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TITLE: Home-Based, Online, Mindfulness and Cognitive Training for Soldiers and Veterans with TBI

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14. ABSTRACT

Objectives: We examined whether a home-based, adaptive cognitive training, and problem-solving training program would lead to changes in performance on untrained cognitive and functional tasks in TBI Veterans.

Scope: 23 veterans with MCI (age = 50.43, SD=12.77) were randomly assigned to either combined cognitive and problem-solving training (Intervention Group, IG, BrainHQ + Movingforward) or an active control group (AC, casual computer games + VA information session). Participants were instructed to train on their assigned programs for 40 minutes per day, five days per week, over 12 weeks (40 hours of total program usage). Participants completed tests of cognitive (processing speed, memory, and executive control) and functional abilities before, after 12 weeks of training, and after 6 months from the initiation of training to measure the retention benefit from the training.

Up-to-date report of progress: We successfully developed a training website with embedded problem-solving and cognitive training programs. Participant recruitment was initiated in the middle of 2017. Fifteen out of 23 randomized participants completed the training and 13 participants completed entire post-training and 3-month follow-up assessments, and 2 participants completed only partial post- and follow-up assessments due to COVID-19. The mean number of sessions completed was 32.6 out of 60 total sessions (SD = 23.88).

Major Finding: There was no group difference in baseline performances demonstrating successful participants' randomization. The intervention group showed strong improvement on the trained task performance, suggesting that TBI participants are capable of learning home-based computerized tasks. Although there was some numerical improvement favoring IG over AC, there was no significant interaction found between-group (IG and AC) and time (baseline vs. post-training) in untrained cognitive performance and functional ability. Three out of fifteen completed participants performed pre- and post-fMRI sessions. Due to the limited sample size, there was no significant change found in fMRI using the N-back task as a functional task. Although the relative benefit on the intervention group was not found compared to the active control group, the current results show that home-based online training can be applied to veterans with MCI. The lower-than-expected enrollment rate indicates that further assistance in enrollment for the target population of Veterans with MCI is required to achieve an optimal result from an online RCT.

Problems/Issues: Participant recruitment was challenging due to the specificity of the target population. Due to the COVID-19 pandemic, all in-person activities were suspended from March of 2020. During the period, the survey-type assessments were performed online, and the computer-based assessments were not collected.

15. SUBJECT TERMS

Cognitive Training, Problem-Solving Training, TBI, Cognitive and Functional Changes

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1. INTRODUCTION:

To test the efficacy of online, home-based brain training Program (Intervention Group, IG, BrainHQ + Movingforward) compared to an active control group (AC, casual computer games + VA information session) in improving cognitive and functional performance, we conducted double-blinded, randomized controlled trial. Twenty-three veterans suffering from TBI-related cognitive impairment were randomly assigned to either IG or AC group. Participants’ cognitive and functional performance were tested before and after the 12-weeks of training to examine the immediate training benefit and after 6 months from the initiation of training to measure the retention benefit from the training. Three out of 23 participants completed MRI/fMRI before and after the training to test the brain changes from the training.

2. KEYWORDS:

Cognitive Training, Problem-Solving Training, TBI Veterans, Cognitive and Functional Changes

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Table 1. Major goals

Developmental Aims 1-3	% completion	Completion date
Major Task 1: Develop Programs and Initiate Trial		
Subtask 1: Brain Exercise Selection	100%	October, 2016
Subtask 2: Wrapper development and testing	100%	December, 2016
Subtask 3: Build study and caregiver portal	100%	January, 2017
<i>Milestone(s) Achieved: Release study and caregiver portal</i>	100%	
Regulatory review and approval by the USAMRMC Human Research Protection Office	100%	March, 2017
Local IRB Approval	100%	October, 2016
Scientific Aims 1-2		
Major Task 2: Conduct Trial		
Subtask 1: Participants recruitment and enrollment	100%	January, 2020
Subtask 2: Assessments and training	100%	May, 2020
Subtask 3: 6-months post-training assessment	100%	August, 2020
<i>Milestone: Enrollment and Data collection is complete.</i>	100%	
Major Task 3: Analyze and Interpret Data		
Subtask 1: Prepare data for analysis and analyze neurobehavioral and imaging data.	100%	October, 2020
<i>Milestone(s) Achieved: Completion of Data Analysis and Prepare for Publication</i>	100%	

What was accomplished under these goals?

YEAR 1 (09/15/2016 – 09/14/2017)

Major Task 1: Develop Programs and Initiate Trial

1. **Task 1:** Create a training website

- a. Training website was created for both experimental and active control group

- Subtask 1: Brain Exercise Selection

In this study, we selected 17 brain training exercises. Core training targets included visual and auditory processing accuracy, speed, and sequencing; phasic, sustained, and divided attention; memory and memory association; and executive control abilities. Participants progressed from an initially limited performance ability that was supported by continual positive feedback and an individually adapted challenge level to maintain ~75-85% accuracy. As participants progressed, improvements in processing speed and/or performance accuracy *and* in their controlled, higher-order performance operations were challenged at progressively more cognitively demanding task levels. By this adaptive training strategy, virtually all trainees, regardless of the learning rate, were continuously challenged at an appropriate difficulty level as their abilities improved. Participants received training exercises designed to improve the speed and accuracy of visual/auditory information processing early in training (i.e., to improve the quality of information *feeding-forward* to the higher-level cognition and executive control), using strategies that had been repeatedly shown to improve lower-system-level, modulatory system and attention control processes that crucially support higher-level cognition and executive control.

Although targeting different cognitive domains, all training exercises were designed to enhance the quality and quantity of information processing and decision making at speed. Among other training strategies, speed-of-processing training showed the most potential for real-life benefit. Speed-of-processing training was strongly associated in the trial with better driving safety as measured by sustaining driving and at-fault crashes¹⁻³, was shown to positively impact self-reported health-related quality of life and sustained independence, reduced the probability of onset (and the severity of) senior depression⁴, and reduced the probability of a progression to dementia⁵.

Furthermore, cognitive decline is often explained by the mediational model such that working memory and executive control are largely mediated by its effect on processing speed⁶. As an individual has slow and degraded sensory input, the quality of information fed to higher-level cognitive function is also degraded, and so does the higher-level cognitive process itself (i.e., memory, and executive function). By improving the fundamental processing speed abilities and directly practicing other higher cognitive abilities, we expected to induce higher cognitive benefit on TBI veterans from this training program (please see Table 4 for description of brain training exercises).

- Subtask 2: Wrapper development and testing

All training exercises and the "Start Moving Forward program" were embedded in the training system as continuous training. Both Brain training and Active control group participants logged into the same website and were moved to different training programs depending on their login id (see Figure 1).

Figure 1. General Scheme of Training Program



- Subtask 3: Build study and caregiver portal

A caregiver portal was created providing the progress of each participant on each cognitive domain. Participants and their caregivers could access the portal by just clicking on the “Progress” button on top of their training program. Caregiver portal included 1) BrainHQ Calendar that showed the dates that participants used a training program, with darker colors representing more training. Participants can get more details (e.g., minutes of training) by hovering over a day; 2) BrainHQ Activity Quotient (your BrainAQ) represented participants’ overall gains from training. When starting, the quotient started at zero. Each time participants completed a new training level, the BrainAQ would tick upward. As participants’ performance improved, the BrainAQ would increase proportionally, reflecting cognitive gains from training; 3) Stars earned and Levels completed across different exercises in different domains. By hovering over the map of the stars and the map of levels earned, participants could see the details of performance for each task.

