TITLE: Dual-task Augmented Reality Treatment (DART) for individuals with Parkinson's disease and deep brain stimulation

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Project Goal: The goal of this project is to evaluate the safety and preliminary effectiveness of utilizing a digital therapeutic, Dual-task Augmented Reality Treatment (DART) protocol, for the treatment of postural instability and gait dysfunction (PIGD) in individuals with PD with a previously implanted deep brain stimulator (DBS).

Rationale: Postural instability is a cardinal motor symptom of Parkinson's disease (PD), and is often accompanied with non-motor symptoms such as cognitive impairment.[1] Activities of daily living (ADL) frequently involve the simultaneous performance of two or more tasks, such as crossing the street while holding a conversation. The cognitive demands of dual-tasking to perform routine daily activities may lead to increased fall rates relative to healthy peers.[2]

Multi-Modal Training in PD patients: In order to treat dual-task impairment (difficulty performing two tasks at once), multi-modal treatment (MMT)[3] was designed to target PD-specific declines in the areas of cognitive function and gait and posture impairments. Briefly, MMT training consists of simultaneously training a motor and cognitive task. The motor aspect of MMT stresses high velocity, high amplitude training principles while the cognitive aspect stresses commonly impaired cognitive domains in PD such as attention and executive function. An example of an MMT task is marching while spelling words backwards.

Delivery of a Digital Therapeutic via Augmented Reality for the Treatment of PIGD: The MMT intervention is well-suited for integration into an augmented reality (AR) platform as it consists of the patient performing a series of cognitive and motor tasks simultaneously while the patient receives knowledge of performance and results from a therapist. The Microsoft HoloLens is an untethered, AR headset used in applications as broad as teaching anatomy, displaying fine art and gaming. With AR, the user maintains contact with the physical world and the people in it. The HoloLens uses AR technology to place holograms, objects made entirely of projected light, into the user's physical environment; hence creating a first-person mixed reality environment. These holograms can be viewed from different angles and distances, can be two-dimensional or three-dimensional, can appear life-like, can move, be shaped, and change according to interaction with users' or the physical environment in which they are projected, depending on the programming. We previously developed the Dual-task Augmented Reality Treatment (DART), which delivers MMT training on a head-mounted AR display. The DART platform was successfully piloted in 50 individuals with PD who did not have DBS (IRB # 20-207). The results of the project indicate that DART is an effective method of training for individuals with PD. We plan to expand the impact of that project through the investigation of DART in individuals with PD who have previously undergone DBS surgery.

APPROACH: We will conduct a preliminary study with up to 5 participants to determine the safety and preliminary efficacy of the DART platform on individuals with PD and DBS. It is hypothesized that the DART platform will result in few adverse events and will be well-tolerated by individuals with PD and DBS.

Inclusion criteria:
1) Adult with a diagnosis of idiopathic PD
2) History of deep brain stimulator placement for treatment of PD

Exclusion criteria:
1) Medical diagnosis of dementia or any neurocognitive impairment that compromises the ability to provide informed consent.
2) >2 errors on the Short Portable Mental Status Questionnaire[4]
3) Musculoskeletal or cardiopulmonary issue that limits one's ability to engage in exercise
4) Neurological disease other than Parkinson's disease that impacts motor or cognitive function

DART Platform and Intervention: Up to five individuals with PD and DBS will receive the DART intervention. The 16 DART sessions will be delivered over an 8-week period (but not more than 10-weeks). Each DART session will consist of approximately 30-minutes of dual-task activity and will be scheduled over a 1 hour period. A physical therapist or physical therapist assistant will oversee each session. Exercises will be progressed based on results from the DART platform, feedback from the participant, and the clinical expertise of the physical therapist or physical therapist assistant.

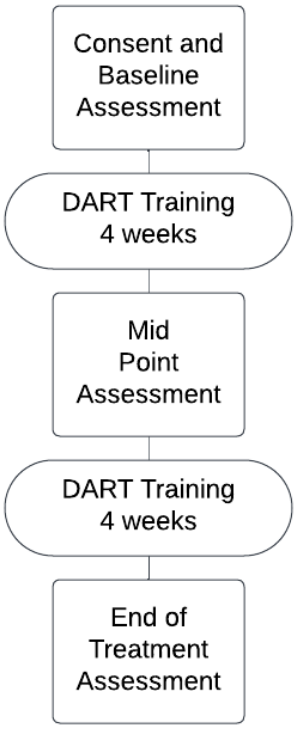

Figure 1: Study flow diagram.

Data Collection: Assessments of motor and non-motor function will be completed for all participants at the following time points: enrollment, midpoint, and end of treatment. Motor and non-motor outcomes are provided in Table 1. Assessments will be conducted in the "on-medication" state (PD medication ~1 hour prior to testing) and with the DBS set to their clinical settings. Research personnel will inquire with the patient during a scheduling telephone call, the timing of their PD medications. All appointments will be scheduled approximately 1 hour after dosage so as to not disrupt the participants standard medication schedule. The outcomes assessor (Dr. Anson Rosenfeldt, DPT) will not have access to training performance data; the physical therapist (Dr. Ryan Kaya, DPT) performing the training will not be privy to the outcome assessments. Medication reconciliation will be completed at each assessment and levodopa equivalent daily doses (LEDDs) will be determined. Demographic and outcomes variables will be recorded in RedCap. Training and some motor outcome variables will be collected on the HoloLens2. Only a subject ID will be associated with the HoloLens 2 and no PHI is stored on the device. Optional photo/videos will be recorded on willing participants with Dr. Kaya utilizing his CCF phone. Immediately after the appointment, any photo/videos will be uploaded and stored on a Cleveland Clinic computer behind CCF firewalls.

Table 1: Outcome Metrics		
Assessment	Description	Primary Outcome
Adverse events	Such as falls, dizziness, and others as a result of the intervention	Number of serious and non-serious adverse events related to the intervention
Two Minute Walk Test	Distance traveled during a 2-minute period under single- and dual-task conditions	Distance (meters)
MDS-UPDRS III	Clinical assessment of PD motor symptoms	Total score
Timed Up and Go Test (TUG)	Stand from chair, walk 3 meters, turn, return to chair under single- and dual-task conditions	Duration (seconds)
Postural sway	Amount of sway in multiple directions	Sway distance (cm)
Cognitive performance	During single- and dual-task conditions	Number of correct responses
System Usability Scale and other usability/satisfaction surveys	Usability of HoloLens and DART protocol technology	Total score
Activities-specific balance confidence scale (ABC)	Balance confidence during daily tasks	Total score
Fall Diary	To track fall events	Number of falls

Power and Statistical Analysis: The sample size (N=5) is reflective of the preliminary nature of the study. A repeated measured ANOVA will be used to compare the group at the three different time points (baseline, midpoint, and end of treatment).

References:

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4. Pfeiffer E. Short Portable Mental Status Questionnaire for Assessment of Organic Brain Deficit in Elderly Patients. *Journal of the American Geriatrics Society*. 1975;23(10):433-441. doi:DOI 10.1111/j.1532-5415.1975.tb00927.x