Evaluation of a hybrid treatment for veterans with comorbid traumatic brain injury and
posttraumatic stress disorder: Study protocol for a randomized controlled trial

Amy J. Jak^{a,b,d}, Robin Aupperle^e, Carie S. Rodgers^{b,d}, Ariel J. Lang^{b,d}, Dawn Schiehser^{b,c,d},

Sonya B. Norman^{a,b,d,f}, & Elizabeth W. Twamley^{b,d}

^aPsychology Service, VA San Diego Healthcare System

^bCenter of Excellence for Stress and Mental Health, VA San Diego Healthcare System

^cResearch Service, VA San Diego Healthcare System

^dDepartment of Psychiatry, University of California, San Diego

^eLaureate Institute for Brain Research, University of Tulsa

^fNational Center for PTSD, White River Junction, VT

Amy Jak (corresponding author): 3350 La Jolla Village Dr., 151B, San Diego, CA 92161

ajak@ucsd.edu

Robin Aupperle: East 67th Street, Tulsa, OK 74136. raupperle@laureateinstitute.org

Carie Rodgers: 3350 La Jolla Village Dr., 151B, San Diego, CA 92161. carie.rodgers@va.gov

Ariel Lang: 9500 Gilman Drive #0855, La Jolla CA 92093. ajlang@ucsd.edu

Dawn Schiehser: 3350 La Jolla Village Dr., 151B, San Diego, CA 92161. dschiehser@ucsd.edu

Sonya Norman: 3350 La Jolla Village Dr., 151B, San Diego, CA 92161. snorman@ucsd.edu

Elizabeth W. Twamley: 3350 La Jolla Village Dr. 116A, San Diego, CA 92161.

etwamley@ucsd.edu

Abstract

Comorbidity of posttraumatic stress disorder (PTSD) and history of traumatic brain injury (TBI) is high among Veterans of Operation Iraqi Freedom/ Enduring Freedom/New Dawn (OIF/OEF/OND). Cognitive Processing Therapy (CPT) is empirically supported for the treatment of PTSD, but it is not specifically designed to accommodate the memory, attention, or problem solving deficits that are experienced by many Veterans with comorbid PTSD and TBI. Compensatory cognitive rehabilitation, including Cognitive Symptom Management and Rehabilitation Therapy (CogSMART), is effective for cognitive deficits stemming from a variety of etiologies, including TBI. We have integrated components of CogSMART into CPT in order to address the unique challenges faced by Veterans with ongoing cognitive complaints related to PTSD and a history of mild TBI. Here we describe an ongoing randomized controlled trial investigating the efficacy of our novel hybrid treatment, SMART-CPT, as compared to standard CPT, for OIF/OEF/OND Veterans with PTSD and a history of mild to moderate TBI. We describe the development of this hybrid treatment as well as implementation of the randomized controlled trial.

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Keywords: PTSD, TBI, cognitive processing therapy, cognitive rehabilitation, Veterans, treatment

Introduction:

Approximately 8% of Operation Iraqi Freedom/Enduring Freedom/New Dawn (OIF/OEF/OND) Veterans are diagnosed with posttraumatic stress disorder (PTSD) [1], characterized by re-experiencing symptoms, intrusive thoughts, avoidance behaviors, cognitive distortions, and heightened physiological arousal. Cognitive complaints [2, 3] and objective neuropsychological deficits [4, 5] are also commonly present. Strong empirical support exists for use of cognitive-behavioral therapies (CBT) for PTSD, including Cognitive Processing Therapy-Cognitive Version (CPT-C; retains the original cognitive restructuring components of CPT but omits a detailed account of the traumatic event.) [6]. However, little work has examined effects of PTSD treatment on cognitive deficits or how they impact ability to benefit from standard PTSD therapies.