Figure 2. Caregiver portal



b. Study database and electronic data collection system were implemented (FITBIR)

2. Task 2a: Prepare sites for clinical trial

a. Posit Science research team created participant binders with detailed assessment descriptions and material for assessment and training. Participants' binders were shipped to a research site.

- b. Experimenter computers were purchased, and the study site IT team set up the computers.
 - c. Posit Science team trained local site staffs regarding the inclusion criteria, administration of assessment measures, and tracking participants' progress of training.
3. **Task 2b:** Approval of local site and HRPO IRBs

SUBMITTED TO AND APPROVED BY:

HRPO #: A-19775

Title: Home-Based, Online, Mindfulness and Cognitive Training for Soldiers and Veterans with TBI

Target required for clinical significance: 80

Target approved for clinical significance: 80

Two protocols:

1) HRPO #: A-19775.a

-- Western Institutional Review Board (IRB) approval: 2 August 2016

-- VA Connecticut Healthcare System Human Studies Subcommittee Approval: 6 October 2016

-- HRPO approval: NGMR, 16 March 2017 (approval pertains to the Data Coordinating Center for up to 100 subjects enrolled at the clinical performance site, which is reviewed and approved separately as A-19775.b).

2) HRPO #: A-19775.b - (VA Connecticut Healthcare System)

-- HRPO approval: NGMR, 16 March 2017

approved for the enrollment of 100 subjects (goal is 80 randomized subjects)

4. **Task 3:** Initiating participants recruitment

- a. Contacted potential participants and conducted phone screening.
- b. Enrolled participants and conducted baseline assessments.
- c. The current study was preregistered on ClinicalTrials.Gov (NCT02922569)

Table 2. Enrollment table for year 1

Scheduled for Consent Visit	Consented	Randomized	Active	Completed
12	12	8	8	0

- d. Details of the recruitment activities carried out and actions being taken to remedy the enrollment shortfall
 - There was a delay in enrollment for the first 6 months of Year 1 due to IRB and HRPO review and approval. Since all subject-related activities were available only after HRPO and site IRB approvals, our subject recruitment was initiated in March of 2017. Therefore, we have 5 months in year 1 for site preparation, subject recruitment, and enrollment.
 - The site attended weekly meetings with the National Center for PTSD for recruitment. The site had staffing issues (low staff) but had hired a new member to help with recruitment efforts and administering assessments. To help boost

recruitment and enrollment, the site expanded the recruitment to the Newington Campus, which was a part of the VA Connecticut Healthcare System.

YEAR 2 (09/15/2017 – 09/14/2018)

MAJOR TASK 2: Continued participant recruitment and monitored enrolled participants’ progress and performance.

We continued to enroll and randomize veterans with TBI to 12-weeks of in-home cognitive training and Problem-Solving training (CT + PST) vs. an active control intervention (casual video games + online veteran-related information session). Patient outcomes were measured primarily using neuropsychological assessments in processing speed (composite score of Pattern Comparison, Digit Symbol Coding, and Letter Comparison), memory (composite score of N-back task, Spatial working memory, WAIS Digit span task, and Rey Auditory Verbal Learning Test (RAVLT)) and executive function (composite score of Trail Making B, Stroop Cost, and Flanker Cost).

For a subset of participants, functional and structural MRIs were used to measure structural and functional neurological changes attributable to these interventions. The Timed Instrumental Activity of Daily Living was used to document everyday functional activity levels. Self-reported sleep quality, physical activity, levels of social communication, brain-healthy diet, and mood were documented to further measure Quality of Life (QOL) impacts and to help determine the magnitude and endurance of increased resilience after training completion.

Table 3. In-lab Cognitive and Functional Assessment Measures

Assessment Type	Assessment Name	Description
Diagnostic	Ohio State University TBI Identification Method Short Form (OSU TBI-ID-SF)	The OSU TBI-ID is a structured interview developed using recommendations from the CDC for the detection of a history of exposure to TBI.
	Mini International Neuropsychiatric Interview (MINI)	Clinical interview to assess mental health symptoms.
Characteristics	Automated Neuropsychological Assessment Metric (ANAM-4)	The ANAM-4 is a clinician-administered computerized cognitive assessment used by the military to assess cognitive function.
	Ruff Neurobehavioral Inventory (RNBI)	The RNBI is a quantitative self-report measure that measures the decline in various neurobehavioral functions as experienced by the participant, comparing their pre-morbid function to their current function
	Columbia Suicide Severity Rating Scale (C-SSRS)	The C-SSRS is a brief measure used to assess the full-range of ideation and behavior, including intensity of ideation, as it relates to suicidality.
Neuropsychological Assessments	Pattern number comparison, Letter number comparison, Digit Symbol substitution tasks.	PNC, LNC, and DSST are measures of cognitive processing speed.
	N-back task	N-back task is designed to assess working memory.
	Spatial Working memory	Spatial working memory is designed to assess spatial working memory.
	Rey Auditory Verbal Learning Test	The RAVLT is a measure of verbal

Assessment Type	Assessment Name	Description
	(RAVLT)	learning and memory, involving reading a list of words and asking the participant to repeat the list. It has immediate and delayed recall components.
	Digit Span (WAIS-IV)	Digit Span is designed to assess verbal working memory.
	Stroop	Stroop is designed to assess cognitive control and inhibition.
	Trail Making	Trail Making B is a test of executive control.
	Flanker Task	Respond to center target while ignoring adjacent distractors.
Functional Assessments	Timed Instrumental Activities of Daily Living (TIADLs)	The TIADL is a clinician-administered functional assessment that uses several real-world items including medicine bottles, phone books, and food items that measures how quickly a participant can complete everyday tasks related to independent living.
	Mayo-Portland Adaptability Inventory (MPAI-4)	The MPAI is a clinician rating scale designed to assist in the clinical evaluation of people during the post-acute (post-hospital) period following acquired brain injury and to assist in the evaluation of rehabilitation programs. The staff-rated approach will yield a clinical impression measure.
Participant-Reported Outcome Measures	Neurobehavioral Symptom Inventory (NSI)	The NSI is a quantitative self-report measure that asks participants to assess the extent to which symptoms typical of traumatic brain injury have disturbed them over the past two weeks.
Participant-Reported Outcome Measures	Post Traumatic Stress Disorder Check List, Civilian Version (PCL-5)	The PCL-5 is a quantitative self-report measure that asks participants to assess the extent to which symptoms typical of post-traumatic stress disorder have disturbed them over the past month.
	Beck Depression Inventory (BDI-II)	The BDI is assessing depression using a set of standardized questions.
	Quality of Life after Brain Injury (QOLIBRI)	The QOLIBRI is a self-report measure that assesses the health-related quality of life of individuals after traumatic brain injury.
	Frontal Systems Behavior Scale (FrSBe)	The FrSBe is designed to identify and quantify behavioral problems caused by executive dysfunction and frontal lobe damage
	Cognitive Failures Questionnaire (CFQ)	The CFQ is designed to identify and quantify common everyday cognitive errors caused by mild cognitive dysfunction.

