Running Head: COGNITIVE FUNCTIONING AND TREATMENT IN PTSD

Verbal Memory Functioning Moderates Psychotherapy Treatment Response for PTSD-
Related Nightmares

J. Cobb Scott^{1,2*}, Gerlinde Harb¹, Janeese A. Brownlow^{1,2}, Jennifer Greene^{1,2}, Ruben C. Gur^{1,2},
& Richard J. Ross^{1,2}

Abstract

Posttraumatic stress disorder (PTSD) is associated with cognitive deficits in attention, executive control, and memory, although few studies have investigated the relevance of cognitive difficulties for treatment outcomes. We examined whether cognitive functioning and history of traumatic brain injury (TBI) were associated with response to cognitive-behavioral therapy (CBT) for PTSD-related sleep problems. In a randomized controlled trial of Imagery Rehearsal (IR) added to components of CBT for Insomnia (IR+cCBT-I) compared to cCBT-I alone for PTSD-related recurrent nightmares, 94 U.S. veterans completed a battery of cognitive tests. TBI was assessed via structured clinical interview. Mixed-effects models examined main effects of cognitive functioning and interactions with time on primary sleep and nightmare outcomes. Significant verbal immediate memory by time interactions were found for nightmare distress, nightmare frequency, and sleep quality, even after controlling for overall cognitive performance and depression. TBI exhibited main effects on outcomes but no interactions with time. Findings indicated that individuals with lower verbal memory performance were less likely to respond to treatment across two sleep interventions. Veterans with TBI displayed greater symptoms but no altered trajectories of treatment response. Together with prior literature, findings suggest that verbal memory functioning may be important to consider in PTSD treatment implementation.

Keywords: posttraumatic stress disorder; psychotherapy; nightmares; insomnia; memory; neuropsychology; sleep; imagery rehearsal therapy

Introduction

Posttraumatic stress disorder (PTSD) is a psychiatric disorder that can develop after exposure to a traumatic event and affects approximately 8% of the general population (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). A number of psychotherapies, including cognitive processing therapy (CPT), cognitive behavioral therapy (CBT), and prolonged exposure (PE) therapy, have been recommended as efficacious for the treatment of PTSD (Forbes et al., 2010; National Collaborating Centre for Mental Health (UK), 2005). However, a substantial proportion of individuals still show limited benefit from treatment. This seems especially true for PTSD-related sleep dysfunction, such as recurrent nightmares and insomnia, which frequently show inadequate response with PTSD-focused psychotherapy (Gutner, Casement, Stavitsky Gilbert, & Resick, 2013; Haagen, Smid, Knipscheer, & Kleber, 2015).

Given the hypothesized role of sleep disturbance in both the development and maintenance of PTSD (Gehrman et al., 2013), insomnia and nightmares may be critical treatment targets (Brownlow, Harb, & Ross, 2015). Specific psychotherapies have been developed to target sleep symptoms in both PTSD and other mental health disorders, including Cognitive-Behavioral Therapy for Insomnia (CBT-I; Manber et al., 2014) to treat insomnia symptoms and imagery rehearsal (IR; Krakow & Zadra, 2006) to treat post-traumatic nightmares. IR is a cognitive-behavioral treatment that attempts to revise the story line of a nightmare during waking and encourages rehearsal of the new, non-distressing dream script prior to bedtime. Although initial results were promising for IR and CBT-I in the context of trauma (e.g., Krakow et al., 2001), there has been significant heterogeneity in response to such therapies (Harb et al., 2013). In combination with results from PTSD-focused psychotherapy, these results suggest a clear need to identify factors that may influence psychotherapy treatment response for individuals with PTSD.

Cognitive dysfunction may be one such factor. Numerous studies have shown that individuals with PTSD exhibit poorer cognitive functioning than individuals without PTSD,

including those who experienced similar traumas as well as those without trauma exposure. Neurocognitive domains most commonly affected include episodic memory (Brewin, Kleiner, Vasterling, & Field, 2007), attention (Vasterling et al., 2002; Yehuda, Golier, Halligan, & Harvey, 2004), executive functioning (Aupperle, Melrose, Stein, & Paulus, 2012; Koenen et al., 2001), and speed of information processing (Verfaellie, Lafleche, Spiro, & Bousquet, 2013; Wrocklage et al., 2016), with the largest effects observed in verbal immediate memory and attention/working memory (Scott et al., 2015). These deficits appear to be greater in individuals with PTSD seeking treatment compared to community-based PTSD samples (Scott et al., 2015) and are associated with negative occupational and social outcomes, highlighting their potential clinical relevance (Geuze, Vermetten, de Kloet, Hijman, & Westenberg, 2009; Wrocklage et al., 2016). However, cognitive functioning has rarely been explored as an influential factor in psychotherapy.

Cognitive dysfunction may interfere with psychotherapy outcomes through both direct and indirect effects. Psychotherapy (especially CBT) relies heavily on neurocognitive skills to achieve treatment gains through cognitive restructuring, updating of associations, and behavioral changes. At a broad level, theoretical frameworks describing the process of change in therapy often invoke neurocognitive mechanisms, such as memory reconsolidation (e.g., Lane, Ryan, Nadel, & Greenberg, 2015) or executive problem solving (e.g., Pascual-Leone & Pascual-Leone, 2015). Thus, cognitive dysfunction may directly interfere with treatment implementation, comprehension, or a patient's ability to re-contextualize memories or associations. For example, in trauma-focused therapy, deficits in verbal abilities may affect one's ability to effectively verbalize trauma narratives, while verbal episodic memory dysfunction may affect the encoding and recall of treatment content or one's ability to re-contextualize memories, resulting in inefficient consolidation of treatment gains. Deficits in executive functioning could also impact a patient's ability to self-monitor and control attention during therapy. In particular, effective working memory, a core component of executive functioning,

requires individuals to monitor incoming information to determine its relevance and update the no longer relevant information with the new, relevant information as appropriate; similar skills are theoretically required in psychotherapy. Working memory has also been associated with the ability to inhibit intrusive thoughts and memories (Brewin & Smart, 2005), which may be linked to PTSD symptom expression, including intrusive trauma thoughts and nightmares. Cognitive impairment may also have indirect effects on treatment outcomes by affecting treatment engagement or by reflecting illness severity. For example, impulsivity and dysfunctional decision-making may lead to decreased compliance with treatment or increased treatment dropout (Patkar et al., 2004). Additionally, those who have greater symptoms may have greater cognitive symptoms and be more treatment resistant.

Two studies in PTSD have examined effects of cognitive functioning on psychotherapy outcomes, specifically focusing on episodic memory. In a small study of civilians undergoing trauma-focused CBT, Wild and Gur (2008) showed that non-responders had worse verbal immediate memory at baseline, and that improvement in PTSD symptoms was positively associated with verbal immediate memory performance. In a recent study of 140 individuals with PTSD, Nijdam et al. (2015) examined whether pre-treatment verbal memory functioning was associated with treatment response across two kinds of trauma-focused psychotherapies. Results showed that short-term memory retrieval was positively associated with PTSD remission and with the degree of change in PTSD severity over 16 weeks of treatment. The contributions of other areas of cognitive functioning to treatment outcomes in PTSD have not been thoroughly examined.