PTSD is highly comorbid with history of mild TBI (mTBI) in OIF/OEF/OND Veterans (43.9%) [7]. Although symptoms resolve rapidly following mTBI (typically within 7-10 days) in the majority of cases [8], almost 50% of Veterans with a mTBI history continue to report at least one post-concussive symptom after one year [9]. Individuals with both mTBI and psychiatric disorders have significantly poorer functional outcomes than those without comorbid conditions [8, 10, 11]. Standard practice for treatment of mTBI includes psychoeducation [12], expectation management regarding symptom recovery [12], and compensatory cognitive strategies for prospective memory, attention/concentration, learning/memory, and executive functioning [13]. These components are included in Cognitive Symptom Management and Rehabilitation Therapy (CogSMART), a 12-week manualized treatment which improves persistent post-concussive symptoms (PCS; namely, cognitive and neurobehavioral symptoms) in OIF/OEF/OND Veterans with TBI [14-16].

Although limited, research suggests providing CBTs (including CPT-C) to people with comorbid TBI is feasible [17], may be prophylactic, [18], and can reduce PTSD, depressive, and post-concussive symptoms [19-21]. However, concerns remain that the cognitive impairment and emotional control problems associated with PTSD and mTBI may complicate or impede recovery from either problem [22-24] and reduce the efficacy of psychotherapy [25]. PTSD and PCS may also share potential causal pathways and the relationship between the two is complex and likely bidirectional [26].

Modifications may need to be made to standard interventions to accommodate shared etiologies and neuropsychological symptoms. Managing the combination of cognitive symptoms and PTSD with either sequential or parallel treatments is cumbersome. As with other comorbidities (such as PTSD with comorbid substance use), it is often unclear in which order to address comorbid problems with a sequential approach (i.e., CPT or cognitive rehabilitation, etc.), and a parallel approach creates time and travel burdens. Due to these reasons, it has been suggested that integrated treatments may be the optimal strategy, though there has been a lack of research on this topic [27-29].

To address the above challenges and optimize the treatment of comorbid PTSD/TBI, we integrated the primary components of CogSMART into CPT-C, resulting in a novel hybrid treatment, SMART-CPT. Herein we discuss the development and organization of SMART-CPT and describe an ongoing randomized controlled trial comparing efficacy of SMART-CPT to standard CPT-C. The primary aim of the trial is to investigate the efficacy of SMART-CPT in reducing emotional and neurobehavioral symptom severity (including cognitive symptoms) in Veterans with comorbid TBI and PTSD. We hypothesize that those receiving SMART-CPT will have greater reductions in PTSD symptom severity (as measured by the PTSD Checklist [PCL]),

greater improvements in quality of life (as measured by the Quality of Life Interview-Brief Version [QOLI-Brief]) [30], and greater reduction in neurobehavioral symptoms (as measured by the Neurobehavioral Symptom Inventory [NSI]) [31] than those receiving standard CPT-C.

Design and Methods

We are currently conducting a randomized (two condition) single center (VA San Diego Healthcare System) controlled trial of SMART-CPT compared to CPT-C for Veterans with PTSD and a history of mild to moderate TBI with current cognitive complaints. Baseline assessment confirms diagnosis of PTSD and history of TBI, and participants are subsequently randomized (simple randomization) to receive CPT-C or SMART-CPT and enter the study on a consecutive admissions basis. The study was approved by the Institutional Review Board of the VA San Diego Healthcare System.

Participants:

Projected enrollment is 90 OIF/OEF/OND Veterans over four years referred by providers in mental health clinics, medical clinics serving Veterans with TBI, Vet Centers, and Veteran organizations at local institutions of higher education. Both male and female Veterans are eligible for participation. The inclusion and exclusion criteria were minimized to target as ecologically valid sample as possible in this cohort. In addition to being able to provide written informed consent to participate in the study, inclusion criteria are: 1) OIF/OEF/OND-era Veteran; 2) current diagnosis of PTSD; 3) history of mild-to-moderate TBI; 4) current subjective cognitive complaints; and 5) no anticipated/pending medication changes (require 6-weeks on a stabilized medication regimen prior to study enrollment). Exclusions are: 1) active substance dependence, 2) suicidal intent or attempt within the previous month; 3) current psychotic disorder; 4) dementia; 5) non-English speaking; 6) current participation in other intervention

