Grant Funding Research Update: February 2017
Study: DIVIDE Study
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Study Overview

Activities of daily living often require the ability to dual task (DT), or simultaneously perform two attention-demanding motor and cognitive tasks. Individuals with PD demonstrate deterioration in stride length, step width, step variability, and walking speed under DT conditions compared to walking alone. It is unknown how specific cognitive constructs (i.e. memory, attention, executive function, etc.) affect gait and postural stability during DT activities; and less is known about therapeutic treatment of DT deficits in this population.

This study consists of two distinct phases. Phase 1 will involve an in-depth gait analysis on individuals with PD. The purpose of Phase 1 is to generalize characteristics of gait and postural control during DT constructs using the CAREN system, a VR reality system with a fully integrated 3-D motion capture. Phase 2 involves the clinical translation of these findings by creating a clinical intervention based on the objective information gathered from the CAREN system. We will use the biomechanical data gathered from the CAREN system to prioritize interventions during DT interventions. The intervention will take place 3x/week for 8 weeks. Interventional groups will include: 1) DT group (N=10) and 2) Single task group (N=10).

Figure 1: CAREN system. The self-paced treadmill (outlined in red) in front of the projection screen allows the individual to be immersed in an activity or scene.

Phase 1 Aim: To categorize gait and balance deficits during DT constructs in individuals with PD. (N=15)
3-D gait analysis using the CAREN system will be used during single task (ST) conditions (i.e. walking alone) and DT conditions under the following cognitive domains: processing speed, visual memory, verbal memory, executive function, and attention. The CAREN gait analysis will examine spatiotemporal measures of gait as well as measures of gait variability.
Hypothesis 1: Gait parameters will be impaired under DT conditions compared to ST.

Phase 2 Aim: To create a DT clinical intervention based on biomechanical analysis from the CAREN system that improves motor and non-motor function of individuals with PD. (N=20)

Twenty individuals with PD will be divided into two intervention groups: 1) DT group (N=10) and 2) Single task group (N=10). Outcomes similar to Phase 1 on the CAREN system will be captured at baseline, end of the 8 week intervention, and 4 weeks post intervention. *Hypothesis 2:* The DT clinical group will demonstrate greater improvements in motor and non-motor function compared to the ST groups.

Study Progress Report: Phase 1

We were able to exceed target enrollment for Phase 1 due an enthusiastic response from the local PD community. With data collection complete, our analysis supports Hypothesis 1: Gait parameters will be impaired under DT conditions compared to ST conditions. Both spatiotemporal and kinematic gait parameters were impaired under DT conditions; results presented below. Demographic variables from 23 participants are presented in Table 1.

Table 1: Participant Demographics (N=23)	
Age, yrs, mean (SD)	63.6 (7.0)
Males, n	11
Disease duration, years, mean (SD)	6.2 (4.0)
Hoehn & Yahr, stage, mean (SD)	2.2 (0.5)
MDS-UPDRS III, mean (SD)	33.0 (13.1)
Number of falls in previous 12 months, mean (SD)	3.9 (9.0)

Data Dissemination: Phase 1

Poster presentations relating to the results of Phase 1 have been presented at the following national and international conferences:
1. World Parkinson's Conference (Portland, OR – September 2016)
2. Society for Neuroscience (San Diego, CA – November 2016)
3. American Physical Therapy Association Combined Sections Meeting (San Antonio, TX – February 2017)

A manuscript titled "Gait deteriorates under dual task conditions during a two-minute walk test in individuals with Parkinson's disease" is currently under review in *Archives of Physical Medicine and Rehabilitation*, a peer reviewed journal. Below is the submitted abstract with accompanying figures:

Background and Purpose:
Spatiotemporal gait impairments become exaggerated under dual task (DT) conditions in individuals with Parkinson's disease (PD). The aim of this study was twofold: 1) To determine how gait kinematics are impacted under DT conditions in individuals with PD; 2) To determine the validity of using overground ambulation distance relative to self-paced treadmill ambulation distance under single task (ST) and DT conditions in this patient population.
Methods: Twenty-three individuals with PD completed the Two Minute Walk Test (2MWT) under ST and DT conditions in two environments: overground and a self-paced treadmill in a biomechanics laboratory. Serial 7s arithmetic was performed during the DT condition. Primary outcomes were distance walked over both environments and kinematic measures during treadmill walking.