Study Population:

The study population was composed of veterans who have persistent post-concussive symptoms (PPCS) following traumatic brain injury (TBI). Participants were recruited from the VA Connecticut

Healthcare System through flyers, newspapers, and patients' referrals for an online training study for veterans' TBI symptoms. Applicants were first screened via email with a questionnaire that surveyed demographics (e.g., age, English language proficiency). If not excluded based on the survey, a phone interview checked for medical and non-medical conditions affecting neuropsychological testing. Eligible participants were (1) age over 18, (2) a diagnosis of TBI (including blast exposure) confirmed by the Ohio State University TBI Identification Method-Short Form (OSU TBI-ID-SF), (3) persistent cognitive dysfunction confirmed by an objective measure (as recommended by the ICD-10 definition for post-concussion syndrome) or a subjective measure (as recommended by the DSM-V definition of post-concussional disorder), (4) at least six months out from their most recent TBI, (5) fluent English speakers and (6) adequate in sensorimotor capacity to perform training, including the visual capacity to read a computer screen at normal viewing distance, the auditory capacity to understand normal speech, and motor capacity to control a computer mouse (please refer to clinicaltrials.gov for detailed inclusion and exclusion criteria).

Randomization.

After screening and baseline testing, participants were assigned to either the Intervention or AC group using the minimization method⁷ with probability 0.8 to the group minimizing symmetric Kullback-Leibler discrepancy on five prognostic variables (baseline age, education, gender, PTSD status, and depression status). The largest allowable discrepancy in subject counts between the two groups was set to four participants. Given the small sample size used in our study, allocating participants to groups based on minimizing the imbalance on prognostic variables was considered a better method compared to traditional stratification randomization.

Study Design.

All participants completed cognitive and function testing, with the task order fixed within the cognitive session. A part of the participants received the MRI/fMRI session occurring on a separate day following cognitive testing. To maintain participant blinding, consent forms described the study as comparing two distinct types of cognitive training. Site staff (i.e., training coach) directly interacting with participants during training were not blinded to effectively handle any training-related issues but were instructed to describe each program's features as potentially beneficial. Post-training assessments were administered by staff who were separate from training coaches and blinded to the training condition.

Participants completed the assigned home-based training program with their computer or loaned computer. The training was restricted to one session per day, with at least 5 sessions in 7 days. The training coach interacted with participants regarding their training only when participants experienced technical difficulties or when participants had an extended period of training absence. If participants had not trained in a week, the training coach sent a standard reminder email. In cases where participants did not respond to the reminder email, the coach called the participant to determine their reason for training absences.

When training programs were finished, participants completed a post-training assessment session. After 6 months from the beginning of the trial (i.e., 3 months from the completion of the training), participants were invited for the retention assessment session that measures the longer-term benefit from the training.

Diagnostic Assessment.

Ohio State University Traumatic Brain Injury Identification Short Form was used for the detection of history of exposure to TBI. A Mini International Neuropsychiatric Interview (MINI) and the Wechsler Test of Adult Reading (WTAR) were used to determine premorbid IQ.

Cognitive Assessments.

Assessments administered before and after training were grouped into three categories: Processing Speed (Digit Symbol Substitution, Letter Comparison, Pattern Comparison), Memory (N-back, Spatial Working Memory, Digit Span, Rey Auditory Verbal Learning Test) and Executive Control (Trail Making, Flanker, Color Stroop).

Functional Assessments.

Functional ability was measured with Timed Instrumental Activities of Daily Living (TIADLs) and The Mayo-Portland Adaptability Inventory (MPAI-4). TIADLs are a test of real-world performance in five key domains specifically designed to assess mild cognitive impairment levels by measuring the time taken to complete each task (which is sensitive to mild dysfunction) rather than whether the task is completed successfully or not (because the task is virtually always completed successfully in people with mild dysfunction and is thus not sensitive). MPAI-4 is designed to assist in the clinical evaluation of people during the post-acute (post-hospital) period following acquired brain injury.

Exploratory Measures.

Psychological Well-Being was measured with Neurobehavioral Symptom Inventory (NSI, a measure of symptom report), the PTSD Check List (PCL-5, a symptom rating scale for PTSD in common use at VA centers), the Quality of Life after Brain Injury (QOLIBRI, a measure of Health-Related Quality of Life), the Beck Depression Inventory (BDI-II), the Frontal Systems Behavior Scale (FrSBs), and the Cognitive Failures Questionnaire.

Training Programs.

Experimental Treatment (Cognitive and Mindfulness/Problem Solving Training). Each session began with a 10-minute-long Problem-Solving training program (Moving Forward). The Moving Forward web-based session was integrated into and controlled from the training website. The moving Forward program emphasized resilience and prevention of mental health conditions and skills-building for problem-solving that was particularly appropriate for TBI patients. Following the 10 minutes Moving Forward session, participants initiated 30 minutes of cognitive training (CT). The cognitive training program included 17 computerized exercises delivered from the study website. Core training targets included visual and auditory processing speed and accuracy; attention; memory; and executive control abilities. On each session, participants were given 5 games each lasting ~6 minutes. During a 6-minute game, participants played a certain level multiple times (usually 2-3 times, varying based on participants' response speed and the number of trials). The baseline was set as performance on the first attempt. On repetition, initial difficulty was set by the previous trial's best performance to promote performance improvement. Participants progressed from an initially limited performance ability (i.e., easy trial) that is supported by continual positive feedback to individually adapted challenge trials to maintain ~75-85% accuracy. As sessions progressed, processing speed and/or performance accuracy and/or higher-order performance operations were challenged at progressively more demanding levels. The adaptive training ensured virtually all participants, regardless of the learning rate, were continuously challenged even as their abilities improved. Early in training, participants completed exercises designed to improve the speed and accuracy of visual/auditory information processing and attention. Later in training, participants progressively trained more on working memory capacity and executive control. The following table includes a detailed description of each training exercise.

Table 4. Description of Brain Training Exercises

Domain	Exercise	Description	Adaptive features
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			Within session	Between session
Sensory Processing Speed	Visual Sweeps	See two sweep patterns, either inwards or outwards. Indicate the direction of the two sweep-patterns in sequence.	Exposure duration	Color, direction, and frequency of visual stimuli
	Audio Sweeps	Listen to two sweep sounds. The sound can sweep up from a lower to a higher frequency or down from the higher to lower frequency. Indicate the direction of the two sweep sounds in sequence.	Exposure duration	Frequency and sweep ratio of auditory stimuli
	Fine Tuning	Listen to sound and indicate the heard sound among examples.	Exposure duration	The similarity of syllable pairs
	Hawk Eye	See briefly presented items and locate the item which is slightly different from others.	Exposure duration	Eccentricity, target-distractor similarity
Attention	Double Decision	Watch for a vehicle in the center of the screen and a road sign in the periphery. Indicate the central vehicle target and the periphery target location.	Exposure duration	Number of distractors, eccentricity, target-background similarity
	Target Tracker	Keep track of objects in motion and indicate the tracked objects.	Number of memory items	Number of distractors, stimuli-background similarity, moving speed of stimuli
	Freeze Frame	Remember the target image and withhold a response for the target and commit a response for distractors.	Exposure duration	Number of distractors, target saliency
	Mixed Signal	Listen to a number, letter, color, or other pieces of information while looking at a set of numbers, symbols, letters, words, or other information, and indicate if the auditory information matches to visual information.	Response duration	Target-distractor compatibility, stimuli category
	Divided Attention	Watch two items presented on the screen and respond if they have the same color, shape, or pattern.	Exposure duration	Stimuli category, response rule
Memory	To-Do list training	Listen to a series of items presented in an auditory format and select the items in the presented order on a visual grid.	Number of memory items	The complexity of auditory presentation
	Memory Grid	Click on a card and remember the sound associated with the card. The goal is to find a pair of cards having the matching sound.	Number of memory pairs	Type of voice, the familiarity of sounds

