AWARD NUMBER: W81XWH-16-1-0685

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

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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

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6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Posit Science Corporation
160 Pine Street Suite 200, San Francisco,
CA 94111

VA Connecticut Research and Education
Foundation (VACREF)
950 Campbell Avenue
West Haven, CT 06516

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

We are currently conducting a double-blinded, randomized controlled trial in our research site (VACREF) to examine the efficacy of integrated brain training compare to active control with TBI Veterans. Since it is designed as a double-blinded study, PIs are blinded to participants' group allocation, and therefore, intermediate data analysis was not performed. However, the training improvement on the intervention group, and the baseline differences between groups were tested for the data quality check.

14. ABSTRACT

Objectives: We examine 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: Veterans with TBI are randomly assigned to either brain training (Cognitive Training + Problem Solving training) or an active control group (AC, casual computer games + TBI information session). Participants are 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 complete tests of cognitive (processing speed, working memory, and executive control) and functional performance (Timed Instrumental Activities of Daily Living and The Mayo-Portland Adaptability Inventory) before and after 12 weeks of training. For a subset of participants, structural and functional neuroimaging assessments are performed to examine the brain mechanism of cognitive rejuvenation. The longer-term benefit of the brain-training is measured by 3-months post-assessment.

Up-to-date report of progress: We successfully developed training website with embedded problem-solving and cognitive training programs. Participant recruitment was initiated from the middle of 2017. Currently, our training site is actively recruiting, enrolling, monitoring and testing participants. The 12-month no-cost-extension was approved, and the project end date is now extended to September 14th of 2020.

Major Finding: Data analysis testing the group by time interaction will be done around the end of data collection. The baseline group difference and the improvement on the trained tasks were tested for quality check of the data. 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.

Problems/Issues: Participant recruitment is challenging due to the specificity of target population. To help boost recruitment, study site attends weekly meetings with the National Center for PTSD, which they will continue to do. The site is continuing to post flyers at the Newington Campus, which is part of the VA Connecticut Healthcare System. In addition, they have been making efforts to reconnect with potential participants who had previously contacted the site but were not able to make initial contact. The site has found success with recruitment at their local Outpatient Day Program, College Outreach Program and the VITAL Program, a Veterans outreach program, and will continue to recruit from these programs. Also, the site is looking into recruiting from other VAs in the region. Also, we have submitted the protocol modification including non-veteran TBI into enrollment. Currently, we are waiting for an official approval for the change.

15. SUBJECT TERMS

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

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

To test the efficacy of online, home-based brain training program compared to active control group in improving cognitive and function performance, we are conducting double-blinded, randomized controlled trial. Veterans suffering from TBI-related cognitive impairment are randomly assigned to either brain training (Cognitive Training + Problem Solving training) or an active control group (AC, casual computer games + VA information session). Participants' cognitive and functional performance are 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.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

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

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

For year 3, the major goal is to conduct randomized controlled trial.
Subtasks include 1) Participants recruitment and enrollment, 2) Conducting pre-, post- and 3-month follow-up assessments and 3) monitor participants' training on their assigned program.
The milestone for this major goal is to complete the participant enrollment by the middle of year 4.

As of September 14, 2019, we have consented 41 participants.

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Major Task: Continue participant recruitment and monitor enrolled participants' progress and performance.

The current study is preregistered on ClnicalTrials.Gov (NCT02922569)

We randomize veterans with TBI to 12-weeks of in-home cognitive training and Problem-Solving training (CT + PST) vs. a control intervention (casual video games + online veteran-related information session). Patient outcomes are 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 are used to measure structural and functional neurological changes attributable to these interventions. The Timed Instrumental Activity of Daily Living is used to document everyday functional activity levels. Self-reported sleep quality, physical activity, levels of social communication, brain healthy diet, and mood are documented to further measure Quality of Life (QOL) impacts, and to help determine the magnitude and endurance of increased resilience after training completion.

