Cognitive Training as a Novel Neuroscience-based Treatment for PTSD

NCT03316196

January 9, 2024

Human Protocol (Version 1.66)

General Information

***Please enter the full title of your study::**

Cognitive Training as a Novel Neuroscience-Based Treatment for PTSD

***Please enter the Study Number you would like to use to reference the study:**

CT for PTSD
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

Add departments

and Specify Research Location:

Is Primary?	Department Name
◉	**VASDHS** - VASDHS

Assign key study personnel(KSP) access to the study

***Please add a Principal Investigator for the study:**

Bomyea, Jessica A., PhD

3.1 If applicable, please select the Research Staff personnel

A) Additional Investigators

Jak, Amy J., PhD
Co-Investigator
Simmons, Alan N., PhD
Co-Investigator
Stein, Murray B., MD
Co-Investigator

B) Research Support Staff

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Northup, Sara
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Student
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***Please add a Study Contact**

Bomyea, Jessica A., PhD

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

Section 1 - Preliminaries

Principal Investigator:

Jessica A. Bomyea, PhD

Protocol Title:

Cognitive Training as a Novel Neuroscience-Based Treatment for PTSD

IRB Protocol Number:

H170098

Protocol Nickname:

CT for PTSD

Form Template Version:

v20150115

Date Prepared:

01/09/2024

Please be advised that this protocol application form has changed as a result of the 2018 Common Rule. There are new questions and sections, and you may be required to provide additional information to previous sections.

1a) Is this study considered human research?

- (•) Yes
- ( ) No
- ( ) I don't know

1b) Please select:

- ( ) This is an application for a NEW human subject research protocol
- (•) This is a revision of an existing protocol

Was this study initially approved prior to January 21, 2019?

(•) Yes ( ) No

Were you instructed to convert to the 2018 Common Rule Requirements?

( ) Yes (•) No

Section 2 - Research Subjects

2a) What is the total planned number of VA-consented subjects?

Include the total number of subjects who will prospectively agree to participate in the study (e.g., documented consent, oral consent, or other).

130

2b) What is the total number of VA subjects who WILL NOT be consented?

Include the total number of subjects that will be included without consent (e.g., chart review). *Note: Data about people are still considered "human subjects" by the IRB, so even if you do not intend to contact the patients whose charts you will review, you still should enter the number of charts as your "planned subjects."*

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Section 2.1 Consented Subject Groups

2.1) For each of the subject categories listed below, indicate whether or not these subject groups will participate in the study:

2.1a) Children under the age of 18
Note: If neonates or children will be involved in this study, certification by the Medical Center Director will be required. Only minimal risk research may be performed with children. Only non-invasive monitoring and/or prospective observational and retrospective record review studies that are minimal risk can be conducted in VA involving neonates.

○ Yes ◉ No

2.1b) Pregnant women

○ Yes ◉ No

2.1c) Individuals with cognitive/decisional impairment

○ Yes ◉ No

2.1d) Non-English-speaking individuals

○ Yes ◉ No

2.1e) Prisoners of War (explicitly targeting this group)

○ Yes ◉ No

2.1f) Non-Veterans (Note: Justification for inclusion of non-Veterans will be required)

○ Yes ◉ No

2.1g) Incarcerated individuals (Note: VA CRADO approval will be required)

○ Yes ◉ No

2.1h) VA employees - including VA paid, IPA, or WOC (Note: Union review and authorization may be required)

○ Yes ◉ No

2.1i) Students of the institution (e.g., resident trainees) or of the investigator

○ Yes ◉ No

2.1j) Patients with cancer (or high cancer risk) [explicitly targeting this group]

○ Yes ◉ No

Section 3 - Study Features (these items default to "No" for convenience)

3) This section consists of several Yes/No questions addressing protocol characteristics. Click on *Save and Continue*.

Section 3.1 Protocol Basics

Select all that apply

3.1a) The research **intends to change** the participant.

◉ Yes ○ No

3.1b) **Interactions** with living participants to collect data or specimens with no intent to change them.

○ Yes ◉ No

3.1c) This is a study that **never** has any **subject contact and does not collect subject identifiers**

○ Yes ◉ No

3.1d) This is a **chart review** study involving retrospective or prospective medical records.

○ Yes ◉ No

3.1e) This is a **multi-site** study occurring in-part or in-full at other locations.

○ Yes ◉ No

3.1f) There is an **international** component to this research. *International research includes sending or receiving human derived data or specimens (identifiable, limited data set, coded, or deidentified) to or from an international source. International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator.*

○ Yes ◉ No

3.1g) This study includes **off-station activity** (not including VA-leased space or CBOC clinics) conducted under VASDHS IRB approval. *Note: this does not include research conducted by a collaborator at their home institution under their institutional approval.*

◉ Yes ○ No

3.1h) VA subjects will **participate** in part or in full **at other locations** (not including VA-leased space or clinics) under VASDHS IRB approval. *Note: if this study involves remote participation of subjects, please indicate "no" and describe their remote participation in section 9 of the application. This question is intended to understand whether participants must physically go to a non-VA location to participate in this VA research study.*

◉ Yes ○ No

Section 3.2 Specimen Use and Data Repository

Indicate whether or not each of the following applies to this protocol

3.2a) Involves specimens that are left over from pathological or diagnostic testing (**non-research specimens**)

○ Yes ◉ No

3.2b) Involves **specimens collected for research** purposes **only**

○ Yes ◉ No

3.2c) This study includes **specimen banking** (specimens are retained for use outside of the purposes of this protocol)

○ Yes ◉ No

3.2d) The study involves **DNA** genotyping or other **genetic analysis**

○ Yes ◉ No

3.2e) Biological **specimens/material** will be sent outside of the VA.

○ Yes ◉ No

3.2f) A **data repository** is maintained (data are retained after completion of the protocol for other uses, IMPORTANT: see **?** before checking "yes")

○ Yes ◉ No

3.2g) **Data will be shared outside** of the VA (identifiable, coded, limited data set, or deidentified)

○ Yes ◉ No

Section 3.3 Treatment and Clinical Trials

Indicate whether or not each of the following applies to this protocol

3.3a) Includes a **treatment** component (a research treatment)

(•) Yes ( ) No

3.3b) Study is a **clinical trial.** *Note: A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.*

(•) Yes ( ) No

3.3c) Has a data safety monitoring board (**DSMB)** or data safety monitoring committee.

( ) Yes (•) No

3.3d) Has a **data safety monitoring plan** (but not a DSMB) (this is not the data security plan, it is a safety plan).

(•) Yes ( ) No

Section 3.4 Drugs and Devices

Indicate whether or not each of the following applies to this protocol

3.4a) **Drugs** that require **FDA** action such as an Investigational New Drug (IND) approval or exemption or 510 (k) approval.

( ) Yes (•) No

3.4b) Other drugs, supplement, etc. that **do not require FDA** action for inclusion in the study.

( ) Yes (•) No

3.4c) Medical **devices requiring FDA** IDE approval or waiver

( ) Yes (•) No

3.4d) **Other** medical **devices**

( ) Yes (•) No

Section 3.5 Risk and Hazards

Indicate whether or not each of the following applies to this protocol

3.5a) Study places subjects at **greater than minimal risk** (do not include risks that are due to standard care)

( ) Yes (•) No

3.5b) Human subjects are exposed to **radioisotopes** (do not include standard care).

( ) Yes (•) No

3.5c) Subjects have other **radiation exposure** (e.g., x-rays) (do not include standard clinical use).

( ) Yes (•) No

3.5d) Target population has psychiatric diagnosis, behavioral complaint, or chronic pain.

(•) Yes ( ) No

Section 3.6 Clinical Facilities and Standard Care

Indicate whether or not each of the following applies to this protocol

3.6a) Study **uses VA clinical services** (e.g., adds required tests run in the VA lab for study purposes; research procedures concurrent with clinical care)

○ Yes ◉ No

3.6b) Includes procedures or drugs that will be considered **part of standard care.**

○ Yes ◉ No

3.6c) Involves **lab tests done for research** purposes.

○ Yes ◉ No

Section 3.7 Subject Expenses and Compensation

Indicate whether or not each of the following applies to this protocol

3.7a) There may be expense or added **costs to the subject** or the subject's insurance.

○ Yes ◉ No

3.7b) This is a **qualifying cancer treatment trial** and subjects may be billed for study drugs or procedures.

○ Yes ◉ No

3.7c) This is a cancer treatment trial but **subjects will not be billed** for study drugs or procedures.

○ Yes ◉ No

3.7d) Subjects will be **compensated** (either in cash or other means such as a gift certificate).

◉ Yes ○ No

Section 3.8 Subject Activities

Indicate whether or not each of the following applies to this protocol

3.8a) Involves **surveys or questionnaires** completed by subjects

◉ Yes ○ No

3.8b) Includes the use of **recruitment materials** such as flyers, advertisements, or letters

◉ Yes ○ No

3.8c) Involves facial **photographs** or audio or video **recordings** of **patients**

◉ Yes ○ No

Section 3.9 Sponsors and Collaboration

Indicate whether or not each of the following applies to this protocol

3.9a) This research is a funded research project **(commercial (industry) sponsor, NIH, VA, other).**

○ Yes ◉ No

3.9b) Other **commercial (industry) non-financial support** is provided (e.g., drugs or supplies).

○ Yes ◉ No

3.9d) The protocol has **Department of Defense** involvement (e.g., subjects or funding).

○ Yes ◉ No

3.9c) The PI or other study staff member has a financial interest or other **real or potential conflict** related to this study.

○ Yes ◉ No

3.9e) This study involves **collaborative** research activities (research conducted at other institutions under the authorities or approvals of the other institution/s). *Note: this may include other VA and/or non-VA institutions, but does not include off-site VA research.*

○ Yes ◉ No

Section 4 - Estimated Duration

4) What is the estimated duration of the entire study? (From IRB approval to IRB closure)

5 years

Section 5 - Lay Language Summary

5) Provide a summary or synopsis of the proposed study using non-technical language (not more than 1 paragraph)

The proposal aims to evaluate the effect of a cognitive training intervention program on emotional and cognitive symptoms of posttraumatic stress disorder in Veterans. The proposal also seeks to examine neurobiological mechanisms of generalization to symptom reduction. Using functional magnetic resonance imaging, the neural regions involved in neutral and affective cognitive
control functioning will be examined before and after the intervention, and associations between activation in neural regions and symptom reduction will be examined. The planned study will provide critical information about the efficacy of this type of program for Veterans with PTSD, while simultaneously informing neurobiological and cognitive models of the disorder that will allow for more precise treatment development and personalization.

