT clinical training will be created based on the interventional gait analyses during various DT conditions. The DT clinical group will train in a traditional clinical rehabilitation environment. A variety of motor-cognitive or motor-motor tasks will be administered during balance and gait training (treadmill or over ground). Cognitive tasks will include processing speed, attention, memory, cognitive flexibility, and executive function tasks. Depending on the results of Phase 1, examples of a motor-cognitive tasks involving verbal memory may include recounting what he/she ate for breakfast this morning while navigating an obstacle course. Tasks will be graded based on the participant's baseline level of motor and cognitive function. The purpose of this group is to determine if a clinical

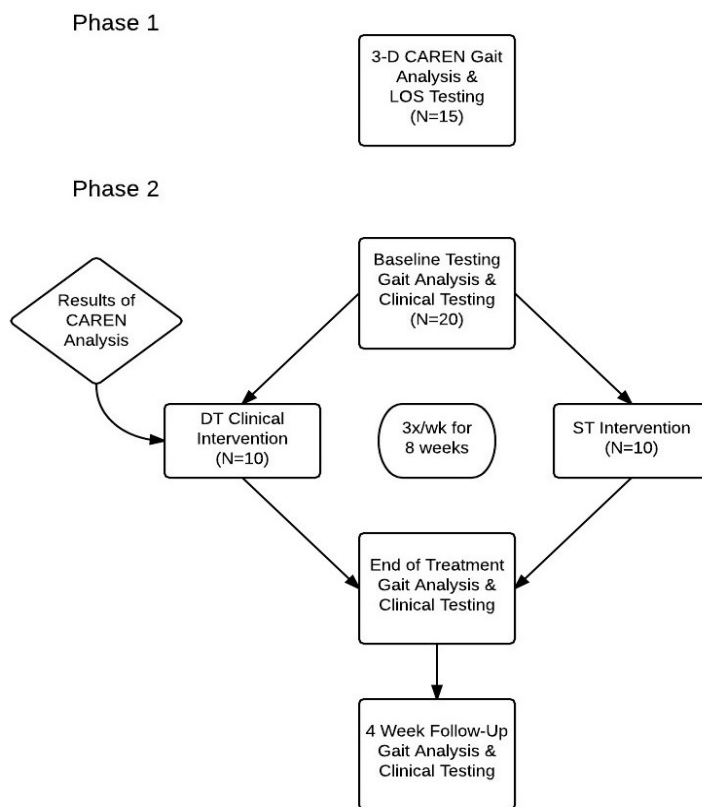


Figure 2: Study Flow Chart

intervention based on a biomechanical outcome is feasible and efficacious. The intervention will last approximately 45 min.

Single Task (ST): For this 45 minute session, individuals will perform 1) motor tasks; 2) cognitive tasks. An equal amount of time will be spent on the motor and cognitive tasks. Each task will be performed in a ST construct, where the participant will only have to focus on one task at a given time. Examples of ST motor include walking, static and dynamic balance activities such as single-leg stance or tandem stance, and reaching in various planes. Cognitive tasks will be administered with the participant in a seated position and include the same cognitive domains: processing speed, visual memory, verbal memory, executive function, and attention.

Table 1: Outcome Measures	
Outcome Measure	Function Evaluated
Motor Outcomes	
CAREN 3-D gait analysis during ST and DT (listed below) conditions to capture spatiotemporal gait characteristics	Objective quantification of gait during ST and DT conditions (e.g. step length, gait speed, step variability, kinetic and kinematic analysis and evaluation of ground reaction forces).
N-back test	Executive function, attention, and visual memory: participant is presented with a visual sequence of letters and is required to confirm the letter that is from N steps earlier in the sequence.
Stroop test	A measure of information processing speed; the participant is required to name the color that the word is printed, not the word itself. E.g. <b>BLUE</b> The correct response is red.
Repeating digit sequence	Verbal memory; participant is asked to repeat a string of increasingly longer digits
Serial 7s and arithmetic problems	Mathematical reasoning
Verbal fluency	Naming as many words as possible beginning with the letter “x”
2 Minute Walk Test (2MWT) under ST and DT conditions 1. ST walking only 2. DT Motor-Cognitive: 2MWT while performing serial 7 countdown 3. DT Motor-Motor: 2MWT while holding a cup of water $\frac{3}{4}$ full	Clinical measure of walking endurance both during isolated walking and during DT conditions; iPad will be worn on a belt on the back to capture asymmetry and sway
Limits of stability (LOS) test in the CAREN system (Phase 1)	Measure of postural control that quantify the maximum distance an individual can displace their center of mass within their base of support
Steps per day	Measure of physical activity behavior
Non-motor Outcomes	
Quality of Life in Neurological Disorders (Neuro-QOL) questionnaire	Quality of life measure specific to PD

