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

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13. SUPPLEMENTARY NOTES**14. ABSTRACT**Study and HRPO IRB were approved. Online training programs for both brain training and active control groups were created. Study site started participant enrollment and consented 12 participants by September 21st of 2017.**15. SUBJECT TERMS**

Training program, IRB approval, Participants enrollment

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Introduction

In this study, online individualized brain training program (cognitive training + mindfulness/stress-reduction training) with caregiver support portal and lifestyle monitor is evaluated as a Quality of Life (QOL) enhancing strategy by comparing it to an active control condition (casual video games + online TBI information session) for veterans with TBI. Our main project goals are a) to determine the effectiveness of this advanced brain training approach; b) to initiate strategies that encourage and document other key lifestyle changes known to contribute to brain health; c) to further optimize delivery strategies to ensure near-universal access; d) to assure that training *has* restored brain health and brought the patient to a better, safer brain-health level; and e) to determine long-term patient fates. To achieve these goals, we randomize 80 veterans with TBI to 12-weeks of in-home brain training vs. a control intervention. Patient outcomes are measured primarily using neuropsychological assessments in processing speed (composite score of Pattern Comparison, Digit Symbol Coding, and Letter Comparison). As secondary measures, we use neuropsychological assessments in attention (composite score of Attentional Blink, and Stroop), working memory (composite score of Picture Sequence Memory Test, and the Rey Auditory Verbal Learning Test), and executive function (composite score of Trail Making B and Task Switch). Functional and structural MRI are used to measure structural and functional neurological changes attributable to these interventions. The Functional Activities Questionnaire is used to document everyday function activity levels. Self-reported sleep quality, physical activity, levels of social communication, brain healthy diet, and mood are documented using daily program-embedded questionnaires delivered throughout the training to further measure QOL impacts, and to help determine the magnitude and endurance of increased resilience after training completion.

Keywords

traumatic brain injuries, cognitive training, and mindfulness training

Accomplishments

1. Task 1: Create training website

a. Training website is ready for both experimental and active control group

Training website: <https://app.brainhq.com>

- Subtask 1: Brain Exercise Selection

In this study, we have selected 18 brain training. Core training targets include visual and auditory processing accuracy, speed, and sequencing; phasic, sustained, and divided attention; memory and memory association; and executive control abilities. Participants progress from an initial limited performance ability that is supported by continual positive feedback and an individually adapted challenge level to maintain ~75-85% accuracy. As participants progress, improvements in processing speed and/or performance accuracy *and* in their controlled, higher-order performance operations are challenged at progressively more cognitively demanding task levels. By this adaptive training strategy, virtually all trainees, regardless of learning rate, are continuously challenged at an appropriate difficulty level as their abilities improve. Participants receive 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 have 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 are 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 crashes^{1, 2}, 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 depression³, and reduced the probability of a progression to dementia⁴.

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 speed. 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 expect to induce higher cognitive benefit on TBI veterans from this training program.

Table 1. Description of Brain Training Exercises	
Processing Speed	
Visual Sweeps ⁵	See two sweep patterns, either inwards or outwards. Indicate the direction of the two sweep-patterns direction in sequence.
Audio Sweeps	Listen to two sweep sounds. The sound can sweep up from a lower to higher frequency or down from the higher to lower frequency. Indicate the direction of the

	two sweep sounds in sequence.
Fine Tuning	Listen to sound and indicate the heard sound among examples.
Hawk Eye	See briefly presented items and locate the item which is slightly different from others.
Eye For Detail	See briefly presented three items in order and locate two items which are identical.
Attentional Control	
Double Decision ^{6, 7}	Watch for a vehicle in the center of the screen and road sign in the periphery. Indicate the central vehicle target and the periphery target location.
Target Tracker ⁶	Keep track of objects in motion and indicate the tracked objects.
TAPAT ⁸	Remember the target image and withhold a response for the target and commit a response for distractors.
Mixed Signal	Indicate if the two figures on the screen have the same color or not as fast as possible
Divided Attention	Watch two items presented at the screen and respond if they have the same color, shape or pattern.
Memory	
To-Do list training	Listen to a series of items presented in auditory format and select the items in the presented order on a visual grid.
Memory Grid	Click on a card and remember the sound associated to the card. The goal is to find a pair of cards having the matching sound.
Rhythm Recall	Listen to and watch a song, then repeat the timing sequence by pressing keyboard keys.
Scene Crasher	Watch a briefly presented image and indicate the missing item on the current image from memory
Executive Function	
Card Shark ^{9, 10}	Match if the 1, 2 or 3 back visual item is matching to the current visual item
Juggle Factor	Maintain and update specific locations depending on the given situation
Mind Bender	Respond to stimuli differently depending on changing rules.
Auditory Ace	Match if the 1, 2 or 3 back auditory stimuli is matching to the current auditory stimulus

- Subtask 2: Wrapper development and testing
- All training exercises and “Start Moving Forward program” were embedded into training system as a continuous training. Both Brain training and Active control group participants log into the same website and are moved to different training program depending on their login id (see Figure 1)

Figure 1. General Scheme of Training Program



- Subtask 3: Build study and caregiver portal
 Caregiver portal was created providing the progress of each participant on each cognitive domain. Participants and their caregivers can access the portal by just clicking on the “Progress” button on top of their training program. Caregiver portal includes 1) BrainHQ Calendar that shows the dates that participants used 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) represents participants’ overall gains from training. When starting, the quotient starts at zero. Each time participants complete a new training level, the BrainAQ will tick upward. As participants’ performance improves, the BrainAQ will increase proportionally, reflecting cognitive gains from training; 3) Stars earned and Levels completed across different exercises in different domain. By hovering over the map of the stars and the map of levels earned, participants can 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. Create participant binder with detailed assessment description and material for assessment and training
 - Participants binder is ready and shipped to research site.
 - b. Set up experimenter computers and install assessment related software
 - Experimenter computers were purchased and study site IT team set up the computers.
 - c. Set up training computers
 - Training computers were purchased and Posit IT team set up the computers.
 - d. Train site staff on study procedures
 - Site staff training was completed.
- 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. Contact potential participants and conduct phone screening.
 - b. Enroll participants and conduct baseline assessments.

Enrollment Table

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

- c. 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 attends weekly meetings with the National Center for PTSD for recruitment, which they will continue to do. The site had staffing issues (low staff) but have recently hired a new member to help with recruitment efforts and administering assessments. To help boost recruitment and enrollment, site will look into recruitment at the Newington Campus, which is a part of the VA Connecticut Healthcare System.

Impact

Nothing to Report

Changes/Problems
Nothing to Report.

Products

Nothing to Report

Participants & Other Collaborating Organizations

<i>Name:</i>	<i>Hyun Kyu Lee</i>
Project Role:	<i>PI</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>4</i>
Contribution to Project:	Dr. Lee has worked on preparing study design and material and training study site staff.
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:	<i>Clinical Trials Manager</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>4</i>
Contribution to Project:	Ms. Kim has worked on preparing study material and training study site staff.
Funding Support:	

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

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

Funding Support:	assessments.
<i>Name:</i>	<i>Wes Jackson</i>
Project Role:	<i>Software Engineer</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	Dr. Jackson has developed study website.
Funding Support:	
<i>Name:</i>	<i>Jose Gallegos</i>
Project Role:	<i>Game Programmer</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	Dr. Gallegos has worked on training program design and development.
Funding Support:	

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 \$ 354,030 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

Other.

Special Reporting Requirements
Nothing to Report

Appendices

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