Section 6 - Specific Aims

6) Provide a statement of specific aims and hypotheses that serve as the basis for this protocol. Emphasize those aspects that justify the use of human subjects.

Research design. The proposed study is a randomized controlled trial of 80 Veterans with PTSD who will be assigned to cognitive training (COGENT) or a sham training (ST). 130 participants will be consented and evaluated for eligibility with the goal of achieving 80 randomized participants.

Aim 1: To examine the effects of COGENT versus ST on PTSD symptom outcomes.
Primary outcome: PTSD re-experiencing symptoms will be measured using the Clinician Administered PTSD Scale (CAPS) interview.
Hypothesis: Individuals completing COGENT will demonstrate a significantly greater reduction in symptoms relative to those in ST.
Secondary outcome: Cognitive symptoms will be measured using subtests of the Delis Kaplan Executive Function System (DKEFS). A composite score for subtests will be created based on scaled scores for each.
Hypothesis: Individuals completing COGENT will demonstrate a significantly greater improvement in performance relative to those in ST.

Aim 2: To examine the effects of COGENT versus ST on neural functioning during cognitive control.

Primary Outcomes: Change in neural activity using % signal difference between a) a reappraisal task (reappraisal versus maintain conditions)and b) a cognitive function task (Reading Span task; interference versus baseline condition).
Hypotheses: COGENT will result in greater neural activation relative to ST in regions including the dlPFC, dACC, parietal cortex, and IFG during both tasks, and less activation in amygdala and insula regions in the reappraisal task.

Section 7 - Background and Significance

7) Provide a succinct discussion of relevant background information to justify performing the proposed study.

PTSD is one of the most prevalent service-related mental health conditions in treatment-seeking Veterans, and is associated with negative outcomes including greater healthcare utilization, physical health comorbidities, and greater risk for suicide (e.g., Hidalgo & Davidson, 2008; Seal et al., 2007). Current empirically supported treatments for PTSD utilize time-limited, manualized interventions based on cognitive-behavioral principles (e.g., Prolonged Exposure [PE] and Cognitive Processing Therapy [CPT]). Numerous studies indicate that PE and CPT are effective (Ponniah & Hollon, 2009), yet even these first-line interventions are not uniformly tolerated or accepted. Non-response and drop-out rates have been estimated as high as 30-50%, and residual symptoms remain even among treatment responders (Bradley et al., 2005; Schottenbauer et al., 2008). Psychotherapy also requires substantial time and effort from patients both during sessions and while completing home-based exercises. Thus, though there are treatments that are very effective for some Veterans with PTSD, many individuals do not access or complete empirically supported approaches, and therapies are not effective for all patients, suggesting a need for continued therapeutic development. Veterans would be greatly served by research examining novel intervention approaches for PTSD, particularly those that could be translated into a transportable, efficacious, and low-burden program for wide dissemination.

Recent theoretical accounts suggest that PTSD symptoms stem from deficits in cognitive systems that regulate, manage, and manipulate information generally (e. g., Anderson & Levy, 2009; Bomyea & Lang, 2015, Verwoerd, de Jong, & Wessel, 2008). By this account, individuals with poor *cognitive control* are more likely to experience intrusive cognitions. Cognitive control refers to domain-general control mechanisms that govern cognitive sub-processes used in higher order cognition, including updating and monitoring information, controlling interference from unwanted or unnecessary information, and shifting between mental sets (Miyake et al., 2000). Individuals with poor cognitive control may be vulnerable to intrusions because they lack adequate cognitive resources to down-regulate irrelevant or unwanted thoughts and memories when prompted with perceptual or semantic retrieval cues. Common, shared cognitive and neural mechanisms are thought to be responsible for affectively-neutral cognitive control (i.e., “cold” regulation), which is reflected in neuropsychological abilities and cognitive task performance, and affectively-valenced cognitive control (i.e., “hot” regulation) which is reflected in the ability to manage emotional information such as traumatic memories (Banich et al., 2009; Bomyea & Lang, 2015; Ochsner & Gross, 2006, 2008). These shared mechanisms may account for the link between cognitive control ability and re-experiencing symptoms in PTSD.

The emerging field of neurotherapeutics, which uses computerized cognitive training techniques to modulate cognitive processing, has shown promise for improving cognition and symptoms in mental health disorders. Several studies indicate that it is possible to improve cognitive control using training programs in diverse populations such as children with attention deficit hyperactivity disorder (e.g., Klingberg et al., 2005), older adults (Buschkuehl et al., 2008), individuals with schizophrenia (Vinogradov et al,. 2012), and healthy participants (Jaeggi,

Buschkuehl, Jonides, & Perrig, 2008). Training-related changes can be observed via neural changes during task performance, suggesting that modification of neurobiological circuitry may be a mechanism of generalization from task to symptoms (Kane & Engle, 2002; Olesen et al., 2004; Schweizer et al., 2013). In addition, several studies indicate that computer-based programs designed to modify cognitive biases (e.g., attention) decrease anxiety symptoms (e.g., Amir, Beard, Burns, & Bomyea, 2009). Given that cognitive control supports complex cognition, which includes regulating thoughts and memories, it may be an ideal initial target for neurotherapeutic development in PTSD.

In spite of evidence for the potential efficacy of neurotherapeutics, to date only one study has evaluated the efficacy of cognitive control training in PTSD, and no published studies have evaluated its efficacy in Veterans. The applicant developed a cognitive control neurotherapeutic intervention tested in a relatively small, homogeneous group of women with PTSD secondary to sexual trauma (Bomyea et al., 2015). A critical next step is the evaluation of the program in a larger, diverse group. In particular, the efficacy in a Veteran population has not yet been evaluated, and the neurocognitive mechanisms of symptom reduction following this intervention remain to be established. Also, understanding how cognitive training culminates in symptom reduction is a critical next step for improving the efficacy of this program. Neural systems used for cognitive control functions targeted in the training described (e.g., dlPFC) are also recruited for reappraisal functions during emotion regulation as described above. PTSD is characterized by aberrant affective and neurobiological patterns during reappraisal, which may contribute to persistent re-experiencing and hyperarousal symptoms. Modifying functioning in these substrates with training may thus reduce symptoms by improving neural functioning during affective processes that are critical to managing trauma-related information and emotions.

The current proposal aims to bridge research on basic neurocognitive mechanisms of PTSD with intervention research by conducting a randomized controlled trial (RCT) of the cognitive control training program developed by Dr. Bomyea and colleagues in Veterans with PTSD. The primary aim will be to examine the effects of the training program on PTSD and cognitive symptoms (neuropsychological performance) in Veterans. A secondary aim will explore hypothesized mechanisms by which symptom reduction occurs by examining training-related changes in the neurobiological substrates of cognitive control on an affectively-neutral cognitive control task (i.e., Reading span task; Rspan) and on an affectively-valenced cognitive control task (i.e., reappraisal task).

Section 9 - Design and Methods

9) Describe the research design and the procedures to be used to accomplish the specific aims of the project. Provide a precise description of the planned data collection (include what systems or databases will be used/accessed to gather data), analysis and interpretation. For chart review studies, include the timeframe of collection. Address sample size, inclusion of women and minorities. Define in clear terms exactly what will be done to the human subjects.

Due to COVID-19 related changes, the lab will be able to recruit active duty participants through the community directly using Build Clinical. VASDHS staff will collect all study data directly from participants. Therefore, due to COVID-19, in addition to items specified above, VASDHS staff will also be responsible for the below:
1. Recruitment of active duty service members through various online community platforms
2. Determining preliminary eligibility for the study.

The proposed study is a randomized controlled trial of 80 Veterans with PTSD who will be assigned to cognitive training (COGENT) or sham training (ST). Data collection will consist of interview measures, self-report measures, neuropsychological test measures, and fMRI data. Participants will begin the study by completing an eligibility assessment, where diagnostic status and fMRI safety will

be confirmed via interview. If eligible, participants will then complete additional self-report measures that will assess symptoms severity. It is anticipated that approximately 130 participants will be evaluated for eligibility to randomized a total of 80 participants. Primary self-report assessment time points will occur at baseline pre-treatment, immediately post-treatment (2-months post-baseline), and at a 2-month follow-up (4 months post-baseline). One additional intermediary assessment will also be conducted at the mid-treatment time point (1 month post-baseline) for clinical monitoring purposes. Neurobiological fMRI assessments and neuropsychological assessment will occur at the baseline and post-treatment assessment time points. During fMRI participants will complete cognitive control tasks probing affectively neutral and affectively-valenced cognitive control processing (cognitive control task, reappraisal task). During neuropsychological testing, participants will complete standard measures of executive functioning. Analyses will be conducted to examine change from pre- to post-intervention across the active and control groups.

Visit	Time Commitment	Materials
Visit 0: Telephone Screening	< 20 minutes	MRI safety screening by phone/zoom
Visit 1: Study enrollment interview	< 2 hours	MINI and CAPs interview
Visit 1: Pre-treatment assessment if eligible	1 hour	Self report battery, neurocognitive battery
Visit 2: Pre-treatment fMRI session	< 2 hours	Cognitive control tasks in scanner
Visits 3-19: COGENT or ST (8 weeks of treatment)	< 30 minutes ea.	COGENT or ST program; Self report battery at visit 9 for monitoring
Visit 20: Post-treatment fMRI visit	< 2 hours	Cognitive control tasks in scanner
Visit 21: Post-treatment assessment time point	< 3 hours	CAPS interview, self-report battery, neurocognitive battery
Visit 22: Follow-up assessment time point (8 weeks post-treatment)	< 3 hours	CAPS interview, self-report battery, neurocognitive battery

130 Veterans between the ages of 21-55 will be recruited in order to achieve a recruitment goal of 80 randomized participants. Eligible Veterans will contact our study coordinator in response to 1) flyers posted in VA mental health, primary care, and general community areas as authorized by VASDHS, 2) advertisements in print and web-based media in the general community, 3) referrals from the VA mental health and primary care clinics and research studies.