In-lab Cognitive and Functional Assessment Measures

Domain	**In-lab measures**
Processing Speed	Pattern number comparison Digit symbol coding Letter comparison
Memory	N-back Task Spatial working memory Digit Span (WAIS-IV) Rey Auditory Verbal Learning Test (RAVLT)
Executive Function	Trail Making A and B Flanker Task Stroop
Functional Outcomes	TIADL MPAI-4

Study Population:
The study population is composed of veterans who have persistent post-concussive symptoms (PPCS) following traumatic brain injury (TBI). We note that we expect this population to have substantial co-morbidities, including but not limited to PTSD, depression, chronic pain, and hearing loss, and intend to focus on "treating the symptoms rather than on determining the etiology of the symptoms" as recommended by VA/DoD Clinical Practice Guideline For Management Of Concussion-Traumatic Brain Injury.

Specific objectives
i) Contact potential participants and conduct phone screening.
ii) Schedule consent visit and enroll eligible participants.
iii) Conduct in-lab pre-training assessment and explain home-based training program.
iv) Conduct in-lab post-training assessment
v) Conduct 3-month follow-up assessment

Approval of local site and 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)

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 describe the opportunity to volunteer for a clinical trial to advance the science and treatment of TBI in veterans. The emphasis of the benefit is on advancing science and on helping people like the potential participant. Applicants are first screened via phone interview checked for eligibility and medical and non-medical conditions affecting neuropsychological testing.

Initial Contact	368
Phone Screened	171

Specific Objective 2*:* Schedule consent visit and enroll eligible participants.

During the consent/enrollment meeting, the Site Study Coordinator and the potential participant discuss 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 are offered the opportunity to join the study by signing a written consent using a consent form approved by the site's local IRB in order to participate.

After consent, participants undergo Screening to determine eligibility.

Consented and Screened	41

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

After completing pre-training assessments, we randomize participants into groups. Given the potential importance of PTSD status and depression status on the etiology of the PPCS as well as the response to cognitive training use, we employ the minimization method of adaptive stratified randomization to minimize the imbalance between the number of participants in each group over

the PTSD and depression factors. The minimization method addresses the general problem ensuring stratification across multiple factors in small or moderate sized trials. Five prognostic variables are considered: baseline age, education, gender, PTSD status, and depression status. All consent visit and pre-training assessment data for each participant are fully monitored, with all queries resolved, because allocation depends on obtaining data for all prognostic variables.

Scheduled for Pre-Assessment	0
Completed Pre-Assessment	20
Randomized	20

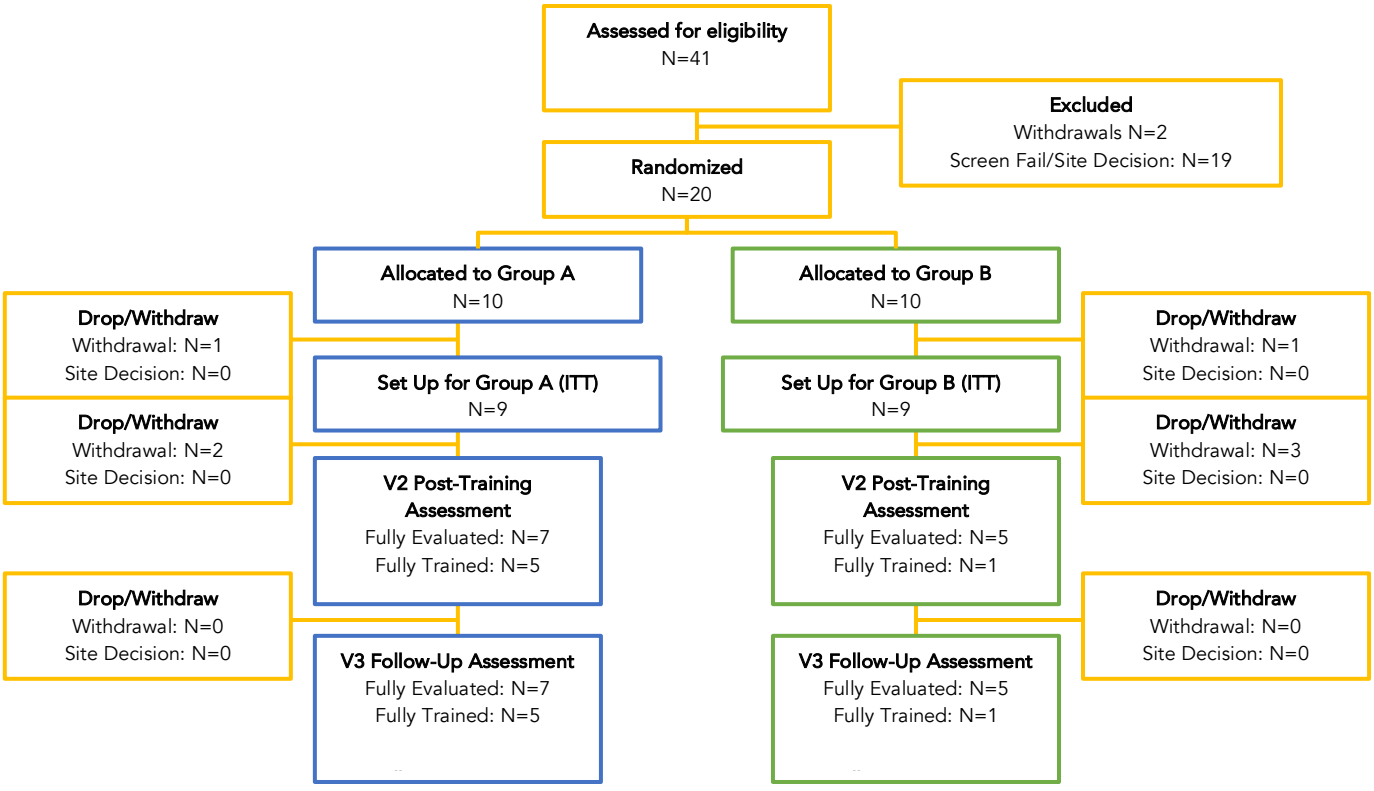
Site Study Coordinator orients the participant to the training program by sitting with them, in lab, and completing the first session. This is helpful for participants to become familiar with the program and using a computer, and be given the opportunity to ask questions about the training.