Concerns have also been raised regarding whether veterans with traumatic brain injury (TBI) may have reduced treatment efficacy during psychotherapy. Individuals with mild and moderate TBIs have been shown to evidence cognitive deficits in memory, processing speed, and executive functioning, as well as greater mental health symptom severity, chronic pain, and emotional regulation difficulties; all of these symptoms have the potential to reduce

psychotherapy treatment effectiveness (Bryant et al., 2010). Yet few studies have investigated the effects of TBI on treatment outcomes in PTSD. Studies of veterans with PTSD in exposure-based therapies have shown that treatment attendance may be lower in those with mild TBI (Davis, Walter, Chard, Parkinson, & Houston, 2013), although significant reductions in PTSD severity may nonetheless occur (Wolf, Strom, Kehle, & Eftekhari, 2012). However, studies to date have been small and used modified versions of the therapies that include cognitive rehabilitation components (Chard, Schumm, McIlvain, Bailey, & Parkinson, 2011) or increased session length and enhanced structure, such as providing smartphones, coaching between sessions, or additional support services (Wolf et al., 2015, 2012). Moreover, despite applying cognitive supports during therapy, no studies have examined cognitive functioning in predictive models.

Here, we extend prior literature in a number of ways. First, we examine the influence of cognitive functioning and TBI on treatment outcomes across two short-term treatments for PTSD-related recurrent nightmares, Imagery Rehearsal (IR) therapy and components of CBT for insomnia (cCBT-I). Second, we examine critical follow-up data for up to six months after the end of treatment, as previous studies have only examined outcome data at treatment cessation. [Third, we utilize a relatively comprehensive neurocognitive battery, which allows us to examine whether working memory and verbal episodic memory have specific roles in treatment outcomes while controlling for the influence of overall cognitive functioning.](#) Fourth, we explore whether veterans with PTSD and TBI showed treatment benefits equivalent to those with PTSD only. Such analyses take a critical step towards personalized treatment by identifying which individuals may be more or less likely to respond to treatment. Given prior results (Nijdam et al., 2015; Wild & Gur, 2008), estimated effect sizes in PTSD (Scott et al., 2015), and theoretical frameworks described above, we hypothesized that verbal immediate memory and working memory would moderate treatment response (including nightmare distress, nightmare frequency, and sleep quality) across both psychotherapy treatments, such that those with worse

cognitive functioning would have worse symptom trajectories. Given previous results and the heterogeneity of TBI symptomatology (Levin & Diaz-Arrastia, 2015), we also hypothesized that TBI status would have a main effect on these treatment outcomes but would not moderate treatment response (i.e., individuals with TBI and PTSD would be more symptomatic at all time points).

Methods

Participants

One-hundred and eight Operation Enduring Freedom/ Operation Iraqi Freedom/ Operation New Dawn (OEF/OIF/OND) veterans were recruited. All were enrolled in mental health care at the Corporal Michael J. Crescenz VA Medical Center (CMCVAMC) or its community-based outpatient clinics (n=102), or at the VA Connecticut Health Care System (VACHS) Mental Health Clinic (n=6). Participants were recruited between 2009 and 2015 for a randomized clinical trial of IR+cCBT-I vs. cCBT-I for recurrent, PTSD-related nightmares. Here we report data on 94 (out of 108) participants who received neurocognitive testing at baseline. Further details of the study design are described in the Supplemental Methods and will be described elsewhere.

Inclusion criteria were: (1) current Diagnostic and Statistical Manual, Fourth Edition (DSM-IV; American Psychiatric Association, 2000) PTSD as assessed with the Clinician-Administered PTSD Scale (CAPS; Weathers, Keane, & Davidson, 2001); (2) recurrent deployment-related nightmares (at least one every two weeks for at least six months); and (3) global sleep disturbance, defined as ≥ 5 on the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).

Additional exclusion criteria were: nightmares and PTSD primarily related to military sexual trauma, bipolar disorder, severe TBI, dementia or amnestic disorder not related to head injury, and schizophrenia or psychotic disorders. Individuals with substance dependence in the

preceding 12 months and those with “at risk” drinking behavior over the past month were excluded. For men, at risk drinking was defined as >4 drinks on a given day, drinking >3 days a week, or having >14 drinks in a week; for women, at risk drinking was defined as >3 drinks on a given day, drinking >3 days a week, or having >7 drinks total in a week (National Institute on Alcohol Abuse and Alcoholism, 2010). Comorbid anxiety or depressive disorders, alcohol and cannabis abuse, and mild and moderate head injury were allowed in order to recruit a representative sample of veterans with PTSD. Concurrent psychoactive medications were allowed if started more than two weeks before beginning the assessment. Enrolled veterans were allowed to continue mental health treatment as usual, although veterans concurrently receiving Prolonged Exposure or Cognitive Processing Therapy were excluded.

Participants provided written informed consent, and the study received Institutional Review Board approval from both CMCVAMC and VACHS.

Psychiatric Assessment

Participants were administered the CAPS, considered the “gold standard” assessment for PTSD, and the Structured Clinical Interview for DSM-IV (SCID-IV; First, Spitzer, Gibbon, & Williams, 2002) at baseline and end of treatment by clinical psychologists or master’s level clinicians. Assessors were blinded to randomization and received extensive training, including didactic workshops, a minimum of four observations of experienced assessors, and assessments observed and rated by experienced assessors. The four CAPS raters across sites exhibited excellent reliability during reliability training (ICC = 1.0 for presence of PTSD diagnosis and of 0.95 for CAPS total score).

Military-related concussions were evaluated with a structured clinical interview querying retrospective self-report of blast exposures, details of head injuries with loss or alteration of consciousness, and post-concussive symptoms. TBI severity was determined using published criteria (Ruff et al., 2009).

Neurocognitive Assessment

At baseline, participants received neuropsychological testing with the Penn Computerized Neurocognitive Battery (CNB), a battery of tests assessing multiple cognitive domains, including attention, executive control, episodic learning and memory, and spatial processing (Gur et al., 2001, 2010; Moore, Reise, Gur, Hakonarson, & Gur, 2015). Numerous studies support the CNB's validity and reliability in assessing neurocognitive functioning across a wide age range, in healthy individuals and those with neurological and psychiatric illness (Almasy et al., 2008; Gur et al., 2001; Roalf et al., 2014; Thomas et al., 2013). The CNB was administered by certified assessors who received hands-on didactic training, including several mock sessions observed by experienced assessors, feedback after each practice assessment, and standardized certification procedures. See Table 1 for a list of tests administered.

[INSERT TABLE 1 HERE]

Neurocognitive analyses focused on the Penn List Learning Test (PLLT) and the Letter N Back (LNB) test. The PLLT is an episodic memory measure similar to the California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 2000), with 16 semantically-related words read by the test administrator across five learning trials, as well as delayed recall. For the PLLT, we used total words recalled across trials 1-5 given prior associations with treatment outcomes (Nijdam et al., 2015; Wild & Gur, 2008), as well as robust effect size in PTSD, including greater effect sizes than delayed verbal memory (Scott et al., 2015). The LNB assesses working memory monitoring and updating by briefly displaying sequences of uppercase letters in three different conditions. In the 0-back condition, participants respond to a single target letter, 'X'. In the 1-back condition, they respond if the presented letter is identical to the one that preceded it. In the 2-back condition, they respond if the letter is identical to one presented two trials before. For the LNB, we used d-prime (d'), a measure of discriminability from signal detection theory that factors in both sensitivity and false alarms (Cohen, Braver, & O'Reilly, 1996).