studies; 7) prior CPT or CogSMART treatment (> 5 sessions). Thorough medical chart review and detailed screening questions were used to assess the exclusion criteria. Prior non-CPT psychotherapy for PTSD is not exclusionary as long as the Veteran still meets diagnostic criteria for current PTSD. Because PTSD is highly comorbid with other medical and mental health conditions [32], during study participation, Veterans may continue to receive other medical and mental health care (e.g., support groups, family therapy, occupational therapy). Eliminating Veterans receiving stable doses of pharmacological agents or those engaged in other supportive mental health services or services for conditions only distally related to PTSD would ultimately not be representative of the vast majority of this target OIF/OEF/OND population. Given the duration of the treatment, limiting or withholding treatment across multiple comorbidities was also felt to be ethically contraindicated.

Treatment:

Eligible Veterans are assigned to one of the two treatment conditions (CPT-C or SMART-CPT) via simple randomization using random number generation, with equivalent allocation to each treatment group. Both treatments are manualized, 12-week interventions, delivered individually by a Ph.D.-level psychologist.

Cognitive Processing Therapy-Cognitive Only: CPT-C is a cognitive behavioral treatment targeting PTSD. CPT, from which CPT-C is derived, has been successfully implemented with patients exposed to a range of traumatic events, including combat [6, 33]. The treatment is drawn from a social cognitive theory of PTSD/trauma, and focuses on the content of trauma-related thoughts. Specifically, it centers on whether thoughts are or are not consistent with the individual's prior world beliefs, and the subsequent impact that thoughts have on emotions and behaviors. CPT-C does not include a detailed account of the traumatic event. It was chosen for use in this study because it is

equally effective to CPT [20], but has potentially lower rates of drop-out and earlier symptom reduction [6]. Eliminating the written account of the traumatic event also allowed more time to incorporate CogSMART components into the hybrid treatment. During the first session, the Veteran is educated about PTSD symptoms, cognitive theory, and treatment goals. The Veteran is also asked to write a one-page “Impact Statement” focusing on how the identified trauma has influenced thoughts and beliefs about oneself, others, and the world. In sessions 2 and 3, the Impact Statement serves as the basis for identifying "stuck points" or distorted thoughts about the trauma. The Veteran is then taught to recognize the connection between thoughts and feelings. Sessions 4 and 5 focus on recognizing and challenging cognitive distortions. Sessions 6 through 12 teach and reinforce cognitive restructuring skills, emphasizing themes of safety, trust, power and control, self-esteem, and intimacy [34]. All sessions are designed to be 50 minutes in length.

SMART-CPT: The hybrid treatment (SMART-CPT) keeps all of the components and structure of CPT-C and adds the following elements from CogSMART: psychoeducation regarding TBI and comorbidity with PTSD; brief instruction in compensatory strategies for attention, memory, and executive functioning and their specific application to CPT-C; more concrete language; repetition and reviews of key points through written summaries and mini-reviews at the beginning, middle, and end of treatment sessions; built-in short rest breaks during each session; and simplified and restructured homework pages that break assignments into smaller parts to aid understanding and ease of completion. These components of CogSMART were specifically chosen for incorporation due to their relevance for the concentration/attention, executive function, and prospective memory difficulties often reported for both TBI and PTSD. These strategies were also most relevant for enhancing compliance and retention of information presented through CPT-C. To incorporate the additional components, each SMART-CPT session

is 75 minutes in length, although the intervention as a whole remains a 12-week treatment (see Table 2).