Actively Training	0

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

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

Study Consort Table.



Baseline Demographics between groups: Average and standard deviations shown below; all group differences were non-significant p>0.5

	A (N=10)	B (N=10)
Age	46.4 (15.05)	55.4 (10.10)
Education	15.0 (2.44)	13.6 (1.50)
Gender (% male)	90%	80%
Race (% White)	70%	70%
ANAM	-1.98 (2.1)	-2.27 (1.7)
RNBI Attention	73.1 (14.5)	65.7 (21.6)
RNBI Executive	64.8 (11.7)	60.5 (18.6)
RNBI Learning & Memory	77.5 (16.6)	74.5 (19.9)
RNBI Speech & Language	69.8 (14.3)	69.9 (18.1)
PCL-5	44.3 (12.15)	45.60 (25.18)

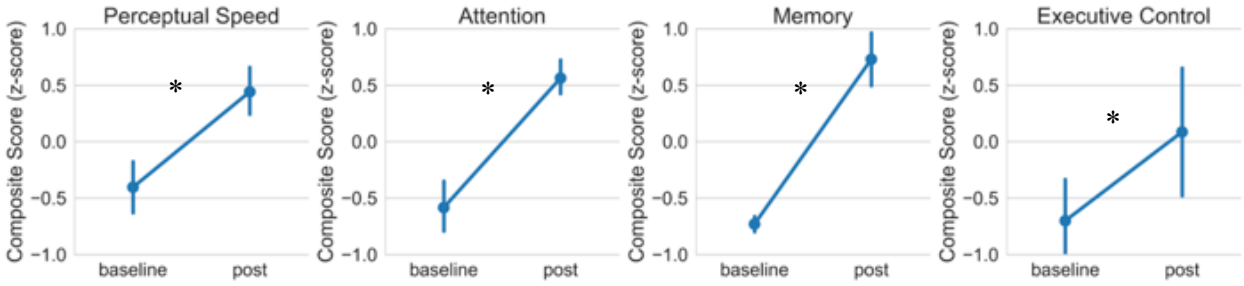
Baseline Outcome measures between groups: Average and standard deviations shown below; Primary measures were following: Pattern Number Comparison, Digit Symbol Coding, Letter Comparison: number of correct answers; Digit Span, RAVLT: total score; N-back, Spatial Working memory: Composite score of RT and ACC (Z-score); Trail A and Trail B: total time in seconds; Flanker Cost, Stroop Cost: Composite score of RT and ACC cost (difference between incongruent and congruent, Z-score); TIADL: Composite score of all tasks (Z-score); all group differences were non-significant, p>0.5