Results: Gait performance under the DT condition was characterized by a decrease in joint range of motion at the hip, knee, and ankle (Figure 2). Both methods of assessment, overground and self-paced treadmill, resulted in similar distances walked under ST conditions, 158.1±25.9 m and 149.2±25.0 m, respectively and under DT conditions, 131.7±29.9 m and 121.9±35.8 m, respectively (Figure 3).
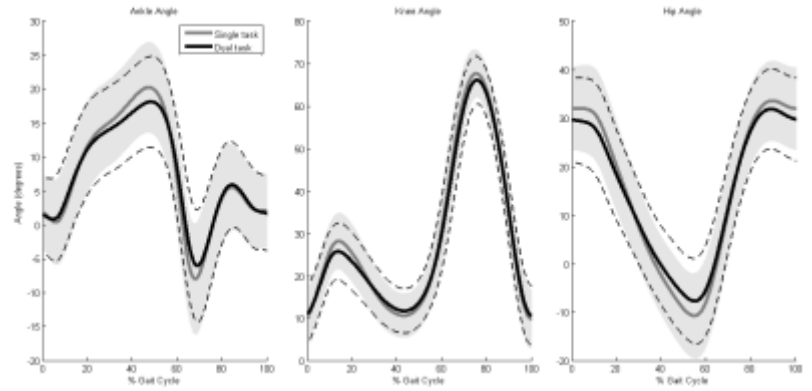

Figure 2: Mean range of motion (ROM) of the ankle, knee, and hip over a gait cycle. The grey line and shaded area represent the mean ROM, SD for the ST condition. The black solid and dashed lines represent the mean ROM, SD at each joint for the DT condition. Overall, ROM at the ankle, hip, and knee was significantly less during the DT condition. 0% of the gait cycle represents heel strike.
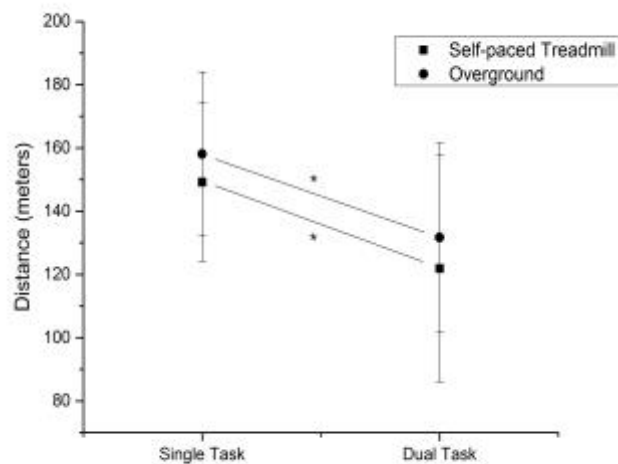

Figure 3: Distances walked during single and dual task conditions overground and over a self-paced treadmill on the CAREN system.

Discussion and Conclusions: Decreased distance and change in kinematic gait variables as a result of cognitive loading provides evidence that the automaticity of gait is significantly impacted by basal ganglia dysfunction in PD. The similarity between distances covered during overground and self-paced treadmill walking across ST and DT conditions supports using an overground paradigm for evaluating DT effects on gait in a clinical setting.

Study Progress Report: Phase 2

Upon analysis of Phase 1 data, we developed a physical and cognitive intervention to be implemented in Phase 2. We are currently in the recruitment and data collection stage of Phase 2. Individuals in the ST group receive 20-25 minutes of gait training, followed by 20-25 minutes of cognitive training in a seated position. Total training time is 45 minutes. Individuals in the DT group receive 45 minutes of simultaneous gait and cognitive training. All individuals exercise 3x/week for 8 weeks.

The cognitive training addresses 4 major domains: attention, memory, language, and executive function. Within each domain, there are varying tasks that can be graded by the study administrator based on the individual's baseline level of cognitive function. The gait training, overground or on a treadmill, addresses gait impairments that were observed in Phase 1 such as decreased velocity, cadence, step length, and arm swing. The gait training is administered by Dr. Rosenfeldt, a neurologically certified physical therapist.