Table 2: Treatment Overview

Session	Standard CPT-C Content	Additional Content for SMART-CPT
1	Introduction to treatment and psychoeducation about PTSD	TBI Psychoeducation, Choosing a calendar
2	Impact of trauma, identifying trauma-related cognitive distortions (“stuck-points”), psychoeducation about emotions	Identify a ‘home’ for important items, calendar use
3	Identifying thoughts and feelings, initial stuck point challenging	Taking breaks, sleep and fatigue strategies
4	Continuation of Session 3 topics	Prospective memory techniques, routines, linking tasks, automatic places
5	Specific work on challenging stuck points	Calendar – weekly planning session, prioritizing to-do lists
6	Identification of patterns of problematic thinking	Attention strategies - Active effort, breaks, self-talk
7	Continued work on challenging stuck points, introduction of generating alternative thoughts	External (e.g., calendars, note taking, alarms) and Internal (e.g., categorizing, visual imagery) Memory Strategies
8	Challenging safety stuck points, generating alternative thoughts	Overlearning, name learning, and retrieval strategies; organization strategies

9	Challenging trust stuck points, generating alternative thoughts	Goal setting and planning
10	Challenging power/control stuck points, generating alternative thoughts	Cognitive flexibility and problem solving, brainstorming
11	Challenging esteem stuck points, generating alternative thoughts	Review and use of cognitive strategies
12	Challenging intimacy stuck points, generating alternative thoughts, termination	Additional resources

Assessments: To document diagnosis and symptom presentation, participants are assessed prior to treatment (baseline). To assess any treatment gains, Veterans are assessed immediately following completion of treatment (3-month). Three months following the end of treatment (6-month), Veterans undergo a final assessment to determine maintenance of any treatment gains (see Table 1). Symptom ratings and treatment compliance information are also collected weekly during the active treatment portion of the study. All assessments are administered by experienced, blinded examiners, who are trained to high levels of inter-rater reliability (>.90). Participants are compensated for completion of assessments but not for treatment sessions. A combination of gold-standard diagnostic interviews (i.e., CAPS, WARCAT) and brief self-report severity measures (i.e., PCL, NSI) were used to confirm and assess diagnosis as well as ongoing symptom change during the active intervention. The primary outcomes of interest for reduction in PTSD symptoms are measured by the CAPS and PCL

(DSM-IV), reduction in post-concussive/neurobehavioral symptoms by the NSI, and improvements in quality of life by the QOLI-Brief.

Table 1: Assessment Overview

Domain	Pre-tx	Weekly	Post-tx	Follow-up
PTSD diagnostic interview	X		X	X
TBI Diagnostic Interview	X			
Symptom Severity	X	X	X	X
Quality of Life	X		X	X
Treatment compliance (attendance and homework)		X		
Treatment Satisfaction			X	
Objective Cognitive Functioning	X		X	X

PTSD Diagnostic Interview

The Clinician-Administered PTSD Scale for DSM-IV [CAPS; [35]] is the primary clinician-rated diagnostic and outcome measure administered at the pre-, post- and extended follow-up assessments. The CAPS is used to confirm the diagnosis of PTSD in study participants, if not already completed clinically within the past year (accessed via VA clinical records). The F1/I2 method of scoring is used to quantify severity [36]. This scoring method requires a specific symptom to be rated at a frequency of “1” (occurring “once or twice”) and an intensity of “2” (“moderate” intensity of symptoms) in order to be counted towards meeting diagnostic criteria. The number of symptoms meeting this criteria are then summed and compared to the number of symptoms required for each symptom cluster noted within DSM-IV (at least one re-experiencing symptoms; at least 3

avoidance/numbing symptoms; at least two symptoms of increased arousal). The scale also assesses social and occupational functioning, dissociation, and the validity of the items.

TBI Diagnostic Interview

The Warrior Administered Retrospective Casualty Assessment Tool [WARCAT; [37]] is used to obtain standardized data to confirm the history of mild to moderate TBI. This measure is a short, structured interview that allows for diagnosis based on the American Congress of Rehabilitation Medicine criteria, which requires an injury event followed by an alteration in consciousness. Mild to moderate TBI for this study is defined as an injury event, followed by loss or alteration of consciousness of less than 24 hours and posttraumatic amnesia of 7 or fewer days. Clinical confirmation of diagnosis by the Polytrauma Service is used to corroborate the WARCAT, if available.