	A (N=10)	B (N=10)
Pattern Number Comparison	28.4 (5.29)	30.80 (9.0)
Digit Symbol Coding	67.6 (14.81)	60.90 (11.92)
Letter Comparison	19.9 (2.18)	19.5 (6.07)
N-back	-0.02 (0.79)	0.02 (0.47)
Spatial Working Memory	0.12 (0.96)	-0.12 (0.69)
Digit Span	9.10 (2.72)	10.10 (2.96)
RAVLT - Immediate	52.60 (8.85)	52.40 (8.83)
RAVLT - Delayed	8.20 (1.22)	7.80 (2.09)
Trail A	34.40 (9.31)	35.70 (12.58)
Trail B	86.34 (36.0)	94.03 (51.04)
Flanker Cost	0.001 (.22)	-.001 (1.00)
Stroop Cost	-0.01 (0.95)	0.009 (0.81)
TIADL Total	0.04 (0.52)	-0.04 (0.45)

Amount of Training Completed: no adverse event was reported.

	A (N=10)	B (N=10)
Number of Training Sessions	35.8 (28.0)	26.1 (21.1)
minimum	1	0
maximum	60	60

Performance Improvement on the Trained Tasks: Baseline and post scores for cognitive training exercises within each cognitive domain (only applied to cognitive training group, N = 10). Error bars are standard error. In CT 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 was 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, CT participants showed improvement from training to their post-score.



* p<.05

Conclusion:

- Experimental treatment and active control groups were well-matched at baseline demographics and assessments.
- TBI patients showed improvement on the brain training performance, suggesting the mild to moderate TBI patients are trainable.
- Participants showed tolerability of intervention and no adverse event was reported.

We upload all collected data on EDC and on FITBIR. We continuously monitor and manage electronic database.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

While the research in this grant proposal is not specifically intended to provide training and professional development, we (the coordinating center's team at Posit Science) completed online-based one-to-one training with staffs in research site of the RCT trial (VACREF).

Our team provided didactics and training regarding the population of interest (i.e., Veterans with TBI) and regarding the assessments used as outcome measures in the study. Specifically, our team trained site's staff on the project protocol; how to properly identify, recruit, and enroll participants, as well as how to conduct assessments and deploy the training/intervention and monitor compliance. Finally, our team trained the relevant site staff on using clinical trial tools that are employed in this trial (e.g. the CT Payer subject payment system; the EDC data monitoring system, etc.).

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

In accordance with the Clinical Trial Registration and Results Information Submission regulation (42 CFR Part 11), the dissemination of the proposed trial will be achieved by ensuring that:

(1) The clinical trial is promptly registered on ClinicalTrials.gov within 21 calendar days after the enrollment of the first participant. Registered information will include descriptive information, recruitment information, location and contact information, and administrative data.

(2) The clinical trial is continuously maintained and updated with the study's current status including summary results within one year after the trial's primary completion date. Summary results will include participant flow, demographic and baseline characteristics, outcomes and statistical analyses, adverse events, the protocol and statistical analysis plan, and administrative information.

(3) The clinical trial will include an explicit statement on all participant consent forms that describe the posting of trial information as well as the ClinicalTrials.gov registration link.

(4) Dissemination is planned following the completion of the RCT, data analysis, and manuscript preparation.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We will continue participant-related activities to meet target enrollment number.
The next major task is to analyze and interpret data. We will prepare data for analysis and analyze neurobehavioral and imaging data. The milestone to be achieved during next reporting period is completion of data analysis and preparation for publication by the end of project period.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Positive results from this trial are expected to make a substantial impact on the medical field, through the deployment of the first effective treatment for TBI-related cognitive decline. This is an area with a large unmet medical need. The deployment of an effective treatment based on a successful trial would improve the lives of everyone suffering from cognitive consequences of TBI.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the results from the trial are positive, there will be a substantial impact on the commercial technology of brain training, as this is the first remotely-administered, cost-effective treatment for cognitive decline in TBI.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report." Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