	Rhythm Recall	Listen to and watch a song, then repeat the timing sequence by pressing keyboard keys.	Number of memory beats	Presence of hints, presentation speed
	Scene Crasher	Watch a briefly presented image and indicate the missing item on the current image from memory.	Number of memory objects	Exposure duration, display eccentricity, target-background similarity
Executive Control	Card Shark	Match if the previously presented visual item is matching to the current visual item.	N/A	Number of memory items (up to 6), the complexity of visual stimuli, stimuli presentation speed
	Juggle Factor	Watch a sequence of numbers that are presented within moving circles and reconstruct the sequence in the right order and the right locations.	Number of memory items	Presence of distractors, the complexity of placeholder, moving speed of circles
	Mind Bender	Respond to stimuli differently depending on changing rules.	Response Duration	The complexity of the rule, stimuli category
	Auditory Ace	Match if the previously presented auditory stimuli are matching to the current auditory stimulus.	N/A	Number of memory items (up to 6), the complexity of auditory stimuli, stimuli presentation speed

Active Control (AC). As in the intervention group, each session started with 10-minute online information sessions followed by 30-minutes of commercially available casual video games. The information session was integrated into and controlled from the training website. The information session included relevant news items and information, and resources for traumatic brain injury. Following the 10 minutes information session, participants initiated 30 minutes of casual game training. We used 13 commercially-available computer games designed to (1) provide a face-valid approach to cognitive training, ensuring participants were blind to group affiliation; (2) match expectation-based influences on performance in cognitive outcomes; (3) match the experimental program in overall program use intensity, staff interaction, reward, and overall engagement; 4) not be continuously adaptive (Though, three out of 13 games could increase in difficulty within the session by discrete levels). The user experience in the AC and CT group was almost identical except for the games played.

Table 5. Description of Active Control Exercises

Exercise Name	Description	Adaptive levels
Bricks Squasher II	The game starts with a ball placed on top of the paddle. The goal of this game is to move the paddle and bounce the ball to destroy the bricks.	YES
War Ship	Participants place 5 vessels in the area at the left-hand side and sink the enemy's hidden ships at the right-hand side by guessing the enemy's ship locations.	NO
Bricks Breaking Hex	The target in this game is to connect and remove bricks of the same color to clear the board.	NO
Chinese Checkers	The target of this game is to move all marbles to the enemy base before the opponent (i.e., computer) does so.	NO
Lineup Four	The object of this game is to connect 4 color discs so that they form a line in a horizontal, vertical, or diagonal direction.	NO
Crossword Puzzle	The goal in this game is to find out the words according to the given meanings.	NO
Gems Swap	The goal in this game is to form a line of 3 or more identical gems so that they can be removed.	YES
Double Klondike Solitaire	Participants are given a deck of 52 standard playing cards and asked to move all cards to 8 foundations at the top right corner by suit from A to K.	NO
A Maze Race	The goal is to reach the exit of the maze before the computer does.	YES
Reversi	In this game, an 8x8 grid board and 64 two-sided pieces are used. Each of the pieces has a side in black color and the other in white. The goal is to finish the game with more pieces flipped to the side of participants representing color rather than that of the computer.	NO
Word Search II	Participants are presented with a large grid that contains numerous letter tiles, and a word list placed on the right of the screen. Participants are asked to click and drag the corresponding letters on the grid.	NO
Sudoku	In this game, the goal is to fill in the blanks with numbers 1 to 9 such that the numbers will not be repeated in each row, each column, and each 3x3 square.	NO
Tri Peaks Solitaire	The goal is to move all cards from the three peaks to the discard pile.	NO

Specific Objective 1: Contact potential participants and conduct phone screening.

Participants are recruited from the Connecticut community through flyers and online advertisements. Study recruitment materials described the opportunity to volunteer for a clinical trial to advance the science and treatment of TBI in veterans. The emphasis of the benefit was on advancing science and on helping people like the potential participant. Applicants were first screened via phone interview checked for eligibility and medical and non-medical conditions affecting neuropsychological testing.

Initial Contact	352
Phone Screened	159

Specific Objective 2: Schedule consent visits and enroll eligible participants.

During the consent/enrollment meeting, the Site Study Coordinator and the potential participant discussed the nature of the study, the purpose of the research, the study procedures, the possible risks and benefits of study participation, participant randomization, participant confidentiality, the voluntary nature of the research and the participant's right to withdraw from the study at any time. Following this discussion, participants were offered the opportunity to join the study by signing a written consent using a consent form approved by the site's local IRB to participate.

After consent, participants underwent Screening to determine eligibility.

Consented and Screened	35
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Specific Objective 3: Conduct an in-lab pre-training assessment and explain the home-based training program.

After completing pre-training assessments, we randomized participants into groups.

Completed Pre-Assessment	15
Randomized	15

The site Study Coordinator oriented the participant to the training program by sitting with them, in the lab, and completing the first session. This was helpful for participants to become familiar with the program and using a computer and be allowed to ask questions about the training.

Specific Objective 4: Conduct in-lab post-training and follow-up assessments

Completed Post-Assessment	9
Completed 6-month Follow-up	8

Uploading collected data on EDC and FITBIR: We uploaded all collected data on EDC and FITBIR. We continuously monitored and managed the electronic database.

YEAR 3 (09/15/2018 – 09/14/2019)

MAJOR TASK 2: Continued participant recruitment and monitored enrolled participants' progress and performance.

Specific Objective 1: Contact potential participants and conduct phone screening.

Initial Contact	368
Phone Screened	171

Specific Objective 2: Schedule consent visits and enroll eligible participants.

After consent, participants underwent Screening to determine eligibility.

Consented and Screened	41
------------------------	----

Specific Objective 3: Conduct an in-lab pre-training assessment and explain the home-based training program.

Completed Pre-Assessment	20
Randomized	20

Specific Objective 4: Conduct in-lab post-training and follow-up assessments

Completed Post-Assessment	12
Completed 6-month Follow-up	12

Uploading collected data on EDC and FITBIR: We collected all collected data on EDC and FITBIR. We continuously monitored and managed the electronic database.