Previous recruitment from our VASDHS studies has obtained 9% Hispanic, 16% African American, and 4% other ethnic groups, for a total of 29% from minority groups. In addition, there are increasing numbers of women in the military seeking VA services and a greater Hispanic proportion of the population in southern California. Thus, there will be continued attempts to oversample these groups to obtain adequate recruitment of females and minorities to examine effect sizes for these groups relative to male and Caucasian counterparts. Inclusion of these groups is critical given the disproportionately higher prevalence of PTSD diagnosis among women (56% of women; 40% of men) and minorities (38% of whites; 52% of minorities) observed in previous studies.

Cognitive Training Programs:
Both COGENT and ST consisted of a modified complex span task, which requires the participant to remember item stimuli presented while doing a secondary problem solving/processing task. The two conditions differ only on the amount of interference control required to successfully remember stimuli on each trial (Daneman & Carpenter, 1980; adapted by Lustig et al., 2001). Each trial begins with a fixation cross in the center of the screen for 500ms. Then, a processing task (e.g., “Jane walks her car in the park”) appears on the screen. The participant must make a determination about the processing task (e.g., "Does the sentence make sense?") by selecting a box on the screen. Once the participant completes the processing task, a to-be-remembered item appears on the screen for 500 ms (e.g., "L"). Then the next trial begins with another processing

problem and item, until the end of the set. At the end of each set participants view a recognition screen listing twelve items and select the items that were previously presented in the correct serial order. Once the recognition for the set is completed, the next set of trials began in the same manner. Complex span tasks require interference control resources to perform accurately as trials progress, and item similarity is one factor that determines the amount of interference that exists within the task – stimuli that are more similar create more interference, while less similar stimuli create less (Bunting, 2006).

COGENT condition: COGENT was designed to require high interference control across trials. All to-be-remembered items are derived from the same category (e.g., all letter stimuli), based on prior data suggesting that maintaining the same type of to-be-remembered items across trials maximizes interference (Bunting, 2006). By requiring repeated practice with utilization of interference control across trials, COGENT is thought to enhance plasticity of cognitive systems and improve performance. That is, training is based on the premise that learning-based neural changes will occur via repeated exposure to a task demanding cognitive control resources.

ST condition: ST was designed to contain relatively less proactive interference across trials by alternating item category (e.g., letters, then numbers) every three trials (Bunting, 2006). Thus, although participants are required to remember the same total number of items as in COGENT (i. e., storage requirements were equivalent), there is relatively less interference inherent in the task because trials with number memoranda interfere minimally on trials with word memoranda and vice versa.

MEG
Participants will be asked if they are interested in an optional MEG study titled "Passive electrical neurofeedback treatment of mTBI: MEG and Behavioral Outcomes" IRB# H17033 (P.I. Mingxiong Huang, PhD). If participants consent to be contacted for the optional study, Dr. Huang's approved research team will contact subjects and, if subjects agree, consent them for the study.

Section 9.8 Questionnaires & Surveys

9.8) Provide the name and a reference for questionnaires/surveys that are standard or identify them here and attach a copy of the questionnaire/survey. ***Questionnaires or surveys that are not clinical standard references must be uploaded. Reference the help link for additional information related to surveys administered to VA personnel and approved platforms for web-based surveys.***

Each of the measures selected in a gold-standard or commonly used assessment for the symptom or problem of interest (measures that are not standard for VA care have been attached to the protocol).

Interview Measures:
1. The Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Weathers et al., 2013). This semi-structured interview is designed to measure PTSD diagnostic status as well as symptoms severity. As part of the CAPS, the Life Events Checklist-5 will be given to assess exposure to potentially traumatic events. Using the list as a prompt, respondents select up to three of the most traumatic events they have experienced, and those events are used as the basis of assessing PTSD. All raters will be thoroughly trained for diagnostic accuracy using the standardized CAPS training procedures, and will be closely supervised by Dr. Stein to confirm diagnostic accuracy (including review of audiotaped assessments). The CAPS can be administered in 30-60 minutes, and it has the advantages of categorical (diagnostic) or dimensional scoring of PTSD plus items for assessing social and occupational functioning, dissociation, and the validity of the items. The CAPS will be given at the baseline, post-treatment, and follow-up assessment time points. CAPS diagnostic status will be used to determine inclusion criteria (i.e., diagnosis of PTSD met), and continuous severity scores from the measure are the primary PTSD symptom outcome.
2. MINI International Neuropsychiatric Interview (Sheehan et al., 1998). The MINI includes questions assessing Axis-I psychiatric disorders and also contains questions assessing general health and current and past treatment utilization (e.g., major medical disorders). The MINI will be administered to determine the presence of other comorbid disorders.
3. fMRI safety screening questionnaire. This interviewer-administered questionnaire is provided by the UCSD imaging center and includes a series of items assessing participant compatibility and safety for completion of fMRI (e.g., shrapnel in body, tattoos, body mass index). It will be administered as part of the phone screening, and again immediately before MRI assessments to confirm that the individual can be scanned safely.
4. TBI assessment. The Ohio State University Traumatic Brain Injury Identification Method Short Form (OSU TBI-ID; Corrigan et al., 2007) will be used to assess TBI history and concussion-related injury features (i.e., loss of consciousness, amnesia).

5. The Emory Treatment Resistance Interview for PTSD (Dunlop et al., 2014). This interview assessment collects detailed information regarding prior treatment history and engagement.
6. A Timeline Follow-Back (TLFB) will be administered to record how much alcohol, tobacco, and recreational drugs subjects consumed during the past 30 days.

Self-report battery measures:
Self-report measures will be given at the baseline, mid-treatment, post-treatment and follow-up assessment points as a secondary measure of outcomes and for clinical monitoring purposes.
1. The PTSD Checklist for DSM-5 (PCL; Weathers et al., 2013). This self-report measure is designed to assess severity of PTSD symptoms.
2. The Beck Depression Inventory II (BDI-II; Beck Steer, & Brown, 1996). This self-report measure is designed to assess symptoms of depression.
3. State Trait Anxiety Inventory (STAI; Spielberger et al., 1983). The STAI is a 40-item self-report measure of anxiety; 20 items reflect current state anxiety and 20 items reflect more general feelings of trait anxiety.
4. Therapy evaluation form (TEF; adapted from Holt & Heimberg, 1990). The TEF is a 5-item scale assessing a number of dimensions regarding patient satisfaction with the intervention (e.g., how logical the treatment seems, expectations of efficacy). It will be used to evaluate subjective responses to the computer programs.
5. Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003) will be used to determine presence and severity of childhood maltreatment.
6. Demographic questionnaire. A brief questionnaire will be administered to assess sociodemographic characteristics (e.g., age, gender, household income) at baseline.
7. Insomnia Severity Index (ISI, Morin et al., 2011). The ISI is a quick self-report measure to assess the presence and severity of sleep problems.
8. PROMIS Pain Scale. The PROMIS is a short questionnaire that assesses whether a subject is experiencing pain and to what extent this pain interferes with daily functioning.
9. Perseverative Thinking Questionnaire (PTQ; Ehring et al.2011). This questionnaire asks about patterns of negative, recurrent, thoughts.
10. The CoRonavIuS Health Impact Survey (CRISIS) to be administered and collected during the pandemic to measure the pandemic's influence on other batteries collected.
11. The Emotion Regulation Questionnaire (ERQ). This questionnaire asks about the tendency to use strategies like emotional suppression to manage feelings.
12. The Positive and Negative Affect Schedule (PANAS). This questionnaire asks about positive and negative emotional feelings.
13. The Attention Control Scale (ACS). This questionnaire asks about difficulties with concentration and attention.

Neurocognitive battery measures:
Measures of cognitive symptoms will be given at baseline, post-treatment, and follow-up assessment time points.
1. The Delis-Kaplan Executive Functioning System (DKEFS; Delis et al., 2001). This neuropsychological battery is designed to assess cognitive abilities. Two relevant subtests, the Trail Making test and Color Word Interference Test, will be used to assess the effect of COGENT /ST on cognitive functioning.
2. Working memory task. This neuropsychological assessment is designed to assess cognitive abilities. The task requires participants to remember items while simultaneously solving puzzles. It will be used as a manipulation check for the effect of COGENT/ST on cognitive performance using novel stimuli.
3. The American National Adult Reading Test. The test consists of 50 words, graded in difficulty, whose pronunciation cannot be determined from their spelling. The ANART has become a widely validated method for estimating premorbid levels of intelligence in neuropsychological research. Scores on the ANART can be converted to prorated IQs for analysis.

fMRI assessment battery:
fMRI scanning sessions will occur at baseline and post-treatment assessment points. Imaging experiments will be performed on a General Electric Signa 3 Tesla MRI scanner at the Keck Center for Functional Neuroimaging at UCSD. Each session will consist of a three-plane scout scan, field mapping, a standard anatomical protocol (for standardizing and localizing activation maps) using a sagittally acquired spoiled gradient recalled (SPGR) sequence. Functional runs will utilize a series of BOLD scans. The tasks will be completed in the order below, as the affective component of the reappraisal task has the potential to adversely impact cognitive performance on the cognitive control assessment.

1. Cognitive control assessment. This will be an fMRI-compatible cognitive control assessment (complex span task). Similar to the COGENT and ST programs, participants are asked to remember items while completing a secondary processing task (reading and/or math). Performance is assessed by totaling the number of items correctly recalled in the correct order. Span sizes tested range from 2 to 7. The task contains two conditions, high and low interference conditions, which vary in item similarity (multiple trials of the same item type versus multiple

trials that switch item type). Behavioral outcomes from this task include memory performance, processing accuracy, and reaction times.
2. Reappraisal task. To evaluate cognitive control over emotional information, a reappraisal emotion regulation task will be used. This task, which is designed to isolate brain activation related to down-regulation of negative emotion via the use of reappraisal instructions, has been validated in numerous studies within our lab. The condition of interest involves instructing participants to reduce negative emotion while viewing negative images by using the deliberate strategy of thinking about the scenario in a different, more benign way (i.e., using reappraisal). In the control condition participants will be given instructions to maintain their natural emotional response. During the task, participants are given instructions to rate their emotions before and after receiving instructions to reappraise or maintain their emotions and then viewing negative or neutral scenes. Image stimuli are from the International Affective Picture System (Lang et al., 1997), which includes ratings of valence and arousal. Participants will complete the task while heart rate response is measured. Outcomes include subjective report of emotional experience, heart rate indices.
3. Implicit affect regulation task. To evaluate implicit emotion regulation (vs explicit reappraisal) participant will complete an affective decision making take. In this task, participants view faces (e.g., frowning, neutral) while making a decision about the direction of a central arrow surrounded by flanker arrows. The task allows for examination of responding during conflict (e. g., central arrow left, flanker arrows right) under neutral and negative conditions. Outcomes include neural activation and reaction times.