Activities-specific Balance Confidence (ABC) Scale	Measure of confidence performing various activities without loss of balance or falls; predictive of recurrent falls
Cognitive measures performed during DT training and in a seated position	Measures cognitive function with and without (in a seated position) the coupling motor task
Tests using an iPad	Assessing information processing, vision, and balance
Questionnaires	Assessing falls, physical activity behavior, and quality of life

**Expected Results:** We anticipate that both DT and ST groups will improve motor and cognitive constructs in ST conditions. It is anticipated that the DT clinical group will improve compared to the ST group in both motor and cognitive performance during DT conditions, quality of life, and fall risk. We do not anticipate that DT constructs will change as a result of ST training due to specificity of training.<sup>8</sup> We anticipate that one of the hallmark findings of this study will be insight to which DT constructs result in specific gait and postural control changes. This will guide clinicians in selecting the most appropriate interventions for individuals with PD, and we anticipate this to be the most important findings of this study to guide future research and clinical decisions.

**Participant Screening:** Participants will be pre-screened by the study coordinator. The following inclusion/exclusion criteria will be used:

Inclusion Criteria:

1. Clinical diagnosis of idiopathic PD
2. Able to provide informed consent
3. Ability to ambulate  $\geq 300$ ft with or without an assistive device
4. Hoehn and Yahr stage 2-4
5.  $\geq 2$  fall related to PD in the past 12 months<sup>16</sup>

Exclusion Criteria:

1. Undergone any surgical procedure for the treatment of PD, such as deep brain stimulation
2. Those who have more than 2 uncontrolled cardiovascular risk factors (uncontrolled heart disease, uncontrolled diabetes, etc.) that would qualify them as a high risk exerciser
3. Musculoskeletal injury or neurological injury other than PD that would restrict physical activity
4. Inability to follow 2 step commands
5. Significant cognitive impairment as designated by  $\geq 3$  errors on the Short Portable Mental Status Questionnaire<sup>17</sup>

**Impact on living well with Parkinson's disease:** From a patient perspective, successful DT performance is required to complete most activities of daily living (e.g. looking both ways while crossing a street and processing information related to the environment, holding a conversation while completing activities of daily living, driving a car in an unfamiliar environment, etc.) and is associated with falls,<sup>3</sup> thus a DT deficit has a direct impact on quality of life. Currently, there is uncertainty whether rehabilitation specialists should incorporate DT training into a therapeutic exercise program, or if clinicians should avoid instructing individuals with PD to simply try to avoid DT activities during activities of daily living.<sup>18,19</sup> The latter approach is not only impractical but would potentially lead to greater isolation for PD patients, which has been shown to have a significant impact on quality of life.<sup>20</sup> A more empowering and sustainable approach is to better understand the DT declines and develop targeted intervention strategies to overcome these declines. The benefits of the DT interventions proposed are that they can be administered over a relatively short time period (conductive

for third party insurance payment) that is feasible in a clinical setting, and it can be modified by the results from high tech (VR) setting.

**Novel Aspects of this Project:** DT interventions are novel therapeutic interventions for PD. There are no studies that have examined DT interventions with the same rigor as proposed. This prospective, randomized study using a ST group as a time-matched control intervention has the potential to directly impact therapeutic treatment of individuals with PD. In addition, the VR intervention is novel technology that has the potential to capture more objective, biomechanical information. If biomechanical data gathered from the CAREN system is able to assist clinicians more appropriately select the ideal intervention, this could have an immediate impact on the way that DT is treated in individuals with PD.

**Data Confidentiality:** Study data that will be collected on the CAREN system will be de-identified using only the participant's study number. For purposes of the 3-D motion analysis, participants are videotaped; however this video will not leave the computer of the CAREN system without further written consent from the participant. Other outcome measures will be collected on Redcap®, a secure electronic database, where only research study personnel listed on this study submission will have access to the study data. Other electronic data will be labeled with only the subject number. The original signed and dated informed consent document along with any paper that may be used for data collection will be maintained in a study binder in a locked storage closet within Dr. Alberts' dedicated laboratory space in the Walker Building. The regulatory binder for this study will be kept in this same location, and only research personnel listed on this study submission will have access to this information.

**Potential Risks:** There are potential risks and discomforts to this study. There is a risk of muscle soreness and fatigue that comes along with exercising. There is a risk of falls in the clinical and VR setting, although in the VR setting participants will wear a harness to prevent falls. With the markers that will be worn for the gait analysis, there is a risk of temporary skin irritation. Although the intensity of exercise will be low, there is a risk of a cardiovascular event. All exercise personnel will be CPR certified and there is a medical emergency team located on site. There may be other risks with this intervention that are not yet known.

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