Symptom Severity

The Neurobehavioral Symptom Inventory [NSI; [31]] a self-report measure used to quantify post-concussive symptom severity. In addition to the diagnosis of PTSD assessed by the CAPS pre- and post-intervention, the PTSD Checklist [PCL; [38, 39]] is also used to track weekly changes in PTSD symptomatology.

Quality of Life

The Quality of Life Interview-Brief Version [QOLI-Brief] [30] is used to assess objective indicators and subjective judgments of quality of life in several domains, including living situation, daily activities, family and social relationships, finances, employment, safety, and health.

Treatment Compliance

Attendance at each weekly therapy session is assessed as a dichotomous variable, either present or absent. To measure time spent on treatment-related tasks outside of session participants complete a weekly questionnaire detailing how often he/she worked on the practice assignments (ranging from not at all to more than 10 times) and how many minutes were spent on these tasks. Participants were allowed to reschedule missed sessions and concerted effort is made to maintain participants in the research treatment protocol, however participants may be discontinued if clinically indicated or due to failure to attend sessions. Increasing suicidality, mental health comorbidities taking precedence, or emergent and significant health conditions are examples of reasons participants may be discontinued. Alternative clinical care can then be coordinated for cases where safety or significant mental health or medical comorbidity warrants a higher level of care than can be provided within the structure of a research trial. As a general rule, individuals who fail to attend four sessions without communicating before or immediately after the missed session the reason for the absence (and therefore warrant additional follow up by study staff to reschedule), will be discontinued from treatment. To remain as flexible as possible with great sensitivity to individual circumstances, this is a guideline as opposed to a definitive cutoff for failure to attend. Individuals who drop out of treatment are not pursued for additional assessments but their data is still included in the intent to treat analyses.

Treatment Satisfaction

The Client Satisfaction Questionnaire (CSQ-8) [40], an 8-item measurement designed to measure client satisfaction with services.

Objective Cognitive Functioning

Cognitive outcomes are assessed via objective neuropsychological testing. Participants are evaluated with an approximately 100-minute neuropsychological test battery, including a test

of premorbid functioning [Wide Range Achievement Test-4 [WRAT4, administered only at the pre-treatment visit] [41], a test of effort [Test of Memory Malinger] [42], and tests of learning and memory [California Verbal Learning Test-II [43]; Rey-Osterreith Complex Figure] [44], attention [Wechsler Adult Intelligence Scale – IV, Digit Span subtest] [45]; processing speed [WAIS-IV Digit symbol, Symbol Search] [45]; and executive functioning [Wisconsin Card Sorting Test, Delis Kaplan Executive Function System, Color-Word Interference Test and Trail Making Test] [46, 47]. In this population, self-reported cognitive complaints have very limited correspondence to objective neuropsychological performance [48] so objective neuropsychological scores serve as the primary cognitive outcome. Because a substantial proportion of Veterans with comorbid PTSD and TBI perform below standard cutoffs on neuropsychological measures of performance validity [49], excluding those who fail validity testing will eliminate a considerable proportion of the sample of interest. Therefore, those who perform below standard cutoffs on performance or symptom validity measures will be eligible for the study but scores on validity measures will be used as covariates in statistical analyses as appropriate.