Section 9.9 Data Safety Monitoring Board or Plan

9.9) Provide a Data Safety Monitoring Plan (DSMP) or the details of a Data Safety Monitoring Board; if a written plan is available, attach a copy of the plan to the submission form.

There will be regular weekly team meetings to discuss project activities to assure adherence with data safety and monitoring procedures. These team meetings will be coordinated by the PI, and will include members of the mentorship team (e.g., Dr. Simmons) and all research personnel. Drs. Simmons and Jak will hold regular individual meetings with the PI to direct study activities. This meeting schedule will be maintained throughout all 5 years of the project. For example, we will address issues of data collection, budget, recruitment, treatment issues, protocols, data management and analysis, and perform training and ongoing review to maintain adherence to all study procedures. We will discuss any human subjects issues related to the ongoing work, including access of minority groups to study participation. Empirical literature will be monitored throughout the course of the study to ensure that up-to-date procedures for participant safety are followed.
Research staff working on the project will report any adverse (or questionable) incidents to the Investigator and Dr. Simmons, and will receive extensive training in research ethics and methodology that will be reviewed annually. As mandated by the IRB the Investigator will report any adverse effect to the committee.
The investigative team will establish a group of two data safety monitors (with expertise in statistical approaches to longitudinal treatment outcome data and psychosocial intervention approaches respectively). The biostatistical consultant Dr. Golshan will provide the committee with interim data analyses to monitor study progress. These monitors will be contacted in instances of adverse or questionable events in order to provide independent consultation. Moreover, the PI will interview any participant who reports any adverse effects and refer the client to VA mental health and/or emergency clinics as required. Anyone wishing to withdraw from treatment will again be given the referrals for VA mental health services. Any participant who reports a significant exacerbation of symptoms will undergo a clinical interview by Dr. Bomyea or other licensed provider.

Section 9.11 Pictures and Audio/Video Recordings of Patients

9.11) Describe the purpose of photographs (facial), or audio, or video recordings of patients. Describe whether the recordings will contain, or potentially contain, identifiers. ***Note: use of photographs or recordings must be covered in the informed consent process and documented consent documents (e.g., consent form, information sheets, telephone screen scripts).***

Audiorecordings of CAPS interviews will be collected so that reliability of the staff members can be evaluated.

Section 9.12 Off Station Activities

9.12) Describe each off-station activity including where it occurs, subject involvement, and any additional required protections. ***Note: if the off-station activity is being conducted under the approval authority of another institution, this is not VA offsite research and should be described as collaborative research effort. Please contact the HRPP office if you have any questions***

fMRI procedures will take place at the UCSD Keck. The electronic data from the Keck center (images from MRI machine, behavioral data from laptop computer), which will not contain any VASI, will be stored per procedures described in section 27.

In cases where the individual completes telehealth procedures, the participant will identify a specific location (e.g., room at home or office) where they can reasonable ensure privacy to conduct procedures. All data will be collected by research staff on site at the VA, in building 13.

Section 10 - Human Subjects

10) Describe the characteristics of the proposed subject population. Include age, gender, ethnicity, and health status as appropriate. ***Note: Data about people are still considered "human subjects" by the IRB, so even if you do not intend to contact the patients whose charts you will review, you still describe the characteristics related to the subjects whose charts you will review.***

- **Provide inclusion and exclusion criteria as appropriate. Provide a statement how non pregnancy is confirmed if pregnancy is an exclusion criteria.**
- **For multisite studies, provide the total number of subjects from all sites and include description of the local site's role as a coordinating center if applicable.**
- **Indicate the number of VA participants to be studied.**
- **Indicate the estimated number of consented subjects that will fail the screening process, if any.**

1.1 Human Subjects Involvement and Characteristics
Eighty Veterans between the ages of 21 to 55 will be randomized from VASDHS. We anticipate consenting approximately 130 participants to determine eligibility, and of those approximately 80 participants who initially begin the study and complete the baseline assessment time point, only approximately 56 will complete the treatment protocol and subsequent assessment time points. Participants will be physically healthy. We anticipate that the racial and ethnic makeup of this sample will reflect the current VA population, particularly the Operation Enduring Freedom /Operation Iraqi Freedom/Operation New Dawn demographic given the age range of the current study (approximately 25-30% minority).

Inclusion Criteria and Exclusion Criteria.
Inclusion: Eligible participants will be Veterans who:
1) meet primary, current DSM-5 criteria for Posttraumatic Stress Disorder
2) are age 21-55,
3) are literate in English,
4) intend to remain in the San Diego geographical area for the duration of the study (if completing in-person visits)
5) are willing to attend assessment and treatment sessions.
Exclusion:
1) for the MRI portion only: inability to safely complete fMRI session – unsafe metal in body (including device such as pacemakers, metal fragments in the skin like shrapnel, history of metal work or welding, history of eye surgery or washes
because of metal, aortic/aneurysm clips, prosthesis, bypass surgery/coronary artery clips, hearing aids, heartvalve replacement, intrauterine devices with metal, shunts, electrodes, metal plates/pins/screws, neurostimulators,
older tattoos with metal ink, piercings the subject is unable or unwilling to remove); uncorrectable vision problems; claustrophobia; inability to lie still on the back for approximately one hour; inability to safely fit
within the dimensions of the fMRI machine; prior neurosurgery; pregnancy or current breastfeeding (within 3 months); current IV drug use due to potential cerebrovascular effects; or any other conditions that are deemed
by Keck Imaging Center staff to be contraindicated to safely complete the fMRI scanning. Individuals who cannot safely complete the MRI scan can complete all other study components.
2) a lifetime history of psychotic disorders, lifetime history of bipolar disorder, severe substance use disorder within the last year, or other psychiatric conditions that may adversely impact

cognition and/or are deemed to require other primary psychological intervention,
3) history of any neurological disorder that might be associated with cognitive dysfunction (e.g., cerebrovascular accident, intracranial surgery, aneurysm, seizure disorder),
4) acute suicidality (defined as intent and/or plan and/or action for severe self harm within the past 3 months per suicide questions that are completed as part of the MINI) or current circumstances that present a direct threat to the individual and require more imminent intervention (e.g.,
current domestic abuse),
5) individuals planning to begin medication changes within the time-frame of the study (individuals who are currently taking psychotropic medications can be included if they are receiving the VA standard of care medication guidelines so long as they have been under this care for at least 6 weeks with no immediate plans to withdraw from or change treatment; in the event of planned changes, participants will be asked to wait to begin the study once the 6 week stability criterion is met),
6) individuals current undergoing or planning to imminently begin evidence-based psychotherapy for PTSD,
7) individuals planning non-PTSD related psychosocial therapy change within the pre- to post-treatment time frame of the study (individuals currently under care can be included if they have been receiving stable psychosocial treatment for other disorders or conditions for at least 6 weeks prior to enrollment),
8) those with life-threatening or acutely unstable medical conditions.

Section 11 - Recruitment

11) Describe, step-by-step, the plans for recruitment of subjects (or selection of subjects as in record review). This description must include how, when, and where potential subjects are approached as well as procedures for identifying potential participants (through medical records, physician referral, third-party sources, etc.). Include how selection is equitable. Indicate if vulnerability to coercion may be present and if so plans to ensure voluntary participation.

Due to COVID-19, recruitment will occur through online platforms by self-referrals submitted in response to advertisements. A marketing company that is specialized in online advertisements for clinical studies will provide this service. Online advertisements will be paid through a PO and will NOT be done through the VA or personal account. An IRB approved advertisement may be posted on popular online platforms that our population of interest frequents. The ads will provide potential participants with brief study information, direct them to https://clinicaltrials.gov/ where they may learn more information about the study, provide the study staff's VA office phone number, and ask them to answer 4 brief questions to express their interests in the study. The questions asks about active duty status, first name, phone number, and best time to receive a phone call.BuildClinical retains the information in their portal throughout the duration of the contract. Upon termination of service, the information is deleted from the portal and it may be downloaded as an excel file to keep for our records behind the VA's firewall. All information captured through the screening form is shared with VASDHS. The information is transferred through their HIPAA Compliant platform that encrypts all data in transit and at rest. There is 2 factor authentication available for use and every researcher will have their own unique login credentials.

All of the points of contact will be monitored by study staff on a daily basis. If the potential participant contacts study staff by phone, they will be immediately screened (using the screening script and combined screening and enrollment forms).

Eligible Veterans will contact our study coordinator or will be contacted in response to 1) flyers posted in VA mental health, primary care, and general community areas as authorized by VASDHS, 2) advertisements in print and web-based media in the community, 3) VA/VMRF website advertisement for research opportunities, 4) referrals from the VA mental health and primary care clinics, 5) referrals through other research studies who provided consent to contact (Dr. Allard's protocol H130021 and Dr. Jak's protocols H130148, and H150015),and 6) a referral from staff or providers in mental health, primary care, MST, and substance use treatment programs via CPRS notes in which the provider will specify that the patient provided verbal confirmation that he/she would like to be contacted by research staff. 8) Additionally, to better target veterans who meet inclusion criteria for our study, research staff will search CPRS and pre-screen VASDHS patients who have previously received information about the current study(or, have upcoming appointments) from the Mission Valley or La Jolla VA PTSD and BHIP clinics, the TBI Cognitive Rehabilitation and Polytrauma clinics, or who were serviced by the MST/IPT clinics in the past for inclusionary criteria. Once patients who meet criteria are identified either by Chart Review or attending their clinic appointment, research staff will send a recruitment letter via mail to these veterans prior to contacting them by phone. Those who are interested in participating

will then undergo the standard phone screen and, if still determined eligible, will be scheduled for consenting.9) letter and follow-up call to potential participants identified through the VA Data Access Request Tracker (DART).