YEAR 4 (09/15/2019 – 09/14/2020)

MAJOR TASK 3: Analyzed and interpreted data

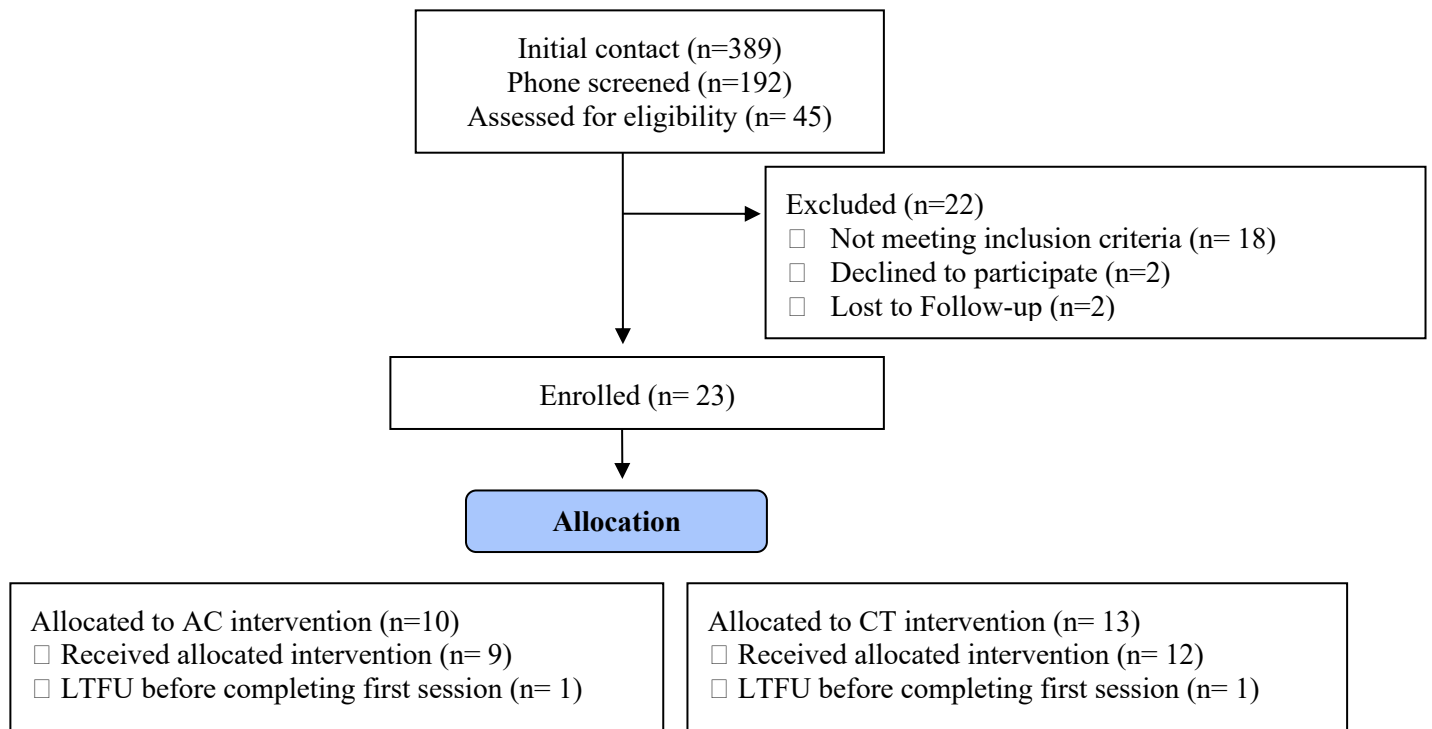
Statistical Analysis Plan.

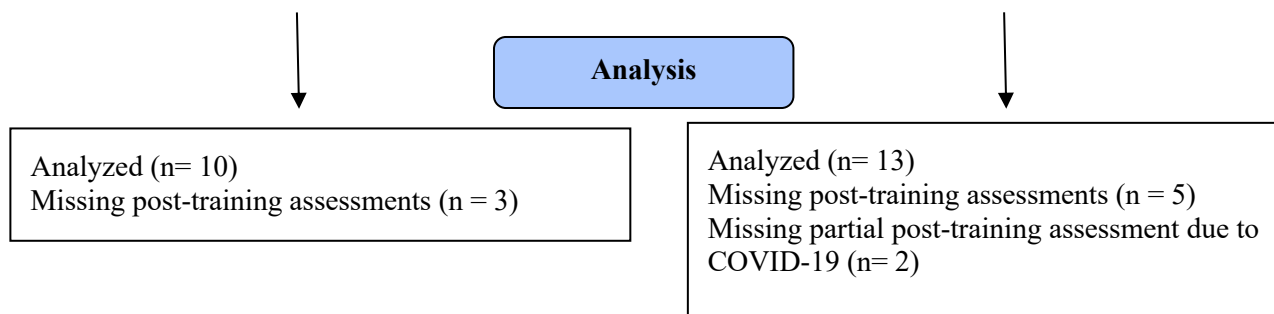
We tested our predictions with mixed-effects linear regressions using normalized baseline and post-training performance calculated with all data points across time. Each model included the treatment group by time interaction term as a fixed factor and each participant's intercept as a random factor. An interaction term (training group by time) estimated the effect of cognitive training on outcome measure change.

RESULTS

Demographics.

At baseline, there were no group differences in demographics (age, gender, education) and other prognostic variables used in randomization (PTSD status, depression status, *ps* > .15).





Attrition.

Fifteen participants out of 23 ITT participants (65.2%) completed their training program and post-training assessments. Among those, 2 participants only completed a partial assessment due to COVID-19 (no in-lab assessments were available). At baseline, non-completers were not significantly different from the completers in age and years of education variables ($ps > .23$). The mean number of completed sessions was 32.6. (SD = 23.88).

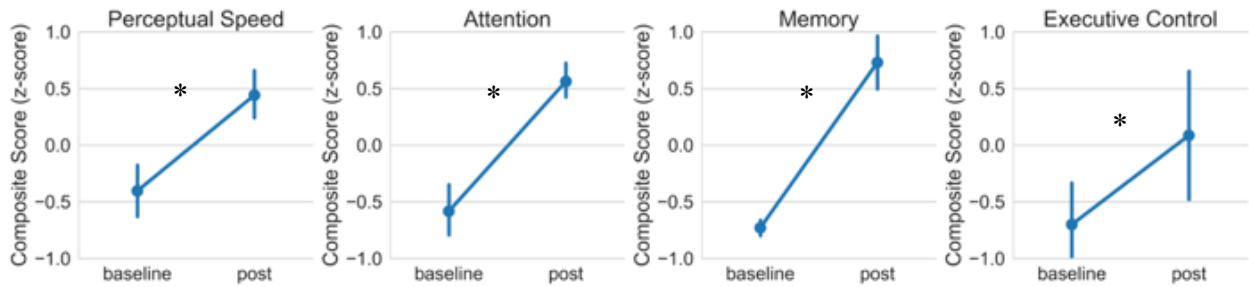
Table 6. Demographics

		Intervention Group (IG)	Active Control (AC)	p-value
Randomized	N	13	10	
	Age	53.53 (10.25)	46.40 (15.05)	$p = .19$
	Gender (% male)	84.6%	90%	$p = .80$
	Years of education	13.76 (1.58)	15.00 (2.44)	$p = .15$
	Race (% white)	61.5%	70%	$p = .65$
	Occupational status (% retired)	69.3%	80%	$p = .91$
	ANAM (z-score)	-2.30 (1.61)	-1.98 (2.13)	$p = .68$
	MRNBI (composite score)	67.5 (17.7)	71.3 (12.5)	$p = .57$
	RAVLT (immediate recall)	51.3 (7.93)	52.6 (8.85)	$p = .72$
	RAVLT (delayed recall)	7.61 (1.89)	8.2 (1.22)	$p = .40$

Game Performance Improvement in IG.

Since the Active Control games were casual games without a data saving system, we could not quantify changes in AC group performance. In the Intervention group, each exercise has multiple levels, presented to participants in a fixed order (i.e., from easy to complex). Participants set the baseline-score during the initial

trial. Post-score was determined by the best performance on the repeated trials at each given exercise level. The baseline and post-score of each game were calculated by averaging baseline- and post-scores of all levels in the game. The composite score for each cognitive domain was calculated by averaging z-scores of all games in each domain. Mixed-effects linear regression was performed for each domain separately with time (pre and post) as a factor and intercept of each participant as a random factor. In all domains, Intervention group participants showed improvement from training to their post-score (processing speed: $z = -15.83, p < .01$, attention: $z = -10.33, p < .01$, memory: $z = -4.69, p < .01$, executive control: $z = -5.44, p < .01$).