Neurocognitive variables were z transformed across the whole sample, with higher scores representing better performance. We also created a variable of “overall cognitive performance” that averaged performance on all CNB measures except the PLLT and LNB; this variable was used to examine the specificity of individual cognitive domains versus effects of overall cognitive functioning.

Primary Outcomes

Primary sleep and nightmare outcomes below were assessed at baseline, within one week of completing the final treatment session (i.e., after 6 weeks of treatment), and during two follow-up visits at three and six months post-treatment. The Nightmare Distress Questionnaire (NDQ; Belicki, 1992b) measures distress associated with nightmares using 13 questions on a 5-point Likert scale assessing anxiety, avoidance, realism, and importance associated with nightmares. These questions are summed to create a total score, with higher scores indicating more distress. The NDQ appears to demonstrate adequate reliability ($\alpha=.83-.88$) and validity (Belicki, 1992a, 1992b; Martínez, Miró, & Arriaza, 2005), with $\alpha=.76$ in this sample. The Nightmare Frequency Questionnaire (NFQ; Krakow et al., 2001) is a self-report, continuous measure of nightmare frequency that generates number of nightmares and number of nights with nightmares per unit time (e.g., week). The NFQ has demonstrated adequate test-retest reliability ($>.85$) and good criterion and discriminant validity (Krakow et al., 2002). The Pittsburgh Sleep Quality Index (PSQI) is a well-validated measure of sleep quality and disturbances during the past month (Buysse et al., 1991, 1989; Carpenter & Andrykowski, 1998), with greater scores indicating poorer sleep.

Analyses

Mixed-effects, repeated-measures analyses with a random intercept for each participant were conducted in Stata 13 to test primary hypotheses. Linear models were used for nightmare distress and sleep quality, and Poisson models were used for number of nightmares given its Poisson distribution. Sex, age, depression status, and overall cognitive performance were included in all models. Time was coded as a categorical factor representing baseline, posttreatment, and two follow-up visits. Separate models analyzed each outcome as a function of TBI x time and cognitive performance x time, as well as main effects of cognitive performance and TBI. Each model also included a treatment x time interaction term. Likelihood ratio tests were used to evaluate the significance of interactions.

Results

Demographic, Mental Health, and Medical Characteristics

There were no important baseline differences between the subsample reported here and the primary sample on sociodemographic characteristics, including age, gender, race, marital status, or education (see Table 2). The most common comorbidities were major depressive disorder (n=61; 64.2%); dysthymia (n=8; 8.4%); depression, not otherwise specified (n=4; 4.2%); and generalized anxiety disorder (n=19; 20.0%). In addition, 68 participants (72.3%) reported a traumatic brain injury (TBI) before, during, or after deployment; most were from blast exposure during deployment (e.g., IEDs and mortar attacks). Most TBIs were classified as mild (n=64; 67.3%), with 34 (35.8%) involving an injury with alteration of consciousness and 30 (31.6%) involving an injury with loss of consciousness. Four participants (4.2%) were classified as having a moderate TBI. Table 3 presents the neurocognitive performance of the participants, including in comparison to normative data.

[INSERT TABLES 2 & 3 HERE]

Cognitive Functioning and Treatment Outcomes

Table 4 shows intent-to-treat, mixed-model analyses examining interactions of cognitive functioning and time on changes in PTSD-associated sleep and nightmare outcomes. There were no main effects of verbal immediate memory on sleep and nightmare outcomes ($ps > .10$). However, as can be seen in the table, there was a significant verbal immediate memory x time interaction for nightmare distress ($X^2(3)=11.7$; $p < 0.001$). Figure 1a shows this interaction with verbal immediate memory performance separated into terciles, indicating that those with the lowest verbal memory performance displayed the least symptom improvement. There was also a significant verbal immediate memory x time interaction for number of nightmares ($X^2(3)=8.0$; $p=0.005$), with a similar pattern of results as nightmare distress (Figure 1b). In addition, there was a significant verbal memory x time interaction for total sleep disturbance ($X^2(3)=9.7$; $p=0.02$) (Figure 1c). Notably, *post hoc* analyses showed that verbal memory at baseline was not associated with nightmare distress, frequency, or sleep quality (see Supplemental Results).

[INSERT TABLE 4 & FIGURE 1 HERE]

There were no significant main effects of working memory performance on sleep or nightmare outcomes ($ps > .10$). There were also no significant working memory x time interactions for nightmare distress ($X^2(3)=1.0$; $p=0.79$) or sleep disturbance ($X^2(3)=2.8$; $p=0.43$). There was a significant working memory x time interaction for number of nightmares ($X^2(3)=10.7$; $p=0.01$). However, as shown in Supplementary Figure 1, this interaction may not be of clinical significance given the pattern of results.

TBI and Treatment Outcomes

There was a main effect of TBI on nightmare distress ($X^2(1)=9.28$; $p=0.002$), number of nightmares ($X^2(1)=5.54$; $p=0.02$), and total sleep disturbance ($X^2(1)=8.14$; $p=0.004$), such that those with TBI were more symptomatic across visits. However, there were no significant TBI x time interactions for any sleep or nightmare-related outcomes (all $ps > .10$).

Discussion

In the current study, we found that baseline verbal memory performance (i.e., immediate memory for a list of words) was associated with treatment response across two types of short-term cognitive-behavioral insomnia and nightmare interventions. More specifically, veterans with PTSD and worse verbal immediate performance were less likely to have favorable responses to both types of psychotherapies than those with higher verbal immediate memory performance. Importantly, this relationship was significant across three different PTSD-related sleep and nightmare outcomes and was not driven by overall cognitive ability or depression status. Taken together with prior findings, our results suggest that verbal memory may be a critical factor to consider in optimizing psychotherapy treatment outcomes in PTSD.

Verbal Memory Is a Specific Moderator of Treatment Response

Our results are concordant with prior studies from Nijdam and colleagues (2015) and Wild and Gur (2008), who found that worse verbal memory performance was predictive of poorer treatment response during trauma-focused therapies for PTSD. However, here we extend prior work to show that such effects: 1) are specific for memory versus overall cognitive ability; 2) extend to short-term psychotherapies not specifically focused on trauma; and 3) appear to be even more robust with longer-term outcomes. Contrary to our hypotheses, however, we did not find that working memory was associated with clinically significant treatment modification, suggesting that working memory, or the transient processes of monitoring and updating task-relevant information, may not alter psychotherapy treatment response in PTSD. In combination with prior work in PTSD, our results suggest that verbal memory may be a specific predictor of cognitive-behavioral treatment response in PTSD. Since performance on the battery used in this study has been linked to specific brain systems (Roalf et al., 2014; Satterthwaite et al., 2013) and is heritable (e.g., Swagerman et al., 2016), this deficit could be a biomarker of treatment response. The fact that this finding has replicated across

three independent samples and three different forms of psychotherapy suggests that verbal memory may be a useful predictor to include in future psychotherapy treatment studies of PTSD. As noted previously (Etkin, 2015), these findings have important clinical implications because verbal memory measures are relatively cheap and easy to administer with limited training.