In regards to the targeted mailings/calls, we will use VA Data Access Request Tracker (DART) requests to identify Veterans with PTSD to be mailed invitational letters informing them of this study. Any potential participant who is identified via a DART request will be sent a modified recruitment letter that provides basic information about the study. The letter will inform Veterans that they will be contacted by phone in the coming days regarding their interest in participating in the study. In the letter, potential participants
will be given an "opt-out" number to call in order to decline participation and/or further contact regarding participation. Two weeks after the mailing, Veterans who have not called the tollfree number to decline participation will be called by the study coordinator to request their participation in the research study.

For potential participants that we contact through the target mailing identified through the DART system, potential participants that call in from the flyers/brochures/websites, individuals that are referred from VA clinics, and potential participants who are recruited through re-contact list from other research studies, we will request a partial waiver of HIPAA Authorization for screening.

As part of referrals through VA clinics, the research assistant working with Dr. Bomyea will attend orientation groups with referring clinicians to present information to patients and provide "Consent to Contact" forms to interested Veterans. Those who wish to be provided with information about the study will be contacted individually to have the study explained and complete screening. In addition, Veterans who do not complete orientation may be given information about the study by treatment providers so that they may self-refer. Alternatively, clinicians from participating clinics may utilize a CPRS note stating that a patient has provided verbal consent during a standard appointment to be contacted via phone by study staff. Staff will be tagged in these notes as a form of notification. After viewing the CPRS note indicating verbal consent to contact has been given, staff will contact the Veteran via phone in order to explain the study and administer a screening.There is unlikely to be undue vulnerability to coercion, and all Veterans will be informed that participation in research is fully voluntary and will not affect their clinical care. As part of research referrals, local investigators will be provided with information about the current research study and recruitment materials to distribute as appropriate to their participants. Research coordinators for our study and other research studies will communicate to provide contact information for participants who have provided consent to be contacted by telephone for other studies. Our research staff will contact these participants by phone to provide information about the study and assess interest in participating.

Veterans may also be recruited via the VA IRB approved registry, VASDHS TBI/PTSD Registry - H170023, allowing themselves to be contacted by future VA IRB studies. In section 12.10, we ask for a waiver of partial HIPAA so we can contact the Veteran via their preferred method of contact. If, at any time, the Veteran enrolled in the VASDHS TBI/PTSD Registry lets this study know that they want to withdraw from the registry and no longer want to be contacted, we will contact H170023's study coordinator as soon as possible.

We will also receive referrals from other VA studies. These studies will provide referrals of veterans that have consented to be contacted for additional studies. Studies we will recruit from include protocol numbers H190062, H170056, H170069, H170105, H220016, H210046 and H160089. Subjects from these studies who appear to be eligible for participation in this study and who have consented to be contacted about future research opportunities will be contacted by our research staff.

MEG
Participants will be asked if they are interested in an optional MEG study titled "Passive electrical neurofeedback treatment of mTBI: MEG and Behavioral Outcomes" IRB# H17033 (P.I. Mingxiong Huang, PhD). If participants consent to be contacted for the optional study, Dr. Huang's approved research team will contact subjects and, if subjects agree, consent them for the study.

Section 11.1 Recruitment Materials

11.1) Identify all recruitment materials (flyers, advertisements, letters, etc.) that will be used; include the web address for any web-based advertisements. The text of all communications with prospective participants must be reviewed and approved by the IRB before it can be used. You will be reminded to attach copies of recruitment materials to the initial submission packet. ***Note: Posting of flyers with pull tabs is not permitted within VASDHS (including the VMRF building). However, you may request to advertise on the e-boards (located at the elevators and throughout the facility) or on the VASDHS Research Opportunities web-page.***

Brochures and flyers will be utilized as recruitment materials. A copy of these materials is attached to the submission packet.

Build Clinical ads are attached for approval.

Section 12 - Informed Consent

12) Indicate whether or not each category of consent is involved in this study:

12a) Will the study team obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without (or prior to) obtaining informed consent of the prospective subject or the prospective subject's LAR?

(●) Yes ( ) No

Check one or both of the below boxes if they apply to this study:

Information will be obtained through oral or written communication with the prospective subject or the subject's Legally Authorized Representative (LAR) and this is not a FDA regulated study.

( ) Yes (●) No

Identifiable information or biospecimens will be obtained by accessing records or stored identifiable biospecimens and this is not an FDA regulated study.

(●) Yes ( ) No

If either or both of the above boxes is checked "yes", an informed consent waiver does not have to be requested for this activity if the protocol is initially approved after 01/01/2019 or if it has been converted to the 2018 Common Rule requirements. However, a request for a HIPAA waiver will still need to be requested and informed consent obtained for any research interventions after eligibility is established. Otherwise, waivers of consent and authorization must be requested for this activity. Waivers of consent and authorization are required for screening purposes for FDA regulated research.

12b) **Signed** informed consent

(●) Yes ( ) No

12c) Waiver of documented consent (e.g., **oral** consent) for all or part of the study.

( ) Yes (●) No

12d) Request for a **waiver** of consent for all or some study activities.

( ) Yes (●) No

12e) Alteration of **other required elements** of consent.

( ) Yes (●) No

12f) **Child** assent to participate (Director approval will be required)

( ) Yes (●) No

12g) Will any language **other than English** be used by those obtaining consent and understood by the prospective participant or the legally authorized representative?

( ) Yes (●) No

12h) **Decisional Capacity Assessment** to determine if participants have the capacity to consent for themselves.

( ) Yes (●) No

12i) **Surrogate** consent (legally authorized representative)

( ) Yes (●) No

Section 12.1 Informed Consent Process

12.1a) Will consent be obtained before any study procedures are performed (including screening procedures except screening procedures with Consent and/or HIPAA waiver when required)?

(•) Yes ( ) No

12.1b) Will the information being communicated to the participant or legally authorized representative during the consent process include exculpatory language through which the participant or legally authorized representative is made to waive or appear to waive any of the participant's legal rights or release or appear to release the Researcher, Sponsor, the VA or its agents from liability for negligence.

( ) Yes (•) No

12.1c) A master list of all VA subjects consented (written or not) under this protocol will be maintained.

(•) Agree ( ) Disagree

12.1d) Identify the circumstances under which consent will be obtained including where the process will take place; any waiting period between describing the research and obtaining consent including sufficient time for the prospective participant to consider participation, and any steps taken to minimize the possibility of coercion or undue influence.

Participants will first hear complete details about the study during the phone screen process, at which time if eligible, they will be scheduled for consenting, and scan. At the time of consenting, the study coordinator or the RA will explain the study to the participant and answer any questions the participant may have. After answering the questions, the participant will decide whether to participate or not. If a participant expresses ambivalence about participating, he or she will not be enrolled at that time. For in-person consenting, the consenting process will take place in building 13, on the 3rd floor. In circumstances where it is not feasible to consent in person (e.g., under current social distancing measures to protect from COVID-19), individuals will be consented using telehealth technology. Copies of consenting and HIPAA materials will be sent electronically using VA-approved encrypted methods (e.g., Azure Rights Management System, myHealtheVet) or by mail if this is the patient preference. All participants will be informed about appropriate use of electronic communication, including instructions to NOT send personal information over unsecured means.

To do remote consenting, research staff will 1) identify the participant via telehealth communication, 2) review the informed consent with the participant and response to any questions the patient may have; 3) confirm that the participant's questions have been answered; 4) confirm that the participant is willing to participate in the trial and sign the informed consent document while the witness is listening via telehealth technology; and 5) obtain verbal confirmation by the patient that they would like to participate in the trial. Based on patient preference, the staff will ensure that the participant has either a)signed and dated the informed consent document that is in their possession via ink signature and expressed their intent to mail the document back via mail or scanned to myHealtheVet, or b) provided a digital image of a wet signature or an electronic signature that is recorded using telehealth technology which will be saved to the R drive, using telehealth technology that is recommended by local and national VA (e.g., SDVA "Interim Policy on Human Subjects Research to Limit COVID-19 Transmission", VA memo: Use of Video Communication Technology Under COVID-19 (VIEWS 02576895), and OIT's Covid-19 response collaboration tools approved for telehealth and administrative meetings, to be updated as newer guidance is available). The staff will confirm that the signature and date are legible, that the version of the consent form is visible within the same image, and that any pages with initials (e.g., audio consent) are visible. If the electronic image cannot be captured or is illegible, the experimenter can witness the signing via telehealth and ask the participant to return the physical copy (or myhealthevet scan). Data collection will not proceed in these instances until the ink signed copy is received.

The research staff will attest on the IRB approved written consent form that the patient

confirmed that they agreed to participate in the study and signed the informed consent using the checkboxes on the consent document and will add his/her digital or written signature to the patient-signed consent document. Similarly, for the HIPAA the individual will sign the form and take a digital image to be saved to the R drive. This digital image will be printed as needed for regulatory review purposes. Allowing individuals to consent offsite will facilitate continued recruitment. A benefit of doing so is that participants interested in receiving this type of computerized training will have continued access given that this treatment is not provided in standard clinical service settings.

Section 12.9 HIPAA Authorization

For each category below, indicate whether or not this study involves the indicated process:

12.9a) **Signed** HIPAA Authorization. ***New Template is available in the ? Help section***

(•) Yes ( ) No

12.9b) HIPAA waiver to cover the entire study

( ) Yes (•) No

12.9c) HIPAA waiver for recruitment, screening, and/or for a portion of the study.

(•) Yes ( ) No

12.9d) HIPAA Authorization or waiver is **not required** for some or all of the study subjects (e.g. no health data).

( ) Yes (•) No

Section 12.10 HIPAA Waivers and Alterations

12.10a) Describe the purpose/nature of the HIPAA waiver or alteration and list specifically, what identifiers and health information are being requested under the waiver/alteration and identify whether the waiver is for access, use, and/or collection of this information.