Design Considerations

We considered other study designs in which CPT-C and CogSMART were administered concurrently or sequentially but rejected those designs for several reasons. Etiology, initial symptom development, and symptom progression and persistence are dynamically intertwined in comorbid PTSD and TBI [26] (see figure 1). Memory, attention, and executive functioning difficulties are present following mTBI [8] and are common in those with PTSD [50], so incorporating compensatory cognitive strategies into a treatment for PTSD targets this overlapping symptomatology. Post-concussive symptoms (e.g., headache, cognitive symptoms,

mood changes) are non-specific, however, and occur in healthy individuals as well as those with chronic pain, and depression, among others [51]. Although post-concussive symptoms are normal and expected immediately following a concussion, *persistent* post-concussive symptoms (lasting longer than 3 months) are not. The extended persistence of such symptoms is most often driven by non-injury factors, particularly psychiatric and iatrogenic factors [8]. For the OIF/OEF/OND population in particular, the injury event may have also been the origin of the psychological trauma and in this way the mTBI impacts PTSD at the same time that the psychological trauma impacts development and persistence of post-concussive symptoms, leading to a bidirectional relationship between PCS and PTSD [26]. In order to prevent patients from having low expectations of PTSD treatment, it is essential to reduce tendencies to attribute all cognitive and other post-concussive symptoms entirely to a neurological insult, build the expectation of recovery, and increase awareness that there are often multifactorial etiologies of post-concussive symptoms [28]. It is also the case that systematically treating one symptom or condition may produce benefits to other symptoms or conditions and so "...it seems logical that providing interventions that aim to reduce traumatic stress and encourage appraisals relating to multifactorial underpinnings of common post-concussion-like symptoms would help reduce symptom burden and improve functioning" (p. 249) [27]. Finally, the structure of SMART-CPT allows the therapist to continue to use and reinforce cognitive rehabilitation principles throughout delivery of CPT-C in a way not possible if the treatments are delivered separately. Therefore, in this population where these two conditions are heavily comorbid, combining treatments was thought to better target the shared etiology and bidirectional influence between PTSD and post-concussive symptoms (see Figure 1).

Figure 1: Model of dynamic relationship between etiology, symptom development and persistence, and treatment in comorbid PTSD and TBI (Adapted from Vasterling, Bryant, and Keane (2012)).

In addition to the theoretical considerations in development of the treatment, there were also pragmatic concerns. CPT-C is an empirically supported treatment for PTSD, has already been established as better than no-treatment conditions, and is considered among the therapies that are the standard of care for PTSD [52]; therefore, it or another empirically supported

intervention for PTSD cannot ethically be withheld. Because all the standard elements of CPT-C are included in SMART-CPT, both groups still receive at least the standard of care for PTSD.

OIF/OEF/OND Veterans have lower attendance and higher ‘no-show’ and drop-out rates for mental health appointments [53], so a streamlined treatment that maximizes clinical benefit in the shortest duration possible is essential. The two separate treatments take 24 hours in total to administer whereas the combined SMART-CPT takes only 15 hours, making it more time and cost-effective. Comparing two treatments that are both 12 weeks in length also reduces impact of a significant difference in social contact. We are nonetheless keeping detailed accounts of exactly how long each session lasts and will control statistically for the differential interaction time between the two treatment groups.

Extended follow up periods range from one to six months in existing trials of CPT in military or Veteran samples, with one-quarter to one-third of participants lost to follow up at these intervals [33, 54, 55]. Three months was therefore chosen as the extended follow up interval to balance achieving reasonable time to examine stability of any symptom change with the likelihood of return for extended follow up decreasing as time increases.

There were also several considerations for how CPT-C and CogSMART were integrated. While incorporating all elements of CogSMART into SMART-CPT would have allowed for fully utilizing an empirically supported cognitive rehabilitation approach [15, 56], it would have resulted each session taking 120 minutes. Feedback received from active duty stakeholders indicated that a treatment session of this length would be unwieldy and negatively received upon implementation. Therefore, the elements of CogSMART that have the strongest empirical support and have been endorsed by clinical patients in a program evaluation survey as most useful were chosen for incorporation into SMART-CPT. All elements chosen did follow the

prescribed content in the original manual. Considerations were then made regarding the order of presentation of the elements of CPT-C and CogSMART. In a given session, presenting all CPT-C elements followed by all CogSMART elements versus interspersing CPT-C and CogSMART elements were explored. Presenting CPT-C elements first, followed by an active break (CogSMART principle), and then presentation of CogSMART elements was ultimately selected as the best therapeutic structure of each session. This order of content was felt to best reduce any unintended contribution to avoidance behaviors by delaying presentation of CPT-C elements within a session, allow time for down-regulation of strong emotion before leaving session, and emphasized in vivo purposeful breaks.