An examination of the specific pattern of effects revealed that individuals with moderate and high levels of memory performance showed significant reductions in sleep and nightmare disturbances at the end of treatment and mostly maintained these treatment gains at 3-month and 6-month follow-up visits. In contrast, those in the bottom tercile of memory performance showed lower gains by the end of treatment and did not maintain gains at short-term follow-ups. Notably, participants with higher and lower verbal memory performance were not different at baseline in nightmare distress, number of nightmares per week, or overall sleep disturbance. Given these baseline equivalencies, differential treatment effects are unlikely to simply reflect illness severity. Though speculative, individuals with lower memory abilities may be less able to consolidate important information acquired in treatment; cognitive deficits from continued sleep disturbances such as insomnia may compound these problems (Goldman-Mellor et al., 2015). Theoretical models of PTSD propose that abnormalities in memory are primary contributors to numerous symptoms of the disorder (Brewin, 2014; McNally, 2006). For example, individuals with PTSD experience involuntary intrusions of vivid, trauma-related memories through flashbacks and nightmares, have difficulties consolidating extinction memories, and, paradoxically, have difficulty voluntarily recalling details of traumatic events (Brewin, 2007). To date, however, delineation of how these memory abnormalities may be associated with difficulties recalling emotionally neutral information in PTSD has been sparse. Future research should also examine how memory dysfunction in PTSD may be associated with memory processes theoretically involved in psychotherapy, such as contextualization or reconsolidation

(Ehlers & Clark, 2000; Lane et al., 2015), or simply memory for therapy content (Harvey et al., 2014).

A prior meta-analysis found that individuals with PTSD seeking treatment had worse neurocognitive performance compared to community-based PTSD samples (Scott et al., 2015). In combination with the current results, this finding suggests that it may be beneficial to examine memory functioning in treatment-seeking individuals with PTSD in order to optimize treatment outcomes. Although prior longitudinal and twin studies have suggested that cognitive abilities may represent both a vulnerability factor for and consequence of PTSD (Gilbertson et al., 2006; Parslow & Jorm, 2007), such distinctions may not be especially useful for understanding treatment effectiveness. In other words, memory dysfunction may be important for PTSD treatment implementation regardless of etiology, and screening for significant memory deficits may be helpful in understanding variability in treatment response. Moreover, the specificity of results to verbal memory suggests that our effects are not driven solely by differences in overall intelligence, which have been associated with PTSD vulnerability (Breslau, Lucia, & Alvarado, 2006; Macklin et al., 1998).

TBI is a Predictor of Symptom Severity but Not Treatment Response

Although verbal immediate memory was associated with treatment response, TBI history was associated with worse PTSD-related sleep symptomatology at each visit (including baseline), but it was not associated with differential treatment response (i.e., there were no TBI x time interactions). Results therefore indicate that mild-to-moderate TBI may be important to consider for treatment planning in terms of symptom severity, although it may not alter an individual's overall capacity for responding to psychotherapy. Prior studies have shown that individuals with TBI and PTSD show significant treatment gains from exposure-based therapies (Chard et al., 2011; Wolf et al., 2015, 2012). These findings may underscore that TBI is a heterogeneous disorder, especially within the mild range of severity, with varying cognitive and

functional symptom profiles and trajectories (Levin & Diaz-Arrastia, 2015). Post-concussive symptoms such as fatigue vary and may be associated more with pre-injury mental health concerns than with TBI-related factors (Meares et al., 2011). Most cognitive deficits from mild TBI (e.g., processing speed, memory) resolve 6-9 months post-injury (Dikmen, Machamer, & Temkin, 2009; Rohling et al., 2011; cf. Bigler et al., 2013), although persistent deficits can be apparent in certain subgroups (e.g., with multiple head injuries; Belanger, Spiegel, & Vanderploeg, 2010). Thus, direct measurement of TBI-related factors hypothetically relevant to treatment may be more germane in future studies than simply studying the category of “TBI.”

Future Studies and Limitations

Although cognitive deficits may adversely affect treatment efficacy in PTSD, to progress to the next stage of intervention planning, research that examines the *pathways* by which cognitive functioning affects treatment is needed. For example, in substance use treatment, worse attention and global neurocognitive abilities have been associated with poorer recall of treatment relevant information (Teichner, Horner, Roitzsch, Herron, & Thevos, 2002), reduced quality of coping skills acquired (Kiluk, Nich, & Carroll, 2011), fewer treatment objectives achieved (Teichner, Horner, & Harvey, 2001) and fewer drink refusal skills learned (Smith & McCrady, 1991). These studies suggest that cognitive functioning plays a direct role in the ability to benefit from the primary “active ingredient” of treatment (i.e., the content of the treatment program). Future research in PTSD and other psychiatric disorders should be conducted to determine which aspects of treatments for these disorders are most affected by cognitive deficits.

Critically, such studies could lead to development of “fine tuned” psychotherapy treatments that are presented at the appropriate neurocognitive level, format, and speed for patients (e.g., utilizing repetition, reducing memory demands by providing reminders or written materials). It may also be beneficial to apply specific strategies to improve memory for therapy

content in those with memory deficits (Harvey et al., 2014). For example, treatments that capitalize on mnemonic devices could help facilitate treatment effectiveness in people with verbal memory deficits through repetition of memorable phrases and content, use of cue-based reminders, or incorporation of visualization/imagery from therapy content. Concurrent pharmacologic intervention could also be explored in the context of verbal memory deficits. For example, selective serotonin reuptake inhibitors have been shown to improve verbal memory and increase hippocampal volumes in PTSD (Vermetten, Vythilingam, Southwick, Charney, & Bremner, 2003). Theoretically, such effects could enhance treatment response in those with lower verbal memory abilities. In addition, cognitive remediation may prove useful for enhancing cognitive functioning during therapy (Jak et al., 2015), although the evidence base for the effectiveness of such techniques is currently limited (Cooper et al., 2015).

Limitations of this study include the exclusive focus on veterans, the small sample of women, and short-term psychotherapeutic interventions. Additionally, because our study did not have a control arm, we cannot rule out the possibility that verbal memory deficits are nonspecific predictors of capacity for recovery absent of any intervention. Although we were underpowered to examine treatment response by type of treatment (i.e., three-way interactions between treatment, time, and cognitive functioning), future studies would benefit from comparing effects of memory functioning on specific psychotherapies, as some types of therapy hypothesized to have fewer cognitive mechanisms (e.g., exposure therapy) may be less affected by memory dysfunction. Moreover, our sample included some psychiatric and medical comorbidities, limiting the specificity of findings to PTSD. However, it should be noted that this comorbidity extends the generalizability of the study for veterans with PTSD.

Conclusions

Our results suggest that individuals with low verbal immediate memory performance, despite having equivalent baseline symptom severity, were less likely to benefit from

psychotherapy for PTSD-related sleep and nightmare disturbances than their counterparts with good verbal memory. In contrast, individuals with TBI were more symptomatic across treatment and follow-up but did not evidence differential treatment response. These findings may inform future personalized treatment for PTSD-related symptomatology, increase understanding of treatment processes in psychotherapy, and guide efforts to enhance treatment. Critically, verbal memory may be an important factor to consider in PTSD treatment implementation and outcomes, and measures of verbal memory could be included in future PTSD treatment studies with relatively low cost and patient burden.