We request a HIPAA/consent waiver for screening purposes only prior to the administration of the phone screen. The phone screen is necessary to determine the eligibility of interested participants prior to a potential in-person screening session. During the phone screen the nature of the study will be explained, portions repeated as necessary, and questions answered. This will involve data including name, contact information, MRI screening information (e.g., weight) and symptom questions as included in the attached phone screening document. If participants are eligible, they will be scheduled for an in-person assessment session, where informed consent (VA form 10-1086) and HIPAA authorization will be completed prior to determining clinical diagnosis and other relevant inclusion/exclusion criteria. Data will only be destroyed according to RCS-10 under Records Control Manager guidance.

In addition, referrals from study H170023, the VA IRB approved VASDHS TBI/PTSD Registry, and protocols H130021, H130148, and H150015 have given their documented consent to be contacted by future studies. We request a partial HIPAA waiver so we can contact the Veteran via his or her preferred method of contact.

Furthermore, participants recruited from mental health, primary care, and MST, program clinics will be offered the option of study involvement via their clinicians at standard appointments (i.e., orientation session, intake appointment, regular psychotherapy/medication appointments). Interested participants will give their clinician their verbal consent to be contacted regarding the study, and their information will be given to the study coordinator. Additionally, these potential participants will be given a flyer about the study, with the study coordinator's information. For these participants, we will request a partial HIPAA waiver prior to the administration of the phone screen. Prior to conducting the baseline assessments, all participants will be asked to complete informed consent Subject's Bill of Rights and HIPAA authorization.

Additionally, a waiver is required for study staff to access VASDHS patient medical records in order to identify eligible patients who have received information (or, have upcoming appointments) about the current study from the Mission Valley or the La Jolla VA PTSD and BHIP clinic orientation meetings or those who have been serviced by the MST/IPT clinics in the past, and to collect names, last four digits of the social security number, mental health information, addresses, and phone numbers for recruitment purposes. Patients identified as meeting criteria will be sent information about our study via mail prior to being contacted by study staff via phone.

12.10b) The proposed access, use, and/or disclosure of PHI involves no more than a minimal risk to the privacy of individuals.

◉ Agree ○ Disagree

12.10c) The plan to protect the identifiers from improper use and disclosure is adequate.

◉ Agree ○ Disagree

Describe the plan

All identifiers will be protected from improper use and disclosure by securing all PHI in locked desks or file cabinets in an access-controlled office or access-controlled computers (keyed and locked office in VA Building 13(#R106, #R146); and VASDHS password protected and encrypted computers within this office). Identifiable health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other permitted research purposes

12.10d) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

◉ Agree ○ Disagree

12.10d2) Describe the plan:

All identifiers will be destroyed per VA requirements.

12.10e) By signing this protocol for submission, the PI is providing written assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy Rule. 38 U.S.C. 7332 Information: If the waiver of HIPAA authorization is for the use of 38 USC 7332 information (applicable to drug abuse, alcohol abuse, HIV infection, and sickle cell anemia records), by signing this protocol for submission the PI is providing written assurance that the purpose of the data is to conduct scientific research and that no personnel involved may identify, directly or indirectly, any individual patient or subject in any report of such research or otherwise disclose patient or subject identities in any manner. (Ref: 38 U.S.C. 7332(b)(2)(B))

◉ Agree ○ Disagree

12.10f) The research could not practicably be conducted without the waiver or alteration.

◉ Agree ○ Disagree

12.10f2) Describe how the waiver/alteration enables the research to be conducted

Potential subjects must be screened for eligibility prior to their consenting to participate in the study. Participants will complete the screening by telephone so that they do not have to make a visit on site to determine basic factors that would preclude enrollment (e.g., unsafe to complete MRI). In cases where the participant is already on-site for some other purpose, they make complete a consent before being asked these screening questions.

12.10g) The research could not practicably be conducted without access to and use of the PHI.

◉ Agree ○ Disagree

12.10g2) Describe why it would be impracticable to conduct this research without the PHI described 12.10a. (v3 /8/18)

Access to and use of individually identifiable health information is necessary for the success of the study, as we cannot recruit individuals who are unsafe to scan to be a part of this study.

Section 13 - Alternatives to Participation

13) Describe the alternatives to participation in this research study (see ? for guidance)

Participants may choose not to participate in the study. Veterans may choose to complete treatment through standard care at the VA.

Section 14 - Potential Risks

14) Describe any potential or known risks or discomforts and assess their likelihood and seriousness (see ? for guidance)

Computerized assessments and computerized training
The main risks associated with these procedures are fatigue, boredom, and irritability with the testing procedure. The investigator and research assistants are trained to frequently check the subjects about their willingness and ability to continue with testing. If the subjects express concerns about continuing with testing or the training program, the investigator has instructed the research assistants to stop testing, offer a break, or, in case the subject is not willing to continue, to terminate the session. Overall, however, previous studies have not resulted in any significant discomfort or anxiety expressed by the participating subjects.

Psychiatric Risks
Images used in task or questions asked during interview may be emotional in nature, this is of specific concern in the PTSD population. These images and interview questions have been well-tolerated in previous studies with high anxious, PTSD, and control subjects. However, to minimize patient distress preliminary practice tasks will be used. In addition, on completion of the testing session patient will be debriefed concerning their emotional state and will have direct contact with a licensed psychologist if they express significant distress or dysphoria.

Confidentiality
Subject information obtained during this study will remain confidential and be disclosed only with a subject's written permission. However, information may be given without a subject's permission to the VASDHS Institutional Review Board (IRB). If some of the information collected, e.g. whether a subject has used illegal substances, were to become public, it may place the subject at risk for criminal or civil liability or may be damaging to the subject's ability to get a job, affect the subject's personal reputation, or have otherwise unforeseen consequences.

Risks associated with fMRI. According to the FDA, there is currently no evidence that MRI with approved scanners of up to 7 Tesla signal strength are associated with adverse effects. However, there are two major sources of risk. First, the subject may experience discomfort being in the confined and sometimes noisy environment of the scanner. Second, the strong magnetic field will affect electronic, magnetic, and metal devices that subjects carry with them or that have been implanted in the subject's body.

Section 15 - Risk Management

15) Describe the procedures for protecting against or minimizing any potential risks/discomforts, and the adequacy of resources for conducting the study and resources participants may need as a consequence of the research. When applicable, include detail of the following safety measures: (a) The type of safety information to be collected, including AEs; (b) Frequency of safety data collection; (c) Frequency or periodicity of review of cumulative safety data; (d) Statistical tests for analyzing the safety data to determine if harm is occurring; and (e) Conditions that trigger an immediate suspension of the research. See ? for further requirements.

The subject will be given frequent breaks if tired and all subjects will be asked if they would like extra cushions for inside the scanner, and be provided with these cushions if requested. Examiners will be clinically trained and sensitive to signs of stress, anxiety, or fatigue so that testing will be immediately terminated should any subject experience signs of discomfort. In cases where conducting procedures is not feasible in person (e.g., due to COVID risk management), clinical assessments may occur via phone or through HIPAA-compliant technology when feasible. Prior to conducting these assessments, all individuals will be required to provide the assessor with contact information and current physical address/location, as well as an emergency contact person. In the event of an emergency this will allow the assessor to provide rapid clinical response should a safety concern arise.

Confidentiality (Legal and Social Risk). Records and data will be linked to coded numbers and anonymity will be rigorously enforced. All record keeping will in accordance with the stipulations of the local Institutional Review Board and Human Research Protection Program. Moreover, when contacting agencies, family, or friends who were provided by the subject, no information will be provided about the nature of the participant, i.e. the research assistant will state that the subject had participated in "fMRI research on brain function". To minimize social and legal risk, all of the data will be kept in locked cabinets or in electronic databases with secured passwords.

In cases where conducting procedures is not feasible in person (e.g., due to COVID risk management), there is a risk of loss of confidentiality if the individual is speaking by phone in a nonprivate environment. The following steps will be taken to ensure that confidentiality is protected. First, all communications with participants will occur via phone for clinical interview assessments, with the assessor on site at the VA using a VA phone. Second, prior to initiating any communications with the participant, staff will ensure that they are currently in a private and distraction-free environment, and that there is reasonable assurance of privacy during responding, consistent with current VA telehealth clinical guidelines.

HIPAA compliant technology will be used for delivery of the computerized training intervention and cognitive tasks and questionnaires. These tasks do not include any identifying information, as they involve recording reaction time and accuracy. In addition, because these interactions will occur via closely monitored screen sharing the data is being collected on the same devices as currently approved by the IRB. All questionnaires/tasks delivered with virtual technology will be identified by subject ID rather than name, and will not include video or audio depictions, IP address, etc. that would be considered identifiable. For activities that do involve PHI, research staff will use VA-approved telehealth technology (e.g., VA video connect) to collect a digital image of the signed consent form or the electronic signature. Together these steps will ensure that data is collected in a way that allow the data to remain at VA (e.g., participants do not need to take equipment or questionnaires home), and that responses from participants that are occurring remotely are unlikely to lead to a lapse in confidentiality.

Discomfort and other risks related to completing computer assessments and fMRI tasks: The computers will be checked regularly for proper and safe operation. Patients and comparison subjects will be carefully screened and subsequently informed about the fact that the principal investigator will be available at all times during the experiment. Subjects are informed that they may end the session at any time and that participation in this research is voluntary. Examiners will be clinically trained and sensitive to signs of stress, anxiety, or fatigue so that testing will be immediately terminated should any subject experience signs of discomfort.In terms of other fMRI related issues, to minimize the risk of fear of closed spaces while in the MR scanner, patients will be extensively interviewed and informed about the nature of the task. We have previously used pictures of the MR scanner to familiarize subjects with the scanner environment. During scanning the investigator can hear the subject at all times and if, at any point in during the scanning, the subject expresses increasing discomfort, the operator will immediately intervene and terminate the scanning procedure. Furthermore, operators will routinely check-in with the subject between each scan task to assess the participant's emotional and physical comfort in addition to reviewing task instructions and logistical checks. If a participant expresses discomfort the operator will work with the participant to determine a possible remediation, and if none is available then the scan will be terminated. There is the possibility of an abnormal finding on the fMRI scan. However, the fMRI scans are not being done for clinical purposes, and the fMRI scan procedure is not sufficient for the clinical diagnosis of a possible brain disorder. The purpose of this scan is not to diagnose abnormalities, but on rare occasions a finding is observed that might be clinically important. Should there be cause for concern, we will forward the imaging information to the participant's physician(typically VA radiology) for followup.