Therapist Training: In this trial, the treatment is delivered by a doctoral level mental health provider, however, it can be delivered by a master's level clinician. The therapist completed formal training with a VA CPT trainer (CSR). The two-day training, which is standard nationally, includes an introduction to the theoretical foundation for the treatment model; specific instructions on implementing each of the twelve CPT sessions; an overview of research results from clinical trials on CPT; and ongoing supervision. The standard CPT training includes a section on the implementation of CPT-C. Identification of stuck points and Socratic questioning was specifically covered and reiterated and practiced in weekly supervision. Additionally, the therapist was trained by the PI (AJJ) on CogSMART and the specific form it takes in the SMART-CPT intervention. Weekly individual supervision is ongoing throughout the trial between the study clinician and a VA CPT trainer (CSR).

Fidelity: Sessions are recorded for participants who consent to audio-recording. 10% of sessions are randomly selected and rated using a structured measure developed by the creator of the treatment [57]. Ratings include four distinct areas: 1) Model Adherence. For each item the rater

assesses if the therapist demonstrates behaviors that are essential to CPT-C for that session. These items are rated as present/absent. 2) Competence. For each of the essential behaviors rated in the adherence section, ratings are made based on how well the therapist carried out the behavior. Ratings in this section are based on a 5-point scale (ranging from poor to excellent, with satisfactory at the midpoint). 3) Essential but not unique elements (i.e., rapport building and time management). These items are also rated on a 5-point scale (1=poor, 5= excellent). 4) Overall Session. Ratings are made as present/absent for difficulties that lead to a departure from the manual, interventions that are implemented that are not in the manual or off-task discussions (sample fidelity form available upon request from the authors). If a therapist fails to achieve an adherence score of 80% or better and competence and skills rating of 4 or above, corrective feedback is provided until these levels are achieved. Fidelity rating forms for SMART-CPT include additional unique and essential items related to the CogSMART modifications (see Table 2 for specific modifications in each session). Otherwise, adherence and competence ratings are completed as detailed above for CPT-C.

Data Analysis:

The effect sizes for CogSMART on targeted cognitive domains and functional skills were medium to large in a previous study. However, we expect that the effect sizes of SMART-CPT on outcomes will be attenuated somewhat, given the effectiveness of standard CPT-C alone in helping alleviate PTSD symptoms. Therefore, we used a medium effect size ($d=.5$) for our power analyses. We estimated the power of the Random Regression Model using the RMASS program provided by Hedeker (<http://tigger.uic.edu/~hedeker/ml.html>). Based on these results, we selected the sample size of 72 subjects, which provides us with a minimum of 70% power for a medium effect size. We will recruit 90 subjects, expecting 25% attrition will result in a usable sample of 72.

For trials comparing two active treatments, use of both intent-to-treat (ITT) and per protocol (PP) analyses are recommended [58]. ITT analyses will include all randomized participants and the PP analyses will include those randomized subjects on whom we have a baseline assessment and at least one post-baseline evaluation. The two treatment groups will be compared on their baseline demographic characteristics and analyses will be adjusted to account for any observed group differences. The groups also will be examined for differential attrition. All dependent variables will be analyzed using a Random Regression Model, a generalized linear model [59-61]. The random effects method has several advantages over more traditional analytic approaches, as it allows the inclusion of subjects with missing data or those who were terminated early in the study, without relying on data imputation procedures. This method provides an estimate of the individual variability around the population trend, the variability of the individual intercepts (baseline values) and slopes (changes across time), and the correlation between them. The model will include a random intercept, a random effect for assessment time, and fixed effects for comparison groups and group-by-time interaction.