* $p < .05$

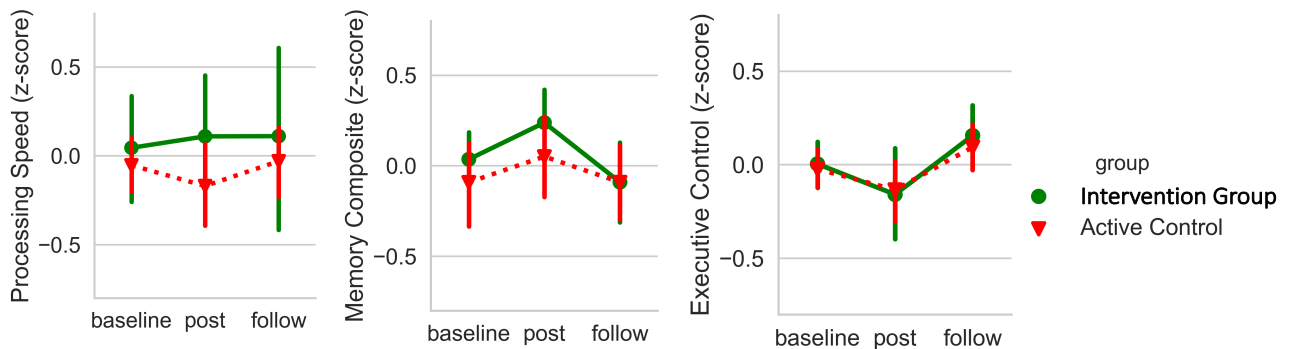
Transfer of Training.

First, we examined whether groups performed equivalently at pre-testing using a one-way ANOVA with the group as a between-subjects factor (IG. vs. AC) for all measures. There were no group differences in any measures ($ps > .05$).

Primary Outcome

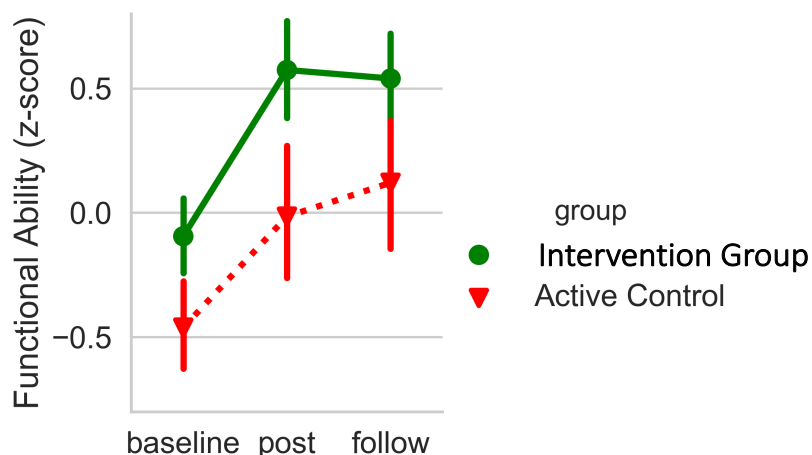
Cognitive Composite Score.

To examine whether cognitive training had any overall effect on cognitive abilities and to better address the issue of measurement error and multiple comparisons, we performed analyses at the construct level using a composite score. The composite measures of processing speed, memory, and executive control were calculated by averaging the z-scores of each domain. We conducted mixed-effects linear regression on those composite scores with the group by time interaction term as a fixed factor, and intercept of each participant as a random factor. Results showed no significant interaction between group and time ($ps > .05$).



Functional Composite Score.

Mixed-effects linear regressions were performed for the composite score of functional measures (TIADL and MPAI-4) as described above. There was no significant interaction between group and time ($ps > .05$).



Self-Reported Exploratory Measures. Mixed-effects linear regression used in the previous analysis was performed for each measure. The interaction between group and time was not significant, except Quality of Life after Brain Injury (QOLIBRI) favoring IG from post-training to 3-month follow-up change ($z = 2.40$, $p < .05$).

Table 7. Detailed results of all assessment measures

Assessment Type	Assessment Name	Pre		Post		Group by Session p-value	Follow-up		Group by Session p-value
		CT (n=13)	AC (n=10)	CT (n = 6)	AC (n = 7)		CT (n = 6)	AC (n = 7)	
Neuropsychological Assessments	Pattern number comparison	15.92 (4.55)	14.20 (2.64)	16.08 (4.30)	14.28 (2.88)	$p > .05$	17.41 (5.47)	14.57 (2.81)	$p > .05$
	Letter number comparison	10.23 (3.45)	9.95 (1.09)	10.0 (2.04)	9.0 (2.02)	$p > .05$	9.91 (4.29)	10.14 (1.72)	$p > .05$
	Digit Symbol substitution tasks	64.23 (15.11)	67.60 (14.81)	67.33 (12.33)	67.57 (8.36)	$p > .05$	63.33 (16.88)	66.28 (9.25)	$p > .05$
	N-back task	0.05 (0.48)	-0.07 (0.80)	-0.03 (0.56)	0.02 (0.92)	$p > .05$	-0.09 (0.52)	0.08 (0.82)	$p > .05$
	Spatial Working memory	-0.06 (0.65)	0.08 (0.98)	-0.16 (0.85)	0.13 (0.65)	$p > .05$	0.02 (0.44)	-0.02 (1.22)	$p > .05$
	RAVLT-delayed recall	7.61 (1.89)	8.20 (1.22)	8.42 (1.71)	7.28 (3.77)	$p > .05$	7.16 (1.83)	9.85 (1.77)	$P < .05$
	RAVLT-immediate recall	51.38 (7.92)	52.60 (8.85)	51.42 (7.65)	49.42 (6.70)	$p > .05$	48.50 (8.98)	52.71 (6.18)	$p > .05$
	Digit Span (WAIS-IV)	10.15 (2.70)	9.10 (2.72)	10.57 (1.51)	8.85 (2.47)	$p > .05$	9.0 (3.09)	8.57 (1.90)	$p > .05$
	Stroop cost	0.04 (0.71)	0.18 (1.04)	0.22 (1.20)	-0.04 (0.84)	$p > .05$	-0.44 (0.59)	-0.15 (0.32)	$p > .05$
	Trail	-0.04	-0.13	0.11	0.34	$p > .05$	-0.20	0.23	$p > .05$