Since last progress report, we have enrolled an additional 9 individuals, bringing our total enrollment to 17 individuals. We are on target to meet our recruitment goal of 20 subjects.

Preliminary Data: Phase 2

Individuals are tested on the CAREN system at baseline, end of the 8 week intervention (EOT), and 4 week follow up period (EOT+4) under the following conditions:

1. ST gait: gait alone
2. N-back: recalling previously presented letters (working memory)
3. Serial 7's: counting backwards by 7s (attention)
4. Digit recall: recalling increasingly challenging span of numbers (attention, memory)
5. Verbal fluency: categorical naming (semantic fluency)
6. Stroop test: naming the color of words. **BLUE** The correct response is red. (processing speed)
7. Motor: carrying a cone with a ball balanced on top

Figure 4 displays representative data from two study participants, one from the ST intervention group and one from the DT intervention group. Both participants improved their gait velocity by a meaningful amount (>0.1 m/s). Similar meaningful improvements were also seen in cadence, step length, and step width. While it is too early to draw conclusions about the interventions, these preliminary data are encouraging.
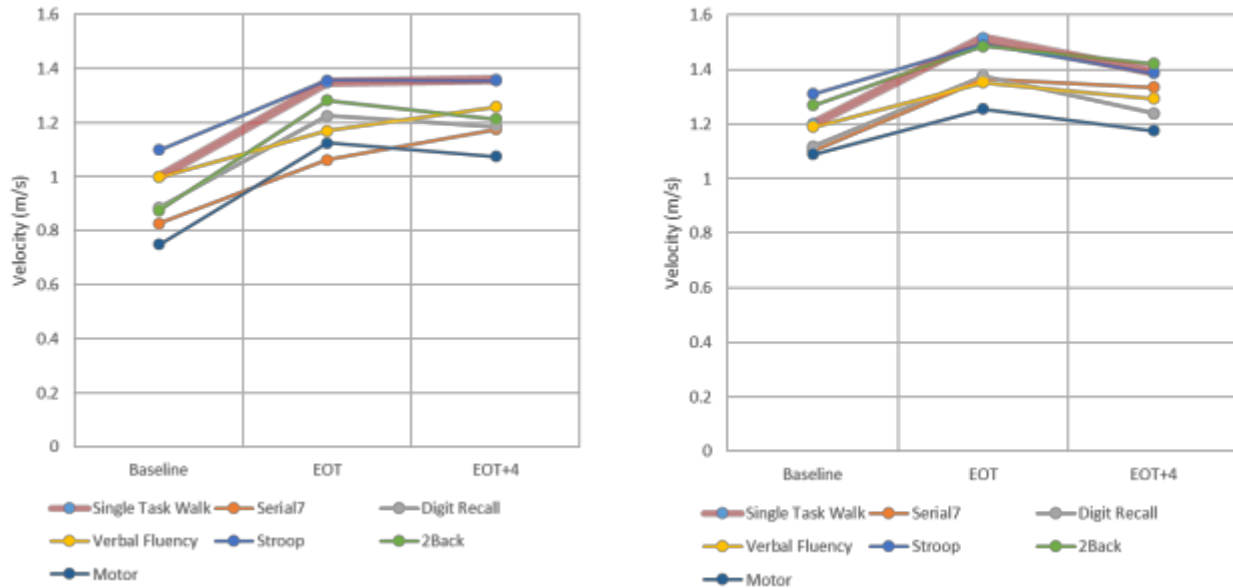

Figure 4: Velocity data from a ST participant (left graph) and DT participant (right graph) during walking alone and during six different dual task conditions. After the 8 week training, both participants significant' increased their gait speed during ST and DT performance, and maintained the gains at the 4 week follow up. EOT, end of treatment; EOT+4; end of treatment + 4 week follow up.

We are extremely thankful to the Davis Phinney Foundation for their support of this project. We anticipate that this study will add significant value to the PD body of literature and translate into improved motor and non-motor symptoms in this patient population.