Discussion

In OIF/OEF/OND Veterans with a history of TBI, approximately 44% also have comorbid PTSD [7] and in those with PTSD, 20% have a history of TBI [62]. Herein we have described the first randomized controlled trial to investigate a modified version of an evidence-based therapy (SMART-CPT) for the purpose of targeting comorbid PTSD and TBI. CPT has good efficacy in Veterans for PTSD and CogSMART has been shown to improve PCS and cognitive symptoms following TBI. There is recently emerging evidence supporting the use of both CPT and cognitive rehabilitation in a residential setting to address comorbid PTSD and TBI

[21]. However, the efficacy of integrating CogSMART directly into CPT-C or examining such treatment combinations in outpatient settings has not been examined.

Several factors led us to believe that the integrated design of SMART-CPT is optimal. An integrated treatment allows focus on overlapping etiologies, and concurrent treatment of overlapping PCS and PTSD symptoms and factors that likely contribute to persistent symptoms. Treating one condition often has reciprocal benefits on other symptoms and conditions and this is expected to be the case particularly when the bidirectional influences of PCS and PTSD are contributing to the maintenance of symptoms (see Figure 1). The hybrid treatment provides the opportunity for discussion of the overlapping cognitive sequelae of TBI and PTSD and direct application and reinforcement of compensatory cognitive strategies to improve attendance, homework completion, and retention of CPT-C skills. The hybrid treatment approach also allows Veterans to receive standard of care for PTSD since both groups receive the full course of CPT-C from the outset of treatment, whereas a sequential approach would result in some Veterans having to wait for PTSD treatment.

Strengths of the study include limited exclusion criteria, thereby making the results of the trial more generalizable to the general treatment seeking population of OIF/OEF/OND Veterans with PTSD and TBI. CPT-C is already a first line treatment for PTSD in the VA and training is widely available. CogSMART, from which the cognitive rehabilitation principles were selected for SMART-CPT, is also publicly available and used widely in the VA system. Training and materials for the essential components of the hybrid SMART-CPT are therefore widely available and dissemination of SMART-CPT would be straightforward.

The study does have limitations. The results of this study may not generalize to individuals with severe TBI or to non-Veteran populations. Though unavoidable, the session

length of the treatment conditions is disparate, and adds a potential confound to any outcome effects. Because the application for funding and initial start-up of the trial was made prior to conversion to DSM5, the DSM-IV criteria are used for the CAPS and PCL and may lead to a slightly different sample composition and symptom assessment than if DSM5 criteria were able to be implemented. The limited exclusion criteria, while providing a more realistic and generalizable sample, also brings with it challenges of examining other common comorbidities, particularly depression and chronic pain, which are frequent presenting concerns in this population [63]. Similarly, the allowance for ongoing treatment of comorbidities was ethically necessary but may confound treatment outcome. However, because comorbidities with PTSD in this Veteran population is the norm rather than the exception, examining treatment in the context of comorbidities does provide for a more ecological and generalizable outcome. Given the level of distress and cognitive symptoms in this population, we anticipate that attendance and subsequent discontinuation of the treatment will be a challenge. To combat this, our protocol includes reminder calls from study staff for all appointments, wide flexibility in scheduling and rescheduling appointments, and coordination with other clinical care as indicated.

Most individuals with mild to moderate TBI have the cognitive skills to successfully participate in psychological treatments for PTSD as long as appropriate modifications are made. Programs with enhanced efficacy for Veterans with PTSD complicated by TBI are key to improving functional outcomes for these veterans. Combining therapeutic approaches in the clinical treatment of comorbid PTSD and TBI by enhancing an existing empirically supported PTSD intervention with cognitive rehabilitation principles has the potential to defragment care and significantly improve treatment for this clinically complicated group. This study will provide valuable information regarding the feasibility and efficacy of augmenting CPT with

CogSMART strategies to treat Veterans with comorbid PTSD and TBI, reduce distress for Veterans, and reduce healthcare costs.

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