Assessment Type	Assessment Name	Pre		Post			Follow-up		
		CT (n=13)	AC (n=10)	CT (n = 6)	AC (n = 7)	Group by Session p-value	CT (n = 6)	AC (n = 7)	Group by Session p-value
	Making Cost	(1.11)	(0.80)	(0.97)	(1.45)		(0.99)	(0.76)	
	Flanker Cost	-0.014 (0.97)	0.009 (0.14)	0.13 (0.34)	0.10 (0.28)	p>.05	-0.08 (0.11)	-0.14 (0.19)	p>.05
Functional Assessments	Timed Instrumental Activities of Daily Living (TIADLs)	-0.39 (0.70)	0.04 (1.31)	0.08 (1.16)	0.45 (0.87)	p>.05	-0.29 (0.92)	0.39 (0.96)	p>.05
	Mayo-Portland Adaptability Inventory (MPAI-4)	37.15 (16.39)	43.20 (10.93)	30.50 (20.59)	41.14 (9.51)	p>.05	35.25 (18.18)	36.00 (8.30)	P<.01
Participant-Reported Outcome Measures	Neurobehavioral Symptom Inventory (NSI)	39.0 (21.22)	48.20 (21.83)	35.5 (19.69)	35.85 (20.49)	p>.05	34.50 (20.68)	35.14 (21.92)	p>.05
	Post Traumatic Stress Disorder Check List, Civilian Version (PCL-5)	42.76 (22.71)	44.30 (12.15)	40.87 (18.36)	31.85 (18.10)	p>.05	42.12 (16.42)	38.0 (15.01)	p>.05
	Beck Depression Inventory (BDI-II)	21.23 (13.88)	28.0 (13.24)	17.11 (11.10)	23.85 (10.85)	p>.05	20.75 (15.18)	25.14 (13.33)	p>.05
	Quality of Life after Brain Injury (QOLIBRI)	48.59 (21.21)	39.39 (15.75)	53.90 (21.95)	46.43 (13.74)	p>.05	55.57 (20.57)	39.96 (16.53)	P<.05
	Frontal Systems Behavior Scale (FrSBe)	56.07 (19.52)	51.00 (14.62)	67.87 (25.54)	74.14 (14.61)	p>.05	66.50 (16.91)	67.71 (10.02)	p>.05
	Cognitive Failures Questionnaire (CFQ)	52.69 (19.19)	61.80 (17.77)	42.55 (17.54)	46.85 (13.75)	p>.05	45.37 (17.17)	49.0 (14.91)	p>.05

Functional MRI with N-back task.

Three participants completed pre-and post- functional MRI sessions. All three participants were in IG.

N-back task: In this task, participants were presented with blocks of trials that consisted of pictures of places, tools, faces, and body parts. Within each run, the 4 different stimulus types were presented in separate blocks. Also, within each run, half of the blocks use a 2-back working memory task and half use a 0-back working memory task (as a working memory comparison). A 2.5-second cue indicates the task type (and target for 0-back) at the start of the block. Each of the two runs contains 8 task blocks (10 trials of 2.5 seconds each, for 25 seconds) and 4 fixation blocks (15 seconds). On each trial, the stimulus is presented for 2 seconds, followed by a 500 ms inter-task interval (ITI). There were two runs (posterior to anterior, and anterior to posterior) for each session.

Structural MRI: High-resolution T1-weighted brain images were acquired using a 3D MPRAGE (Magnetization Prepared Rapid Gradient Echo Imaging) protocol collected in ascending fashion parallel to the anterior and posterior commissures, echo time (TE) = 565 ms, repetition time (TR) = 3200 ms, field of view (FOV) = 256 mm, acquisition matrix 192 mm × 192 mm, slice thickness = 0.8 mm, and flip angle = 120°. All images were collected on 3T Siemens MAGNETOM Prisma MRI Scanner using a 64-channel head coil.

Functional MRI: For all functional scans, T2* weighted images were acquired using a fast echo-planar imaging (EPI) sequence with Blood Oxygenation Level Dependant (BOLD) contrast (TR = 700 ms, TE = 31 ms, flip angle = 55°). All task displays were projected onto a screen and presented to participants via a 45° angled mirror fixed on the head coil; this mirror was adjusted for each participant to enable a view of the screen without head movement.

MRI preprocessing was carried out using FSL 6.0.0 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing were applied: rigid body motion correction using MCFLIRT, removal of non-brain structures using BET, spatial smoothing using a Gaussian kernel of FWHM 6.0-mm, grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, and temporal filtering with a high pass frequency cut-off of 100 s. Regression-based analysis of fMRI data was carried out using FSL's FEAT Version 6.0.0. Of primary interest to this study was the contrast of 2-back > 0-back. For the first individual-level analyses, the hemodynamic response to targeted contrast (2-back > 0-back) was convolved with a double-gamma HRF function in each run. Next, the contrasts were combined across the two runs with smaller motion on a subject-by-subject basis using fixed-effect analysis for each pre- and post-training. Since all participants were in IG, in the third level, we contrasted pre- and post-training within the subject using the second-level contrast images (pre-training > post-training, post-training > pre-training) across participants. All maps were thresholded at a voxel-wise Z-score of 2.33 ($p < .01$) and a cluster-wise threshold of $p < .05$.

Results showed no statistical difference between pre vs. post on the targeted contrast (2-back > 0-back) across three participants.

DISCUSSION

The major goal of the first year was to develop the study platform and to initiate the trial. We created the training website for both intervention and active control groups. Brain training exercises were selected based on the cognitive impairment and underlying mechanism of the TBI-based cognitive impairment. Along with training and active control exercise, we implemented a problem-solving program (i.e., MovingForward.com) and information session (e.g., VA.org) into the training system as continuous training. Both IG and AC participants logged into the same website and the user experience in the AC and IG group was almost identical except for the games played. The training protocol was approved both by HRPO and local site IRBs. The participant enrollment was initiated.

The major goal of the second and the third year was to conduct the trial. Although our vigorous effort to recruit participants, participant recruitment was challenging due to the specificity of the target population. To help boost recruitment, the study site attended weekly meetings with the National Center for PTSD. The site posted flyers at the Newington Campus, which was part of the VA Connecticut Healthcare System. Also, we made making efforts to reconnect with potential participants who had previously contacted the site but were not able to make initial contact.

A total of 45 TBI Veteran participants were enrolled in the study, and 23 participants were randomized home-based online cognitive training. Over 65% of enrolled participants completed the training, and the mean completion rate of training was 54.3%. Participants in IG showed improvement on the trained exercises suggesting the improvement of the cognitive abilities on the trained tasks. Due to the small sample size, the transfer efficacy of the intervention (cognitive training + problem solving) relative to the active control (casual games + information session) cannot be determined. However, there was a trend of relative benefit after training from IG over AC on processing speed and working memory, and functional ability domains between pre- and post-training.

For the current study, the enrollment was the biggest challenge. This study only included one study site, and the target population was young and middle-aged adults with busy life and work. To improve the enrollment rate, it is recommended to have multiple sites in the trial, and also recruit not only Veterans but also civilians with TBI.

HRPO IRBs

HRPO #: A-19775

Title: Home-Based, Online, Mindfulness and Cognitive Training for Soldiers and Veterans with TBI

Two protocols:

1) HRPO #: A-19775.a - (PSC)

-- Western Institutional Review Board (IRB) approval: 2 August 2016

-- HRPO approval: NGMR, 16 March 2017 (approval pertains to the Data Coordinating Center for up to 100 subjects enrolled at the clinical performance site, which is reviewed and approved separately as A-19775.b).

2) HRPO #: A-19775.b - (VA Connecticut Healthcare System)

-- VA Connecticut Healthcare System Human Studies Subcommittee Approval: 6 October 2016

-- HRPO approval: NGMR, 16 March 2017 (approved for the enrollment of 100 subjects)

STATUS:

			Enter information regarding the number of subjects				
<u>HRPO Protocol Number</u>	<u>Protocol PI Name</u>	<u>Organization (Site)</u>	<u># Target</u>	<u># Phone Screened</u>	<u># Consented</u>	<u># Randomized</u>	<u># Completed</u>
A-19775a	Hyun Kyu Lee	Posit Science	0				
A-19775b	Morris Bell	VACHS	80	192	45	23	15

* 2 participants completed remote Post and Follow-up visits

What opportunities for training and professional development has the project provided?