Acknowledgments

This work was supported by a Department of Defense (DOD) CDMRP Award (W81XWH-08-2-0104, Clinical trial #NCT00691626) to Dr. Ross, and a Department of Veterans Affairs Career Development Award (IK2CX000772) to Dr. Scott. The authors also wish to thank Dr. Warren Bilker for statistical consultation. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs. The authors declare no conflicts of interest.

References

- Almasy, L., Gur, R. C., Haack, K., Cole, S. A., Calkins, M. E., Peralta, J. M., ... Gur, R. E. (2008). A genome screen for quantitative trait loci influencing schizophrenia and neurocognitive phenotypes. *The American Journal of Psychiatry*, 165(9), 1185–1192. <http://doi.org/10.1176/appi.ajp.2008.07121869>
- American Psychiatric Association. (2000). *Diagnostic and statistical manual-text revision (DSM-IV-TR)*. American Psychiatric Association.
- Aupperle, R. L., Melrose, A. J., Stein, M. B., & Paulus, M. P. (2012). Executive function and PTSD: disengaging from trauma. *Neuropharmacology*, 62(2), 686–694. <http://doi.org/10.1016/j.neuropharm.2011.02.008>
- Baddeley, A. D., & Hitch, G. J. (1994). Developments in the concept of working memory. *Neuropsychology*, 8(4), 485–493. <http://doi.org/10.1037/0894-4105.8.4.485>
- Belanger, H. G., Spiegel, E., & Vanderploeg, R. D. (2010). Neuropsychological performance following a history of multiple self-reported concussions: a meta-analysis. *Journal of the International Neuropsychological Society*, 16(2), 262–267. <http://doi.org/10.1017/S1355617709991287>
- Belicki, K. (1992a). Nightmare frequency versus nightmare distress: relations to psychopathology and cognitive style. *Journal of Abnormal Psychology*, 101(3), 592–597.
- Belicki, K. (1992b). The relationship of nightmare frequency to nightmare suffering with implications for treatment and research. *Dreaming*, 2(3), 143–148. <http://doi.org/10.1037/h0094355>
- Bigler, E. D., Farrer, T. J., Pertab, J. L., James, K., Petrie, J. A., & Hedges, D. W. (2013). Reaffirmed limitations of meta-analytic methods in the study of mild traumatic brain injury: a response to Rohling et al. *The Clinical Neuropsychologist*, 27(2), 176–214. <http://doi.org/10.1080/13854046.2012.693950>

- Breslau, N., Lucia, V. C., & Alvarado, G. F. (2006). Intelligence and other predisposing factors in exposure to trauma and posttraumatic stress disorder: a follow-up study at age 17 years. *Archives of General Psychiatry*, 63(11), 1238–1245.
<http://doi.org/10.1001/archpsyc.63.11.1238>
- Brewin, C. R. (2007). Autobiographical memory for trauma: update on four controversies. *Memory*, 15(3), 227–248. <http://doi.org/10.1080/09658210701256423>
- Brewin, C. R. (2014). Episodic memory, perceptual memory, and their interaction: foundations for a theory of posttraumatic stress disorder. *Psychological Bulletin*, 140(1), 69–97.
<http://doi.org/10.1037/a0033722>
- Brewin, C. R., Kleiner, J. S., Vasterling, J. J., & Field, A. P. (2007). Memory for emotionally neutral information in posttraumatic stress disorder: A meta-analytic investigation. *Journal of Abnormal Psychology*, 116(3), 448–463. <http://doi.org/10.1037/0021-843X.116.3.448>
- Brewin, C. R., & Smart, L. (2005). Working memory capacity and suppression of intrusive thoughts. *Journal of Behavior Therapy and Experimental Psychiatry*, 36(1), 61–68.
<http://doi.org/10.1016/j.jbtep.2004.11.006>
- Brownlow, J. A., Harb, G. C., & Ross, R. J. (2015). Treatment of Sleep Disturbances in Post-Traumatic Stress Disorder: A Review of the Literature. *Current Psychiatry Reports*, 17(6), 41. <http://doi.org/10.1007/s11920-015-0587-8>
- Bryant, R. A., O'Donnell, M. L., Creamer, M., McFarlane, A. C., Clark, C. R., & Silove, D. (2010). The psychiatric sequelae of traumatic injury. *The American Journal of Psychiatry*, 167(3), 312–320. <http://doi.org/10.1176/appi.ajp.2009.09050617>
- Busse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research*, 28(2), 193–213.

- Buysse, D. J., Reynolds, C. F., Monk, T. H., Hoch, C. C., Yeager, A. L., & Kupfer, D. J. (1991). Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). *Sleep*, 14(4), 331–338.
- Carpenter, J. S., & Andrykowski, M. A. (1998). Psychometric evaluation of the pittsburgh sleep quality index. *Journal of Psychosomatic Research*, 45(1), 5–13.
[http://doi.org/10.1016/S0022-3999\(97\)00298-5](http://doi.org/10.1016/S0022-3999(97)00298-5)
- Chard, K. M., Schumm, J. A., McIlvain, S. M., Bailey, G. W., & Parkinson, R. B. (2011). Exploring the efficacy of a residential treatment program incorporating cognitive processing therapy-cognitive for veterans with PTSD and traumatic brain injury. *Journal of Traumatic Stress*, 24(3), 347–351. <http://doi.org/10.1002/jts.20644>
- Cooper, D. B., Bunner, A. E., Kennedy, J. E., Balldin, V., Tate, D. F., Eapen, B. C., & Jaramillo, C. A. (2015). Treatment of persistent post-concussive symptoms after mild traumatic brain injury: a systematic review of cognitive rehabilitation and behavioral health interventions in military service members and veterans. *Brain Imaging and Behavior*, 9(3), 403–420. <http://doi.org/10.1007/s11682-015-9440-2>
- Davis, J. J., Walter, K. H., Chard, K. M., Parkinson, R. B., & Houston, W. S. (2013). Treatment adherence in cognitive processing therapy for combat-related PTSD with history of mild TBI. *Rehabilitation Psychology*, 58(1), 36–42. <http://doi.org/10.1037/a0031525>
- Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2000). *California Verbal Learning Test - Second Edition: CVLT-II*. San Antonio, TX: Pearson.
- Dikmen, S. S., Machamer, J., & Temkin, N. (2009). Neurobehavioral consequences of traumatic brain injury. In I. Grant & K. M. Adams (Eds.), *Neuropsychological Assessment of Neuropsychiatric Disorders* (3rd ed., pp. 597–617). New York: Oxford University Press, USA.
- Ehlers, A., & Clark, D. M. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy*, 38(4), 319–345.