In order to meet enrollment goal, we have extended project period to another 12 months. The period of participants' enrollment and subsequent participants-related activities was extended until month 42 on SOW. The data preparation and analysis are scheduled to perform during the last two months of project period. Modified SOW is attached in Appendix A.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Problems: Due to specificity of target population, we had very low recruitment rate in year 3. **Details of the recruitment activities carried out and actions being taken to remedy the enrollment shortfall:** In order to increase the enrollment rate, we have submitted the modification on enrollment criteria including non-veteran TBI patients. We are currently waiting for the official approval of this change. The site attends weekly meetings with the National Center for PTSD for recruitment, which they will continue to do. The site is continuing to post flyers at the Newington Campus, which is part of the VA Connecticut Healthcare System. In addition, they have been making efforts to reconnect with potential participants who had previously contacted the site but were not able to make initial contact. The site has found success with recruitment at their local Outpatient Day Program, College Outreach Program and the VITAL Program, a Veterans outreach program, and will continue to recruit from these programs. To help boost recruitment, the site is looking into recruiting from other VAs in the region.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

We submitted the change for inclusion criteria including non-veteran TBI patients.

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: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

Nothing to Report

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

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

https://app.brainhq.com From the following url, you can check training website using following credentials. Experimental group Username and password: CogMindATest2@cogmind.com Active Control Username and password: CogMindBTest1@cogmind.com

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name:	*Hyun Kyu Lee*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*3*
Contribution to Project:	Dr. Lee has worked on supervising overall study progress.
Funding Support:	

Name:	*Morris Bell*
Project Role:	*Co-I*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	Dr. Bell has worked on supervising research staff.
Funding Support:	

Name:	*Sarah-Jane Kim*
Project Role:	*Clinical Trials Manager*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*4*
Contribution to Project:	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:	

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

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

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

Name:	*Cortnie Fleury*
Project Role:	*Clinical Rater*

Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*2*
Contribution to Project:	Ms. Fleury has worked on participant screening and administering neuropsychological assessments
Funding Support:	

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

Name:	*Larry Walker*
Project Role:	*Study Coordinator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	Mr. Walker has worked on participant recruitment for the site.
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?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial

or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

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.

8. COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments*

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

Appendix A: Modified Statement of Work

STATEMENT OF WORK – Month/Day/Year
PROPOSED START DATE Oct. 01, 2016

Site 1: Posit Science Corporation. (PSC)
160 Pine Street Suite 200, San Francisco, CA 94111
PI: Hyunkyu Lee

Site 2: VA Connecticut Research and Education Foundation (VACREF)
950 Campbell Avenue
West Haven, CT 06516
Partnering PI: Morris Bell

Developmental Aims 1-3	Timeline	Site 1	Site 2
Major Task 1: Develop Programs and Initiate Trial	Months		
Subtask 1: Brain Exercise Selection	1	PSC	
Subtask 2: Wrapper development and testing	1	PSC	
Subtask 3: Build study and caregiver portal	1-3	PSC	
Milestone(s) Achieved: Release study and caregiver portal	3	PSC	
Regulatory review and approval by the USAMRMC Human Research Protection Office	6	PSC	
Local IRB Approval	6		VACREF
Scientific Aims 1-2			
Major Task 2: Conduct Trial			
Subtask 1: Participants recruitment and enrollment	6-42		VACREF
Subtask 2: Assessments and training	6-45		VACREF
Subtask 3: 6-months post training assessment	12-48		VACREF
Milestone: Enrollment and Data collection is complete.	48		VACREF
Major Task 3: Analyze and Interpret Data			
Subtask 1: Prepare data for analysis, and analyze neurobehavioral and imaging data.	46-48	PSC	VACREF
Milestone(s) Achieved: Completion of Data Analysis and Prepare for Publication	48	PSC	VACREF

If human subjects are involved in the proposed study, please provide the projected quarterly enrollment in the following table.

	Year 1	Year 2	Year 3	Year 4

Target Enrollment (per quarter)	**Q 1**	**Q 2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q 1**	**Q 2**	**Q 3**	**Q 4**	**Q 1**	**Q 2**	**Q3**	**Q 4**
Site 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Site 2	0	3	9	1	5	8	8	3	1	3	0	0	5	5	0	0
Target Enrollment (Cumulative)	**0**	**3**	**12**	**13**	**18**	**26**	**34**	**37**	**38**	**41**	**41**	**41**	**46**	**51**		

Note: The Government reserves the right to request a revised SOW format and/or additional information.