While the current project was not specifically intended to provide training and professional development, we (Posit Science, the coordinating center's team) provided training regarding the project protocol to study site (VACHS), specifically how to properly identify, recruit and enroll participants, as well as how to conduct an assessment and deploy the training and monitor compliance.

How were the results disseminated to communities of interest?

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?

Currently, there is no plan to apply for other funding for this project. However, given that the low enrollment was the main problem of the current project, multiple sites should be considered to increase the enrollment rate for future studies.

The training program in this project would be classified as a device to enhance the cognitive and functional abilities of TBI patients.

Although the current results could not provide a clear answer for the relative effectiveness of the training intervention over the active control in improving cognitive and functional abilities in TBI veterans, there was a trend of relative benefit after training from IG over AC on processing speed and working memory and functional ability domains. This result suggests the possibility of using online remote training to be a possible remedy for individuals suffering from TBI symptoms.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

The neurological impact of TBI injuries can be long enduring and can affect every aspect of brain function. TBI contributes directly to neurological impairment and sets other progressive neurological changes in motion that can further degrade cognitive abilities and degrade the quality of life (QOLs) for an injured individual. However, there are no medications that currently meet a practice standard for treatment of cognitive impairment in this population, and the need for a new therapeutic strategy that is clinically effective, cost-effective, accessible is high. Even with the studies demonstrating the effectiveness of brain training and problem-solving training in cognitive improvement, there was no established platform or tool that provides effectively integrated cognitive training and problem-solving training that was individually tailored to TBI patients. The current study developed the first individually customized program that provides cognitive training integrated with problem-solving training. The training program is fully remote and delivered online, and anybody with an Internet connection can access and be trained.

What was the impact on other disciplines?

The participants in IG showed improvement in online training performance, suggesting improved cognitive performance on the trained cognitive domain. Although the transfer of the training benefit to the untrained cognitive performance was not found, there was some numerical benefit of IG over AC on a part of cognitive and functional measures.

What was the impact on technology transfer?

The training platform was developed to be delivered fully remotely via an online platform. This fully remote training platform could overcome time and regional barriers. Especially during the COVID-19 pandemic,

when the in-lab visits are discouraged, the fully online training platform could be an optimal means to deliver the training regimen to the target population.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Due to the difficulty of participant enrollment, we changed the inclusion criteria to include not only TBI veterans but also include TBI civilians. We have received the approvals of the modification from IRBs and CDMRP office. After the modification, however, no civilian was enrolled into the study.

Actual or anticipated problems or delays and actions or plans to resolve them

Nothing to report.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS:

• **Publications, conference papers, and presentations**

Nothing to report.

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers and presentations.

Nothing to report

- **Website(s) or other Internet site(s)**

www.brainhq.com

To access the training platform

login id: CogMindATest3@cogmind.com

password: CmATest03

To access the active control platform

login id: CogMindBTest2@cogmind.com

password: CmBTest02

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report

- **Other Products**

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

<i>Name:</i>	<i>Hyun Kyu Lee</i>
Project Role:	<i>PI</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>3</i>
Contribution to Project:	Dr. Lee has worked on supervising overall study progress.
Funding Support:	
<i>Name:</i>	<i>Morris Bell</i>
Project Role:	<i>Co-I</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>1</i>
Contribution to Project:	Dr. Bell has worked on supervising research staff.
Funding Support:	
<i>Name:</i>	<i>Sarah-Jane Kim</i>

Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Clinical Trials Manager</i> 4 Ms. Kim has worked on preparing study material and training study site staff, working with and supporting site coordinators with study tasks, and monitoring site data for completion and accuracy.
Funding Support:	

<i>Name:</i>	<i>Andrea Weinstein</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Study Coordinator</i> 4 Ms. Weinstein has worked on participant recruitment and screening, and supporting participants through training period.
Funding Support:	

<i>Name:</i>	<i>Bharath Muppala</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Clinical Rater</i> 4 Dr. Muppala has worked on participant screening and administering neuropsychological assessments.
Funding Support:	

<i>Name:</i>	<i>Harkirat Kaur</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Clinical Rater</i> 1 Ms. Kaur worked on administering neuropsychological assessments.
Funding Support:	

<i>Name:</i>	<i>Ian Dempsey</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Clinical Rater</i> 1 Mr. Dempsey worked on administering neuropsychological assessments.
Funding Support:	

<i>Name:</i>	<i>Karen Ablondi</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Study Coordinator</i> <i>1</i> Ms. Ablondi has worked on participant recruitment and screening and supporting participants through the training period.
Funding Support:	

<i>Name:</i>	<i>Cornie Fleury</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Clinical Rater</i> <i>2</i> Ms. Fleury has worked on participant screening and administering neuropsychological assessments
Funding Support:	

<i>Name:</i>	<i>Laura Beltran</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Site Data Manager</i> <i>1</i> Ms. Beltran has worked on entering data for monitoring and resolving data queries in the Electronic Data-capturing System for the site.
Funding Support:	

<i>Name:</i>	<i>Larry Walker</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Study Coordinator</i> <i>1</i> Mr. Walker has worked on participant recruitment for the site.
Funding Support:	

<i>Name:</i>	<i>Richard Gorman</i>
Project Role: Researcher Identifier (e.g. ORCID ID): Nearest person month worked: Contribution to Project:	<i>Back-up Clinical Rater</i> <i>1</i> Mr. Gorman served as the back-up Clinical Rater and provided technical support.
Funding Support:	

<i>Name:</i>	<i>Chris Averill</i>
Project Role:	<i>MRI Coordinator</i>

Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>1</i>
Contribution to Project:	Mr. Averill has worked on MRI data collection.
Funding Support:	

<i>Name:</i>	<i>Selin Goktas</i>
Project Role:	<i>MRI Coordinator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>1</i>
Contribution to Project:	Ms. Goktas has worked on MRI data collection.
Funding Support:	

<i>Name:</i>	<i>Jeremy Roscoe</i>
Project Role:	<i>MRI Coordinator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>1</i>
Contribution to Project:	Mr. Goktas has worked on MRI data collection.
Funding Support:	

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report.

What other organizations were involved as partners?

Organization Name: The VA Connecticut Healthcare System (VACHS)/ Magnetic Resonance Research Center (MRRC) at Yale University School of Medicine

Location of Organization: 950 Campbell Ave. Bldg. 35A Room 104 West Haven CT 06516

Partner's contribution to the project: Study Site (Participants enrollment, and assessment center)

Financial support: Subaward for salary support and MRI scanning fee.

In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff); N/A

Facilities (e.g., project staff use the partner's facilities for project activities); N/A

Collaboration (e.g., partner's staff work with project staff on the project); N/A

Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); N/A

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: The quad chart is uploaded as a separate file.

9. APPENDICES:

References cited.

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2. Goode, K. T. *et al.* Useful Field of View and Other Neurocognitive Indicators of Crash Risk in Older Adults. *Journal of Clinical Psychology in Medical Settings* **5**, 425–440 (1998).
3. Ball, K., Edwards, J. D. & Ross, and L. A. The impact of speed of processing training on cognitive and everyday functions. *J Gerontol B Psychol Sci Soc Sci* **62**, 19–31 (2007).
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