- Etkin, A. (2015). Predicting Treatment Response in Posttraumatic Stress Disorder: (Commentary). *The Journal of Clinical Psychiatry*, e1035–e1036.
<http://doi.org/10.4088/JCP.14com09752>
- First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (2002). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P)*. New York: Biometrics Research, New York State Psychiatric Institute.
- Forbes, D., Creamer, M., Bisson, J. I., Cohen, J. A., Crow, B. E., Foa, E. B., ... Ursano, R. J. (2010). A guide to guidelines for the treatment of PTSD and related conditions. *Journal of Traumatic Stress*, 23(5), 537–552. <http://doi.org/10.1002/jts.20565>
- Gehrman, P., Seelig, A. D., Jacobson, I. G., Boyko, E. J., Hooper, T. I., Gackstetter, G. D., ... Smith, T. C. (2013). Predeployment Sleep Duration and Insomnia Symptoms as Risk Factors for New-Onset Mental Health Disorders Following Military Deployment. *Sleep*, 36(7), 1009–1018. <http://doi.org/10.5665/sleep.2798>
- Geuze, E., Vermetten, E., de Kloet, C. S., Hijman, R., & Westenberg, H. G. M. (2009). Neuropsychological performance is related to current social and occupational functioning in veterans with posttraumatic stress disorder. *Depression and Anxiety*, 26(1), 7–15.
<http://doi.org/10.1002/da.20476>
- Gilbertson, M. W., Paulus, L. A., Williston, S. K., Gurvits, T. V., Lasko, N. B., Pitman, R. K., & Orr, S. P. (2006). Neurocognitive function in monozygotic twins discordant for combat exposure: relationship to posttraumatic stress disorder. *Journal of Abnormal Psychology*, 115(3), 484–495. <http://doi.org/10.1037/0021-843X.115.3.484>
- Goldman-Mellor, S., Caspi, A., Gregory, A. M., Harrington, H., Poulton, R., & Moffitt, T. E. (2015). Is insomnia associated with deficits in neuropsychological functioning? Evidence from a population-based study. *Sleep*, 38(4), 623–631. <http://doi.org/10.5665/sleep.4584>
- Gur, R. C., Ragland, J. D., Moberg, P. J., Turner, T. H., Bilker, W. B., Kohler, C., ... Gur, R. E. (2001). Computerized neurocognitive scanning: I. Methodology and validation in healthy

- people. *Neuropsychopharmacology*, 25(5), 766–776. [http://doi.org/10.1016/S0893-133X\(01\)00278-0](http://doi.org/10.1016/S0893-133X(01)00278-0)
- Gur, R. C., Richard, J., Hughett, P., Calkins, M. E., Macy, L., Bilker, W. B., ... Gur, R. E. (2010). A cognitive neuroscience-based computerized battery for efficient measurement of individual differences: standardization and initial construct validation. *Journal of Neuroscience Methods*, 187(2), 254–262. <http://doi.org/10.1016/j.jneumeth.2009.11.017>
- Gutner, C. A., Casement, M. D., Stavitsky Gilbert, K., & Resick, P. A. (2013). Change in sleep symptoms across Cognitive Processing Therapy and Prolonged Exposure: a longitudinal perspective. *Behaviour Research and Therapy*, 51(12), 817–822. <http://doi.org/10.1016/j.brat.2013.09.008>
- Haagen, J. F. G., Smid, G. E., Knipscheer, J. W., & Kleber, R. J. (2015). The efficacy of recommended treatments for veterans with PTSD: A metaregression analysis. *Clinical Psychology Review*, 40, 184–194. <http://doi.org/10.1016/j.cpr.2015.06.008>
- Harb, G. C., Phelps, A. J., Forbes, D., Ross, R. J., Gehrman, P. R., & Cook, J. M. (2013). A critical review of the evidence base of imagery rehearsal for posttraumatic nightmares: Pointing the way for future research. *Journal of Traumatic Stress*, 26(5), 570–579. <http://doi.org/10.1002/jts.21854>
- Harvey, A. G., Lee, J., Williams, J., Hollon, S. D., Walker, M. P., Thompson, M. A., & Smith, R. (2014). Improving Outcome of Psychosocial Treatments by Enhancing Memory and Learning. *Perspectives on Psychological Science : A Journal of the Association for Psychological Science*, 9(2), 161–179. <http://doi.org/10.1177/1745691614521781>
- Jak, A. J., Aupperle, R., Rodgers, C. S., Lang, A. J., Schiehser, D. M., Norman, S. B., & Twamley, E. W. (2015). Evaluation of a hybrid treatment for Veterans with comorbid traumatic brain injury and posttraumatic stress disorder: Study protocol for a randomized controlled trial. *Contemporary Clinical Trials*, 45(Pt B), 210–216. <http://doi.org/10.1016/j.cct.2015.10.009>

- Kessler, R. C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C. B. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry*, 52(12), 1048–1060. <http://doi.org/http://doi.org/10.1001/archpsyc.1995.03950240066012>
- Kiluk, B. D., Nich, C., & Carroll, K. M. (2011). Relationship of cognitive function and the acquisition of coping skills in computer assisted treatment for substance use disorders. *Drug and Alcohol Dependence*, 114(2-3), 169–176. <http://doi.org/10.1016/j.drugalcdep.2010.09.019>
- Koenen, K. C., Driver, K. L., Oscar-Berman, M., Wolfe, J., Folsom, S., Huang, M. T., & Schlesinger, L. (2001). Measures of prefrontal system dysfunction in posttraumatic stress disorder. *Brain and Cognition*, 45(1), 64–78. <http://doi.org/10.1006/brcg.2000.1256>
- Krakow, B., Hollifield, M., Johnston, L., Koss, M., Schrader, R., Warner, T. D., ... Prince, H. (2001). Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: a randomized controlled trial. *JAMA*, 286(5), 537–545.
- Krakow, B., Schrader, R., Tandberg, D., Hollifield, M., Koss, M. P., Yau, C. L., & Cheng, D. T. (2002). Nightmare frequency in sexual assault survivors with PTSD. *Journal of Anxiety Disorders*, 16(2), 175–190.
- Krakow, B., & Zadra, A. (2006). Clinical management of chronic nightmares: imagery rehearsal therapy. *Behavioral Sleep Medicine*, 4(1), 45–70. http://doi.org/10.1207/s15402010bsm0401_4
- Lane, R. D., Ryan, L., Nadel, L., & Greenberg, L. (2015). Memory reconsolidation, emotional arousal, and the process of change in psychotherapy: New insights from brain science. *The Behavioral and Brain Sciences*, 38, e1. <http://doi.org/10.1017/S0140525X14000041>

