Study Protocol/Statistical Analysis Plan
Evaluating Technology-Based Fall Prevention Interventions
NCT03190460

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Objectives

The primary study objective is to explore the effectiveness of a 16-week cognitive training (CT) intervention to reduce risk and incidence of fall in community-dwelling older adults at risk for fall. Additional objectives of the study are to explore the effectiveness of a CT intervention on cognition and functional outcomes and to examine the feasibility and acceptability of the study protocol and intervention in this population.

Outcomes

Primary Outcome. At time of allocation, participants will be provided with a Monthly Fall Calendar and instructed in its use. At the end of each day participants are asked to place one of 3 letters in the box for the day: "N" for no fall; "F" for fall; and "I" for fall resulting in an injury), considered the "gold-standard" for falls assessment (See Table 1). For purposes of this study, a fall was defined as an "unintentional For individuals who experience multiple falls in a single day, they are asked to denote the number (ex. "F-2"). Fall calendars will be collected monthly (See Table 2), and a new calendar provided to the participant during the study period. The time period for primary outcome assessment is falls over the period of 4 months. For any fall resulting in injury, we will request permission from the participant to obtain medical records for any treatment sought at time of injury.

Secondary Outcomes. Of interest as a secondary outcome in this study is reduction in risk of fall at the end of the 16-week intervention (See Tables 1 and 2). This is defined by 1) an increase in the 10M walking speed from baselineor 2) an increase in the Balance test score from baseline.[40] As secondary endpoints, we will measure cognitive outcomes (using the Cambridge Neurological Assessment Battery [CANTAB]), additional gait and postural sway measures (using body-worn inertial sensor system, the APDM Mobility Lab, Portland, OR; See Tables 1 and 2), and disability (Gill Disability Scale). We will explore if there is retention of benefit of the intervention on fall risk, gait, balance and cognitive outcomes one month following end of the intervention. Feasibility and acceptability of the study protocol and CT intervention will also be evaluated.

Table 1. Summary of Outcome Measures and Source of Measurement

Measure	**Source (Instrument/Test[s])**
PRIMARY OUTCOME	
Falls and Injurious Falls	Self-Report (Prospective Fall Calendar)
SECONDARY OUTCOMES	
Fall Risk	10M Walk Test 90 Second Balance Test
Cognition	CANTAB
Speed of Processing & Response Time	Simple Response Time
Attention	Rapid Visual Information Processing
Working Memory	Verbal Recognition Memory
Task Shifting	Spatial Working Memory
Planning and Decision Making	Intra-Extra Dimensional Set Shift

	Cambridge Gambling Task One Touch Stockings of Cambridge Stop Signal Test
Quantitative Gait and Turning Measures Gait speed (m/s) cadence (steps/min) stride length (m) turn duration (s) turn peak velocity (m/s)	APDM Inertial Sensors Walking trials under testing conditions of: Usual Pace 4-Meter walking laps x 4 Usual Pace 7-Meter walking laps x 2 (if space allows) Fast Pace 4 or 7-Meter walking laps x 2 (space dependent)
Postural Balance Measures: (medial heel-to-medial heel distance = 10 cm) ISway JERK (m^2/s^5) ISway PATH (m^2/s^2) ISway Mean velocity (MV; m/s) ISway Root mean squared (RMS; m/s^2)	APDM Inertial Sensors (ISway): (Inertial sensor at 5th lumbar level) Static Standing 30-second trials under six conditions: normal base-firm, eye open and eyes closed; narrow base-firm, eye open and eyes closed; normal base, foam surface, eye open and eyes closed
Disability	Gill Disability Scale

Study Design

The design is a two-group randomized controlled trial following a 1-week run-in procedure comparing 16-weeks of a web-based CT intervention to attention control (See Table 2).

Baseline Visit (-T1)

If eligible for inclusion after the in-person screening, the research staff member discusses the project in detail with the individual to ascertain interest in further participation and to allow for provision of informed consent. Following informed consent, the baseline visit commences. At this visit, participants are asked about a) demographics (age, gender, race/ethnicity, formal education, income level, insurance status); b) pre-existing conditions (Charlson method); c) current medications (brown bag method). Questionnaires are administered to participants at baseline to assess: 1) social support (MOS Social Support Survey) and 2) functional status (Gill Disability Scale). Participants undergo an assessment of cognitive abilities using the Cambridge

Table 2. Study Protocol (*denotes data are collected, but is secondary outcome)

	Study period							
		Enrollment	Allocation	Post-allocation				Exit
Time point	-T2	-T1	T0	T1 (4 wks)	T2 (8 wks)	T3 (12 wks)	T4 (16 wks)	T5 (20 wks)