Subjects that require special risk management procedures include:

1. Women: prior to each MRI scan we administer pregnancy screens in order to insure that they are not pregnant (as detailed in section 10.6). They will also be asked to sign a Pregnancy Test

Verification Form indicating that the test was received and if the result was negative.

2. In terms of other special classes of subjects that would potentially require special risk management procedures, we have excluded older individuals to help insure that all participants have the capacity to give informed consent. We also exclude individuals with sensory deficits that make them inappropriate for MRI, such as individuals with whom reliable communication cannot be established in the scanner (i.e., deaf individuals; as stipulated in the Protocol Application Section 10).

Section 17 - Potential Benefits

17) Discuss benefits that may be gained by the subject as well as potential benefits to society in general (see ? for guidance)

Posttraumatic stress is related to poorer clinical outcomes in our veteran population. The knowledge that can be gained from this study may help us make important strides in the care of our veterans. Veterans participating in the study may experience a reduction in PTSD symptoms.

Section 18 - Risk/Benefit Analysis

18) Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.

Low risk/low benefit. The proposed study has great potential to better understand the neural substrates of posttraumatic stress. The study may also improve the PTSD symptoms of participants, if the intervention is effective.

Section 20 - Compensation for Participation

20) Provide all details and justifications of the compensation plan. See ? for detailed requirements.

Participants will be compensated for pre and post treatment clinical assessments ($100 per assessment). In addition, participants will be given $50 for completion of the follow up visit and participants will be given a matriculation bonus of $50 if they complete all time points. Compensation is provided to offset participant time and burden of attending sessions.

They'll have the option to receive 3-D brain printouts, if they complete all visits. Subjects can also request a digital non-PHI image of their brain which we will send over VA-approved encrypted software.

In addition, travel reimbursement will be provided to subjects who are unable to participate because of travel expense incurred. Travel reimbursement will be provided at the VA listed reimbursement rate (https://www.va.gov/health-care/get-reimbursed-for-travel-pay/#reimbursed-expenses-and-rates). This website will be referred to every time travel reimbursement is required to ensure participants are being reimbursed at the proper rate.

Section 21 - Responsibilities and Qualifications

Here are the identified study staff members

Jessica A. Bomyea, PhD

Alan N. Simmons, PhD, Amy J. Jak, PhD, Murray B. Stein, MD, Alyxandra L. Bartolovich, Danielle N. Dun, BS, Hanna Hovren, BS, Morgan E. Marvin, BA, Ruth Klaming Miller, PhD, Christopher O. Hunt, PhD, Shahrokh Golshan, PhD, Annemarie Angeles Quinto, Edith Jimenez, Hayden B. Hansen, Jared Baumgartner, Mingxiong Huang, PhD, Nathalie N. Dugas, Santana Denali Woodruff, Caitlyn Adams, Eshika Mehta, Jacqueline Bohrer, BA, Jamila N. Piri, Justin Tintiangco, Lucy Chandler, Ruiyan Hu, Sara Northup, Sergio Barretto, Vitaliana Vasquez

21) For each staff member listed above, describe their role and qualifications. Also indicate which of the

study staff are authorized to obtain consent, when applicable to the study.

Jessica Bomyea, PhD - Principal Investigator, expert in cognition in PTSD
Alan N. Simmons, PhD, Co- Investigator, fMRI expert
Amy Jak, PhD, Co-Investigator, expert in neuropsychology, licensed credentialed clinician
Murray Stein, MD, Co-Invetigator, expert in neurobiology and treatment of PTSD
Shahrokh Golshan will provide statistical assistance.
Christopher Hunt, PhD - Post-Doc Research Scientist authorized to access PHI

Ruth Klaming Miller, Clinical Research Coordinator, VA WOC, *
Morgan Marvin, Study Coordinator, VA Employee +
Danielle Dun, Clinical Research Coordinator, VA WOC * + !
Nathalie Dugas, Alyxandra Bartolovich, Hanna Hovren, Edith Jimenez, and Shivani Vasanth, WOC are authorized to
assist in data handling and recruitment of participants.

Denali Woodruff, Study Coordinator, VA Employee

Hayden Hansen, Research Associate
Jared Baumgartner, Research Associate
Annemarie Angeles Quinto, Research Associate
Dr. Mingxiong Huang, Research Associate

All student Research Volunteers are authorized to assist in the handling of data and recruitment of participants.
Jamila Piri, Student Research Volunteer, WOC
Ruiyan Hu, Student Research Volunteer, WOC
Sara Northup, Student Research Volunteer, WOC
Vitaliana Vasquez, Student Research Volunteer, WOC
Eshika Mehta, Student Research Volunteer, WOC
Sarah Hasheem, Student Research Volunteer, WOC
Shoshana Printz, Student Research Volunteer, WOC
Janelle Nelson, Student Research Volunteer, WOC
Isabella Peralta, Student Research Volunteer, WOC
Sergio Barretto, Student Research Volunteer, WOC
Justin Tintiangco, Student Research Volunteer, WOC
Caitlyn Adams, Student Research Volunteer, WOC
Jacqueline Bohrer, Student Research Volunteer, WOC
Lucy Chandler, Student Research Volunteer, WOC

All staff have access to VASI and have access to subjects. All study coordinators are authorized to obtain consent.

+= ATT Approved
!= Research Contacts

Section 22 - Bibliography

22) List relevant articles that the IRB can use to provide necessary background for the protocol. Do not include an extensive NIH-grant-style bibliography. (Up to 5 recommended, but use more if needed to support the protocol or citations above.)

1. Bomyea, J., Lang, A. J., & Amir, N. (2012). The relationship between cognitive control and posttraumatic stress symptoms. Journal of Behavior
Therapy and Experimental Psychiatry, 43(2), 844-848. doi: 10.1016/j.jbtep.2011.12.001
2. Conway ARA, Kane MJ, Bunting MF, Hambrick DZ, Wilhelm O, Engle RW. Working memory span tasks: A methodological review and user's guide. Psychon Bull Rev 2005;12(5):769-786.
3. Etkin A, Wager TD. Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. Am J Psychiatry 2007;164(10): 1476-1488.
4. Gross JJ. Emotion regulation: Affective, cognitive, and social consequences. Psychophysiology 2002;39(3):281-291.
5. New SA, Fan J, Murrough JW, Liu X, Liebman RE, Guise KB, Tang CY, Charney DS. A

Functional Magnetic Resonance Imaging Study of Deliberate Emotion Regulation in Resilience and Posttraumatic Stress Disorder. Biol Psych 2009; 66, Issue 7, 656–664
6. Morin CM; Belleville G; Bélanger L; Ivers H. The insomnia severity index: psychometric indicators to detect insomnia cases and evaluate treatment response. SLEEP 2011;34(5):601-608.

Section 27 - Privacy, Confidentiality, and Information Security

27a) Provide a brief description of how participant privacy and confidentiality will be protected in this study. Describe the circumstance under which it may be possible for a research team member to identify subjects and any related protections or assurances to prohibit or avoid identification. Describe how the number of people with access to identifiers for research purposes is limited in order to protect a participant's privacy.

Records and data will be linked to coded numbers and anonymity will be rigorously enforced. All record
keeping will in accordance with the stipulations of the local Institutional Review Board and Human Research Protection Program. Moreover, when contacting agencies, family, or friends who were provided
by the subject, no information will be provided about the nature of the participant, i.e. the research
assistant will state that the subject had participated in "fMRI research on brain function". To minimize
social and legal risk, all of the data will be kept in locked cabinets or in electronic databases with secured
passwords. A research team member will access identifiers during the recruitment, screening, and consenting process, which is necessary to effectively complete the study. The staff members listed on
this protocol may each access identifiers, as is necessary for recruitment and screening.

27.b) Entry of a CPRS Research Informed Consent Note is required when subjects will be admitted as inpatients or treated as an outpatients for research *and* the study involves research medical care or may affect medical care.

- ***If a Research consent Note is required, then a Research Progress Note should also be entered for each procedure or intervention.***
- ***Scanning the Consent and HIPAA Authorization into CPRS is not required. Linking the Consent to the Research Informed Consent Note may be permitted and can be useful for trials involving the Research Pharmacy or when research will be performed in conjunction with clinical procedures.***
- ***For Non-Veterans, if Research Informed Consent Notes are entered, then the NOPP Acknowledgment must be scanned into the record. Otherwise a copy of the signed NOPP must be retained with the Investigator's research records and a copy sent to the Privacy Officer; see the ? Help for more information.***

27.b1) Is entry of CPRS notes required based on the above criteria?

- (•) CPRS notes are needed for ALL subjects
- ( ) CPRS notes are needed for SOME subjects
- ( ) CPRS notes are NOT needed for any subjects

27c) Select the VA Sensitive Information (VASI) use category

- ( ) This study does not collect or use any VASI
- ( ) This study uses but does not save, collect, copy, or record VASI
- (•) This study does collect or record VASI

Section 27.1 VA Sensitive Information (VASI)

27.1a) For each type of VASI, indicate all that apply:

Indicate which of the following will be collected/recorded:

- [x] Protected Health Information (PHI)
- [x] Names
- [ ] Device identifiers and serial numbers
- [ ] E-mail addresses
- [ ] Medical record numbers
- [ ] URLs (Universal Resource Locator)
- [ ] All elements of dates (except year) or any age over 89
- [ ] Health plan beneficiary numbers
- [ ] IP Addresses (Internet Protocol)
- [x] Telephone numbers
- [x] Account numbers
- [x] Biometric Identifiers including finger and voice print
- [ ] Fax numbers
- [ ] Certificate or license numbers
- [ ] Full face photographic images and comparable images
- [x] All geographic subdivisions smaller than a state
- [ ] Vehicle ID and serial numbers including license plate numbers
- [x] Social security numbers or scrambled SSNs (describe below)
- [ ] Other unique identifying number, characteristic, or code (describe below)

27.1a1) Describe why SSN are needed for this study

SSNs are used in EFT process for payment and for patient lookup in CPRS.