- Levin, H. S., & Diaz-Arrastia, R. R. (2015). Diagnosis, prognosis, and clinical management of mild traumatic brain injury. *The Lancet. Neurology*, 14(5), 506–517.
[http://doi.org/10.1016/S1474-4422\(15\)00002-2](http://doi.org/10.1016/S1474-4422(15)00002-2)
- Macklin, M. L., Metzger, L. J., Litz, B. T., McNally, R. J., Lasko, N. B., Orr, S. P., & Pitman, R. K. (1998). Lower precombat intelligence is a risk factor for posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology*, 66(2), 323–326.
<http://doi.org/http://doi.org/10.1037/0022-006X.66.2.323>
- Manber, R., Friedman, L., Siebern, A. T., Carney, C., Edinger, J., Epstein, D., & Karlin, B. E. (2014). Cognitive behavioral therapy for insomnia in veterans: Therapist manual. *Washington, DC: US Department of Veterans Affairs*.
- Martínez, M. P., Miró, E., & Arriaza, R. (2005). Evaluation of the distress and effects caused by nightmares: A study of the psychometric properties of the nightmare distress questionnaire and the nightmare effects survey. *Sleep and Hypnosis*, 7(1), 29.
- McNally, R. J. (2006). Cognitive abnormalities in post-traumatic stress disorder. *Trends in Cognitive Sciences*, 10(6), 271–277. <http://doi.org/10.1016/j.tics.2006.04.007>
- Meares, S., Shores, E. A., Taylor, A. J., Batchelor, J., Bryant, R. A., Baguley, I. J., ... Marosszeky, J. E. (2011). The prospective course of postconcussion syndrome: the role of mild traumatic brain injury. *Neuropsychology*, 25(4), 454–465.
<http://doi.org/10.1037/a0022580>
- Moore, T. M., Reise, S. P., Gur, R. E., Hakonarson, H., & Gur, R. C. (2015). Psychometric properties of the Penn Computerized Neurocognitive Battery. *Neuropsychology*, 29(2), 235–246. <http://doi.org/10.1037/neu0000093>
- National Collaborating Centre for Mental Health (UK). (2005). *Post-Traumatic Stress Disorder: The Management of PTSD in Adults and Children in Primary and Secondary Care*. Leicester (UK): Gaskell.

- National Institute on Alcohol Abuse and Alcoholism. (2010). *Rethinking drinking: Alcohol and your health* (No. 10-3770). Rockville, MD: NIAAA. Retrieved from <http://rethinkingdrinking.niaaa.nih.gov/>
- Nijdam, M. J., de Vries, G.-J., Gersons, B. P. R., & Olff, M. (2015). Response to psychotherapy for posttraumatic stress disorder: The role of pretreatment verbal memory performance. *The Journal of Clinical Psychiatry*, 76(8), e1023–1028. <http://doi.org/10.4088/JCP.14m09438>
- Parslow, R. A., & Jorm, A. F. (2007). Pretrauma and posttrauma neurocognitive functioning and PTSD symptoms in a community sample of young adults. *The American Journal of Psychiatry*, 164(3), 509–515. <http://doi.org/10.1176/appi.ajp.164.3.509>
- Pascual-Leone, A., & Pascual-Leone, J. (2015). Memory reconsolidation keeps track of emotional changes, but what will explain the actual “processing”? *The Behavioral and Brain Sciences*, 38, e20. <http://doi.org/10.1017/S0140525X14000387>
- Patkar, A. A., Murray, H. W., Mannelli, P., Gottheil, E., Weinstein, S. P., & Vergare, M. J. (2004). Pre-Treatment Measures of Impulsivity, Aggression and Sensation Seeking Are Associated with Treatment Outcome for African-American Cocaine-Dependent Patients. *Journal of Addictive Diseases*, 23(2), 109–122.
- Roalf, D. R., Ruparel, K., Gur, R. E., Bilker, W., Gerraty, R., Elliott, M. A., ... Gur, R. C. (2014). Neuroimaging predictors of cognitive performance across a standardized neurocognitive battery. *Neuropsychology*, 28(2), 161–176. <http://doi.org/10.1037/neu0000011>
- Rohling, M. L., Binder, L. M., Demakis, G. J., Larrabee, G. J., Ploetz, D. M., & Langhinrichsen-Rohling, J. (2011). A meta-analysis of neuropsychological outcome after mild traumatic brain injury: re-analyses and reconsiderations of Binder et al. (1997), Frencham et al. (2005), and Pertab et al. (2009). *The Clinical Neuropsychologist*, 25(4), 608–623. <http://doi.org/10.1080/13854046.2011.565076>

- Ruff, R. M., Iverson, G. L., Barth, J. T., Bush, S. S., Broshek, D. K., & NAN Policy and Planning Committee. (2009). Recommendations for diagnosing a mild traumatic brain injury: a National Academy of Neuropsychology education paper. *Archives of Clinical Neuropsychology: The Official Journal of the National Academy of Neuropsychologists*, 24(1), 3–10. <http://doi.org/10.1093/arclin/acp006>
- Satterthwaite, T. D., Wolf, D. H., Erus, G., Ruparel, K., Elliott, M. A., Gennatas, E. D., ... Gur, R. E. (2013). Functional maturation of the executive system during adolescence. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 33(41), 16249–16261. <http://doi.org/10.1523/JNEUROSCI.2345-13.2013>
- Scott, J. C., Matt, G. E., Wrocklage, K. M., Crnich, C., Jordan, J., Southwick, S. M., ... Schweinsburg, B. C. (2015). A quantitative meta-analysis of neurocognitive functioning in posttraumatic stress disorder. *Psychological Bulletin*, 141(1), 105–140. <http://doi.org/10.1037/a0038039>
- Smith, D. E., & McCrady, B. S. (1991). Cognitive impairment among alcoholics: impact on drink refusal skill acquisition and treatment outcome. *Addictive Behaviors*, 16(5), 265–274.
- Swagerman, S. C., de Geus, E. J. C., Kan, K.-J., van Bergen, E., Nieuwboer, H. A., Koenis, M. M. G., ... Boomsma, D. I. (2016). The Computerized Neurocognitive Battery: Validation, aging effects, and heritability across cognitive domains. *Neuropsychology*, 30(1), 53–64. <http://doi.org/10.1037/neu0000248>
- Teichner, G., Horner, M. D., & Harvey, R. T. (2001). Neuropsychological predictors of the attainment of treatment objectives in substance abuse patients. *The International Journal of Neuroscience*, 106(3-4), 253–263.
- Teichner, G., Horner, M. D., Roitzsch, J. C., Herron, J., & Thevos, A. (2002). Substance abuse treatment outcomes for cognitively impaired and intact outpatients. *Addictive Behaviors*, 27(5), 751–763.

- Thomas, M. L., Brown, G. G., Gur, R. C., Hansen, J. A., Nock, M. K., Heeringa, S., ... Stein, M. B. (2013). Parallel psychometric and cognitive modeling analyses of the Penn Face Memory Test in the Army Study to Assess Risk and Resilience in Servicemembers. *Journal of Clinical and Experimental Neuropsychology*, 35(3), 225–245.
<http://doi.org/10.1080/13803395.2012.762974>
- Vasterling, J. J., Duke, L. M., Brailey, K., Constans, J. I., Allain, A. N., Jr, & Sutker, P. B. (2002). Attention, learning, and memory performances and intellectual resources in Vietnam veterans: PTSD and no disorder comparisons. *Neuropsychology*, 16(1), 5–14.
<http://doi.org/http://doi.org/10.1037/0894-4105.16.1.5>
- Verfaellie, M., Lafleche, G., Spiro, A., & Bousquet, K. (2013). Neuropsychological Outcomes in OEF/OIF Veterans With Self-Report of Blast Exposure: Associations With Mental Health, but not mTBI. *Neuropsychology*. <http://doi.org/10.1037/neu0000027>
- Vermetten, E., Vythilingam, M., Southwick, S. M., Charney, D. S., & Bremner, J. D. (2003). Long-term treatment with paroxetine increases verbal declarative memory and hippocampal volume in posttraumatic stress disorder. *Biological Psychiatry*, 54(7), 693–702.
- Weathers, F. W., Keane, T. M., & Davidson, J. R. (2001). Clinician-administered PTSD scale: a review of the first ten years of research. *Depression and Anxiety*, 13(3), 132–156.
<http://doi.org/http://doi.org/10.1002/da.1029>
- Wild, J., & Gur, R. C. (2008). Verbal memory and treatment response in post-traumatic stress disorder. *The British Journal of Psychiatry*, 193(3), 254–255.
<http://doi.org/10.1192/bjp.bp.107.045922>
- Wolf, G. K., Kretzmer, T., Crawford, E., Thors, C., Wagner, H. R., Strom, T. Q., ... Vanderploeg, R. D. (2015). Prolonged Exposure Therapy With Veterans and Active Duty Personnel Diagnosed With PTSD and Traumatic Brain Injury. *Journal of Traumatic Stress*, 28(4), 339–347. <http://doi.org/10.1002/jts.22029>