Eligibility screening								
Phone screening	X							
In-person screening								
10M walk		X						
90 sec balance		X						
Informed consent		X						
Run-In Period								
Vision screen		X						
Medication review		X						
Home safety check		X						
Allocation			X					
Intervention								
Active Control				XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX	
Web-based Cognitive Training				XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX	
Assessments								
Baseline								
Demographics		X						
Pre-existing conditions		X						
Medications		X						
Social Support		X						
Outcome Variables								
Primary								
Falls/Injurious Falls				**X**	**X**	**X**	**X**	*
Secondary								
Fall Risk								
10M walk		X			X		X	X
90 sec balance		X			X		X	X
Cognition								
CANTAB		X			X		X	X
Gait/Turning								
APDM		X			X		X	X
Postural Sway								
APDM		X			X		X	X
Disability								
Gill Disability		X			X		X	X
Other Variables								
Short Physical Performance Battery		X			X		X	X
Timed Up and Go		X			X		X	X
Exit Interview								X

Neuropsychological Test Automated Battery (CANTAB) to provide an external method of assessment to that provided by the CT intervention (See Table 1 for specific tests). Lastly, in-home gait and mobility measures are assessed. Gait, mobility and postural sway data are

collected using a body-worn *inertial sensor* system, the APDM Mobility Lab system (APDM Wearable Technologies, Portland, OR). Use of the APDM system involves "instrumenting" the participant with 6 body worn inertial sensors (2 ankle, 2 wrist, 1 waist belt, 1 upper torso) that contain tri-axial accelerometers, gyroscopes, and magnetometers. Participants are asked to wear walking shoes during the assessments. A gait belt and guarding technique[61] is used by a trained investigator during all testing for safety. Data are recorded via wireless transmission from the inertial sensors to a laptop computer and processed with Mobility Lab software. For the instrumented walking assessment, participants are first asked to walk continuous laps with approximately 180-degree turns, at their comfortable (or usual) pace. They complete four 4-meter laps and two 7-meter laps (if space allows) at usual pace. Lastly, participants are asked to walk as quickly as possible, but not so quickly that they lose their balance (2 x 4 or 7-meters; see Table 1 for measures). Participants are able to take rest breaks between activities as needed.

For the postural sway assessment, data are collected with APDM ISway during 6 static standing trials: (1) eyes open/normal base/firm surface (medial heel-to-medial heel distance = 10 cm), (2) eyes open/narrow base/firm surface (feet together) (3) eyes closed/normal base/firm surface, and (4) eyes closed/narrow base/firm surface, (5) eyes open/usual base/foam surface, (6) eyes closed/usual base/foam surface. Participants wear walking shoes and are asked to stand still and keep their arms at their sides during testing. During the eyes open standing conditions, participants are instructed to focus on an “x” placed at eye-level on the wall in front of them. Participants do not use an assistive device, but wear a gait belt and are closely guarded and assisted as needed into the starting position. Measures utilized to assess postural sway are detailed in Table 1. In addition to the gait and balance measures, we collected data to obtain instrumented assessment of mobility: a) the Short Physical Performance Battery (SPPB) and b) the Timed Up and Go (TUG). The SPPB includes tests of static balance, gait speed, and sit to stand. For the sit to stand trial, participants are instructed to move from a seated position to a standing position five times as quickly, but as safely as possible. Participants undertake two trials, with the fastest of the two trials used as the measure.

Run-in and Allocation (T0)

During the 1-week run-in period, a trained member of the research team meets with the study subject three times over the course of a week (approximately 20 minutes per visit) to perform: 1) vision screen; 2) medication review and 3) home fall safety check. This run-in period allows the study staff to provide hazard reduction interventions per CDC recommendations prior to randomization to reduce the risk of these issues introducing bias across groups.

Following successful completion of the run-in period, participants are randomly allocated (1:2) to either a group that is the attention control (**n=20**) or to the group that receives cognitive training (CT) intervention for a total of 16 weeks (**n=40**). Participants are not to be informed that they were assigned to "attention control" or "cognitive training" conditions; rather, individuals in both groups are told that the aim of the study is to determine whether participation in "computer learning activities" reduces the risk of falls and improves functional ability. Sealed envelopes, prepared in advance, assign the participants to one of the two groups. The randomization schedule is prepared by the consulting statistician using block randomization (blocks of 6) prior to the research team’s initial visit to interested parties. This approach ensures that consent is obtained prior to disclosure of group assignment and persons consent to participate in the study, regardless of the group they are assigned to. The envelope is not opened until completion of the run-in procedure. The principal investigator, co-investigators and outcome assessors are blinded to allocation until the end of the trial.