27.1b) Consent Forms and/or HIPAA Authorization

(•) Yes ( ) No

27.1c) Images with personal identifiers are used for this study (x-rays, MRI images with patient names, record numbers, dates, etc.)?

(•) Yes ( ) No

27.1c1) Identify where images will be stored (e.g., in the medical record, with study hardcopy records, with study electronic VASI records).

Images are collected but stripped of identifier (date).

27.1d) Photos with faces or audio video recordings are used for this study.

(•) Yes ( ) No

27.1d1) Identify the device or devices that will be used to take/make the photographs or recordings.

Audiorecordings of clinical interview are kept for assessing clinician reliability using a digital recorder
(Sony icd-px470).

27.1d2) Identify where images will be stored (e.g., in the medical record, with study hardcopy records, with study electronic VASI records

These devices are kept in a locked drawer in 312E. Electronic copies are kept in R/Bomyea /CTinVets

27.1e) Biological specimens with identifiers are used for this study.

○ Yes ◉ No

Section 27.2 Data Collection, Tools, and Resources

27.2a) Will any specially obtained software be used?

◉ Yes ○ No

27.2a1) Describe the software, and identify license requirements and the ownership of the software or license. Identify on what computer/network the software will be used (e.g., VA, VA Research/VMRF, local hard drive) and any data that will be stored in temporary files on the computer's hard drive

Eprime software collects behavioral data. Eprime is installed on VMRF computers and VA computers used
in our lab. The software license was purchased by the PI. Files will be moved from the hard drive to the R drive using our VA issued and approved thumb drive immediately after data collection. Questionnaire data may be recorded using VA-approved REDCap on VA devices.
Zoom will be used for deidentified remote procedures where the participant needs to complete tasks that would typically be completed on our laboratory devices (cognitive training paradigms). The UC San Diego Health instance of Zoom is HIPAA-compliant. Zoom has a HIPAA Business Associate Agreement (BAA) in place, which makes it responsible for keeping participant information secure. Zoom does not have access to identifiable health information, and protects and encrypts all audio, video, and screen-sharing data. No PHI will be collected using Zoom. For collecting PHI (e.g., consent depictions) VA videoconnect or other VA approved devices will be used.

27.2b) Will any mobile devices (laptop, tablet, portable hard-drive, etc.) be used in support of this study?

◉ Yes ○ No

27.2b1) Provide details of the device/s. Indicate whether the device is FIPS 140-2 encryption validated and confirm that the device is listed in the VA EIL. Provide details regarding the nature of the data that will be stored or transmitted on the device and confirm whether a copy of all data will be stored on the VA network.

VMRF laptop computer will be used to collect non-VASI behavioral data (RES005512 or EE112941). A copy of all behavioral data will be transported to the R drive using VA-issued encrypted thumbdrive and stored permanently on R/Bomyea/CTinVets.

27.2c) Does the study require use of an electronic data capture system?

○ Yes ◉ No

27.2d) Will any other web-based applications be used (e.g., for recruitment, completing online questionnaires, or processing data)?

○ Yes ◉ No

27.2e) Will coded data that excludes personal identifiers be used? Coded data excludes *all* HIPAA identifiers (per VHA Handbook 1605.1 Appendix B), including dates

◉ Yes ○ No

27.2e1) Identify where the code key is stored and in what format (electronic, paper).

The key that links the number to the subject will be kept in paper copy in suite 312 at VMRF and electronically on R/Bomyea/CTinVets

Section 27.3 Data Sharing and Transportation

27.3a) Does this study involve collecting, sharing or transporting any type of data outside of the local VA?

◉ Yes ○ No

27.3b) This study collects VASI outside of VA (i.e., at a non-VA location).

◉ Yes ○ No

27.3b1) Describe what is collected outside the VA and how it is secured in transit back to the VA. *Note: An approved Authorization to Transport will be required.*

fMRI scans are collected at UCSD Keck Center (see 27.1.c). Participants may verbally respond to questions to provide data offsite from the VA in instances of telehealth assessment, but all data is recorded and stored at the VA, and is never stored on any personal devices. The consent form will be signed by participants at the location of their choosing, and will be promptly returned via USPS mail following instructions provided by study staff if signing by wet signature is preferred, or by sending a digital image (e.g., creating a screenshot, scanning a pdf) through telehealth if that is the preferred method (e.g., myHealtheVet).

Approved and signed Informed Consent and HIPAA Authorization, which contain research participant names, signatures and Social Security Numbers, may be transported securely from the UCSD Center for functional MRI (Keck Center) to office 312E of the Veterans Medical Research Foundation, building 13, for final storage. These forms will be transported by hand in file folders or in a briefcase and will not be left unsupervised at the Keck Center or otherwise outside of the VA facility at any time. Coded electronic data on a thumb drive will also be transported between locations. Laptop will be kept in 312E.

27.3c) VASI is transported outside of VA for any purpose other than sharing.

○ Yes ◉ No

27.3d) PHI may be disclosed to monitoring/auditing agencies by HIPAA Authorization. ***Note: The Research Office must be notified when monitors come to audit***

◉ Yes ○ No

27.3e) Data may be shared with collaborators or others in the conduct of this protocol.

○ Yes ◉ No

Section 27.4 Research Record Storage and Retention

For each type of record, indicate whether it is collected for this study

27.4a) Hardcopy records/data (includes paper, pictures, film, etc.)

◉ Yes ○ No

27.4a1) Identify precisely where hardcopy data will be stored to include physical site, building, and room number, etc. For each location identify whether VASI or non-sensitive information is stored at that location. For VASI, identify how the data is secured.

Paper hardcopy data identified using a code number will be stored in 312E (e.g., questionnaires), and will be housed in a locked filing cabinet.

27.4a2) Are all of the above locations at VA?

◉ Yes ○ No

27.4b) Electronic study records (includes computer files, removable disk files, digital files, etc.).

◉ Yes ○ No

27.4b1) Identify precisely where ***non-sensitive*** electronic records/data will be stored to include the full map drive, network location/server name, etc., and a brief description of what data/information is stored at each location.

Behavioral data (accuracy, reaction time) is stored on R/Bomyea/CTinVets. MRI images will be stored as
described in 274b4.

27.4b2) Identify precisely where ***VASI*** electronic records/data will be stored to include the full map drive, network location/server name, etc., and a brief description of what data/information is stored at each location.

If no VASI is collected or recorded for this study, simply indicate that the "Study does not collect or record VASI".

VASI records will be stored in R/Bomyea/CTinvets. These records will include any identifiers collected
through screening and tracking, and audiorecordings of interviews.

27.4b3) Are any of the locations described in 27.4b outside of the VA Secure Network? *Note: this includes storage on a computer local hard drive.*

(•) Yes ( ) No

27.4b4) Describe the storage method (e.g., in a VA encrypted laptop) and security details, including the device /media location and ownership; describe backup procedures; identify the web applications; security features; and the nature of the data involved. Identify the rationale for needing to store data outside of the VA Network and describe the arrangement and authority (MOU, contract, other) to permit the arrangement.

MRI scans storage will be serviced by UCSD servers as agreed upon by recent contract between VA and UCSD. A copy of de-identified fMRI images, with no participant names, dates in date fields, or other VASI, will be kept on a VASDHS contracted (initial contract #: 36C26218C0160) computer server in the
west datacenter of San Diego Supercomputer Center (SDSC UC San Diego MC 0505, 9500 Gilman Drive, La Jolla, CA 92093-0505). This storage solution complies with all VA directives developed in accordance with FISMA, HIPAA, NIST, and related VA security and privacy control requirements for Federal
information systems. This includes standards for the protection of electronic PHI, outlined in 45 C. F.R. Part 164, Subpart C, information and system security categorization level designations in accordance
with FIPS 199 and FIPS 200 with implementation of all baseline security controls commensurate with the FIPS 199 system security categorization (reference Appendix D of VA Handbook 6500, VA Information Security Program).

27.4c) Record Retention - VHA requires compliance with Records Control Schedule (RCS-10) for retention of electronic and hard copy records. Following study closure, these temporary records must be retained for six years and then destroyed. Longer retention may be permitted if required by other Federal regulations or requirements. Will RCS-10 requirements be followed (i.e., 6-year retention)?

(•) I will adhere to VHA Records Control Schedule-10 requirements
( ) I request an exception to RCS-10 requirements

Section 27.5 Additional Privacy or Information Security Details

Provide any other privacy or information security details here.

Section 27.6 Attestations

In the event of real or suspected breach of security, the Information Security Officer, Privacy Officer, VA Police (if appropriate), and the individual's supervisor will be notified within one hour of learning of the event.

(•) Agree ( ) Disagree

Study staff will be up to date on any required VHA Privacy Policy and Information Security training or they will not be allowed access to VA Sensitive Information.

◉ Agree ○ Disagree

Access to research sensitive information, if any, will be removed when study personnel are no longer part of the research team.

◉ Agree ○ Disagree

At least one copy of all study records (whether sensitive or non-sensitive) will be retained under VA control and only destroyed in compliance with the approved Records Control Schedule

◉ Agree ○ Disagree

The VA retains ownership of the research data. Should the investigator leave the VA, custody of the research records will be assigned to another investigator and the Research Service notified in writing, or custody of the research records will be transferred to the Research Service.

◉ Agree ○ Disagree

Section 28 - Protocol Association to New or Existing Project

28) Is this a new R&D Project? Before you go on to complete the *Initial Review Submission Form* (which is used for attachments), please address the association of this Protocol to an R&D Committee Project. This Protocol may represent a new R&D Project, or it may be an additional Protocol under an existing R&D Project (such as when a single grant supports multiple Protocols). Will this Protocol be submitted to the R&D Committee as a new Project?

○ Yes ◉ No

Section 29 - Existing Project Association

29) The associated R&D Project should already exist in the database. Identify the R&D Project(s) that correspond to this protocol.

Project Status	Proposal Number	Project Title	Principal Investigator
No Projects are Linked to this Study			

The Protocol Application is now complete for a Protocol attached to an existing Project.

Next you will go on to the Initial Review Submission Form. This form is used to collect the Application and any other needed attachments for submission to the IRB for review.

Press *Save and Continue*