- Wolf, G. K., Strom, T. Q., Kehle, S. M., & Eftekhari, A. (2012). A preliminary examination of prolonged exposure therapy with Iraq and Afghanistan veterans with a diagnosis of posttraumatic stress disorder and mild to moderate traumatic brain injury. *The Journal of Head Trauma Rehabilitation, 27*(1), 26–32.
<http://doi.org/10.1097/HTR.0b013e31823cd01f>
- Wrocklage, K. M., Schweinsburg, B. C., Krystal, J. H., Trejo, M., Roy, A., Weisser, V., ... Scott, J. C. (2016). Neuropsychological Functioning in Veterans with Posttraumatic Stress Disorder: Associations with Performance Validity, Comorbidities, and Functional Outcomes. *Journal of the International Neuropsychological Society: JINS, 1*–13.
<http://doi.org/10.1017/S1355617716000059>
- Yehuda, R., Golier, J. A., Halligan, S. L., & Harvey, P. D. (2004). Learning and memory in Holocaust survivors with posttraumatic stress disorder. *Biological Psychiatry, 55*(3), 291–295.

Table 1.

Tests and domains used from the Penn Computerized Neurocognitive Battery (CNB)

Neurocognitive Domain	Cognitive Functions Assessed	Test
Executive Control	Sustained Attention	Penn Continuous Performance Test (PCPT)
	Working Memory	Letter N-Back Test (LNB)
	Abstraction/Mental Flexibility	Penn Conditional Exclusion Test (PCET)
Episodic Memory	Verbal Episodic Memory	Penn List Learning Test (PLLT)
	Visual Episodic Memory	Visual Object Learning Test (VOLT)
Complex Cognition	Language Reasoning	Penn Verbal Reasoning Test (PVRT)
	Visuospatial Ability	Penn Line Orientation Test (PLOT)
Sensori-Motor	Praxis	Motor Praxis Test (MPT)

Table 2.

Demographic and Mental Health Characteristics of the Analyzed and Total Clinical Trial

Samples

	Analyzed sample (n=94)	Total Sample (n=108)
Demographics, n (%)		
Age (years), mean (sd)	37.1 (9.9)	37.1 (9.9)
Education (some college/degree, %)	64.1%	65.7%
Sex (men, %)	85.3%	86.1%
Race (%)		
Caucasian	59.0%	58.3%
African-American	35.8%	37.0%
Other/Mixed/Unknown	5.3%	4.6%
Age (years), mean (sd)	37.1 (9.9)	37.1 (9.9)
Concurrent Diagnoses, n (%)		
Major Depressive Disorder	61 (64.9%)	69 (63.9%)
Generalized Anxiety Disorder	19 (20.2%)	24 (22.2%)
Alcohol Abuse	6 (6.4%)	8 (7.4%)
TBI, n (%)	68 (72.3%)	71 (65.7%)
TBI with Alteration of Consciousness (%)	34 (35.8%)	37 (34.3%)
TBI with Loss of Consciousness (%)	34 (31.6%)	39 (36.1%)
Clinical Characteristics, mean (sd)		
Nightmare Distress (NDQ), mean (sd)	29.40 (5.92)	29.43 (5.79)
Global Sleep Quality (PSQI), mean (sd)	15.38 (2.77)	15.23 (2.84)
Weekly Nights with Nightmares (NFQ), mean (sd)	3.69 (1.68)	3.61 (1.70)
Weekly Number of Nightmares (NFQ), mean (sd)	5.49 (4.18)	5.44 (4.25)

Note. TBI = traumatic brain injury; NDQ = Nightmare Distress Questionnaire; NFQ = Nightmare Frequency Questionnaire; PSQI = Pittsburgh Sleep Quality Inventory.

Table 3.

Performance of the sample on the Penn Computerized Neurocognitive Battery (CNB).

	Raw Score M (SD)	Number Impaired (%) ^a
Penn Continuous Performance Test – Accuracy (%)	93.1% (0.1)	22 (23.4%)
Penn Letter N-Back Test – d'	3.7 (0.7)	15 (16.0%)
Penn Conditional Exclusion Test – Accuracy	2.0 (0.9)	7 (7.5%)
Penn List Learning Test – Total Correct, Trials 1-5	45.8 (12.3)	31 (33.0%)
Penn Visual Object Learning Test – Total Correct	15.7 (2.6)	11 (11.7%)
Penn Line Orientation Test – Total Correct	13.2 (4.3)	19 (20.2%)
Motor Praxis Test – Reaction Time, Correct Responses (ms)	849.9 (365.2)	17 (18.1%)

^a Impairment determined by performance 1.5 standard deviations below age-corrected normative data.

Table 4.

Analyses of the effects of verbal memory and working memory on changes in PTSD-associated sleep outcomes

	<i>Neurocognitive</i>				<i>Time</i>		<i>Time x Neurocognitive</i>	
	<i>Coeff.</i>	<i>SE</i>	<i>z</i>	<i>p</i>	<i>X²</i>	<i>p</i>	<i>X²</i>	<i>p</i>
Nightmare Distress								
PLLT Total (1-5)	-1.19	0.72	-1.65	0.10	59.1	<0.001	11.7	<0.001
LNB d-prime	0.12	0.82	0.15	0.88	56.0	<0.001	1.0	0.79
Number of Nightmares								
PLLT Total (1-5)	-0.14	0.08	-1.74	0.08	29.0	<0.001	8.0	0.005
LNB d-prime	-0.09	0.09	-0.96	0.34	28.3	<0.001	10.7	0.01
Sleep Disturbance								
PLLT Total (1-5)	-0.46	0.39	-1.17	0.24	129.6	<0.001	9.7	0.02
LNB d-prime	-0.15	0.45	-0.34	0.74	128.8	<0.001	3.0	0.39

Note. PLLT = Penn List Learning Test; LNB = Letter N-Back.

Figure 1. Verbal Immediate Memory Interacts with Time to Predict PTSD-Related Sleep and Nightmare Outcomes. (A) Total nightmare distress as measured by the nightmare distress questionnaire. (B) Nightmare frequency (number of nightmares per week) as measured by the Nightmare Frequency Questionnaire. (C) Total Sleep Disturbance as measured by the Pittsburgh Sleep Quality Inventory. Sleep and nightmare outcomes were measured at Baseline, End of Treatment, and 3-month and 6-month follow-up. Verbal immediate memory performance was divided into terciles to display interaction of cognitive performance and time. Data presented are estimated marginal means controlling for age and sex.

Figure(s)

A

B

C