Intervention

Cognitive training, also known as "brain training", involves scheduled completion of specific tests of executive function, visuospatial orientation and perceptual speed. The CT is completed using a web-based computer interface (Cognifit, Inc.), with task difficulty tailored to the participant's abilities. We will use the Cognifit research interface as it allows tailoring of the intervention to specific tasks selected by the research team.

The individual completes a 14-task baseline testing session, after which the program identifies individualized, tailored training goals for the intervention tasks. Individualized feedback is provided to the user regarding progress towards goals during each session. Our intervention includes 48 training sessions over 16 weeks (recommended 3 sessions per week; each session lasts approximately 20 minutes and covers 3 different cognitive tasks tailored to individual baseline ability and progress to date). Training sessions can be completed on either PC or Mac platform and use a user identified login/password allowing secure access at the individual's home or a community setting per user accessibility and preference. The training allows the user to pick up from the last session to promote completion of the intervention. Because of their linkage to fall and injury prevention, we selected the following specific cognitive tasks to target in the intervention:

- Reaction Time (the ability to perceive and process a stimulus and respond)
- Processing Speed (the ability to fluently perform easy/over-learned tasks)
- Awareness (the ability to evaluate one's own cognitive functioning, realization, perception or knowledge)
- Divided Attention (the ability to execute more than one task at a time)
- Inhibition (the ability to ignore irrelevant information while performing a task)
- Planning (the ability to anticipate and develop the best way to execute a task)
- Shifting (the ability to redirect attention from one channel of information to another)
- Updating (the ability to respond in a flexible and adaptive manner to keep up with environmental changes)

We track sessions completed on a weekly basis and provide reminders as needed. Discontinuation of intervention is made on participant request.

Attention Control

Participants assigned to the attention control condition are provided with programmatic activities that are designed to control for nonspecific treatment effects (computer use, interaction with study staff). Participants will engage in an equal number of sessions (3 sessions/week for 16 weeks) watching preselected healthy aging-related video content on the computer (e.g. NIHSenior Health videos on talking with your provider, taking medications safely, and making the most of a medical visit, how to exercise safely).Participants will be asked to briefly note any information gained from each video on a personal discussion board provided to them within the content module. We track sessions completed on a weekly basis and provide reminders as needed. Discontinuation of intervention is made on participant request.

8-, 16- and 20-week Assessments

A member of the research team blinded to intervention/control group assignment conducts participant outcome assessments at the 8-, 16- and 20-week time periods (see Table 2). These assessments occur in same setting and under similar conditions to baseline testing (e.g., same shoes are to be worn). Following the 20-week assessment, an exit interview is

completed in order to gain insight into the protocol's acceptability including participant perceptions of the CT intervention. Participant interviews use a semi-structured interview protocol as a guide to explore their experiences, overall perceived benefits, challenges and attitudes towards the study protocol. All interview sessions are digitally recorded.

ANALYSIS

All planned statistical analyses will be performed using intention-to-treat. The primary time point of interest in this analysis is the 16-week post-randomization outcome assessment; however, means, standard deviations and distributions will be used to describe the outcomes of interest at baseline, midpoint of active intervention phase and 4 weeks post completion of intervention (week 20 post-randomization). A value of $p<0.05$ will be considered statistically significant. Should there be significant differences between groups on baseline demographic variables despite randomization, we will examine the relationship between the variable and the outcome using sensitivity analyses.

The primary outcome of interest in the proposed RCT is reduction number of falls and injurious falls (See Table 1) at the end of the intervention (16 weeks). We are also interested in the retention of effect 1-month post-intervention. Number of falls and injurious falls will be determined from fall calendar data. Between group differences will be assessed using Mann Whitney U test. Of secondary interest as outcome in this study is reduction in risk of fall which is determined by an increase in the 10M walking speed from baseline and an increase in the Balance test score from baseline. Between group differences will be assessed using Student's t-test. In exploratory analyses, we will examine the change in risk of fall over time using linear mixed models for longitudinal data. As secondary endpoints, we will measure cognitive outcomes (CANTAB), functional outcomes (walking Gill Disability, inertial sensor gait and turn measures, and ISway measures; See Table 1). Outcomes will be compared between groups using either t-tests or Mann-Whitney U tests as appropriate. In exploratory analyses, we will examine the change in outcome measures over time using linear mixed models for longitudinal data.

To better understand feasibility of the study, we will estimate the proportion of older adults found eligible for inclusion who actually agree to participate in such a study. Further, we will compare the characteristics of those who are willing to participate with those who are not. We will also evaluate numbers of study who complete the study protocol and note any differences in participant characteristics in those who drop out. We will also note the numbers of older adults who express interest in the study but are not eligible. To evaluate acceptability of the study procedures and intervention, transcripts of interview sessions will be digitally recorded and transcribed verbatim for descriptive content analysis.