CYBERPSYCHOLOGY, BEHAVIOR, AND SOCIAL NETWORKING
Volume X, Number X, 2014

DOI: 10.1089/cyber.2013.0383

ORIGINAL ARTICLE

Effect of Virtual Reality PTSD Treatment on Mood and Neurocognitive Outcomes

Robert McLay, MD, PhD,[1] Vasudha Ram, MPH,[2] Jennifer Murphy, PhD,[2] James Spira, PhD,[3] Dennis P. Wood, PhD,[4] Mark D. Wiederhold, MD, PhD,[4] Brenda K. Wiederhold, PhD, MBA[4] Scott Johnston, PhD,[2] and Dennis Reeves, PhD*

Abstract

Virtual reality (VR) is an emerging tool to help treat posttraumatic stress disorder (PTSD). Previously published studies have shown that VR graded exposure therapy (VR-GET) treatment can result in improvements in PTSD symptoms. Less is known about the impact on depression, general anxiety, and neuropsychological functioning in patients with PTSD. This study examined changes in self-reports of PTSD, depression, and anxiety before and after treatment, and also examined neuropsychological functioning as assessed by a computerized test of simple reaction time, procedural reaction time, and performance on the congruent, incongruent, emotional, and neutral (match the color of the ''nonsense word'') Stroop tests. Results showed that subjects treated with VR-GET showed significant reductions in PTSD and anxiety severity and significant improvements on the emotional Stroop test. Changes in depression and other measures of neuropsychological function were not significant. Change scores on the emotional Stroop test did not correlate with changes in self-report measures of PTSD. Overall, these findings support the use of VR-GET as a treatment for PTSD but indicate that benefits may be narrowly focused. Additional treatments may be needed after or alongside VR-GET for service members with neuropsychological impairments.

Introduction

SINCE SEPTEMBER 11, 2001, MORE THAN 2 million troops have been deployed to Iraq and Afghanistan.[1] Many have come back with what has been called one of the ''signature wounds'' of these conflicts—posttraumatic stress disorder (PTSD). Reports have varied in regard to the exact percentage of service members affected with PTSD,[2] but several studies have documented the severity of this problem.[3] The natural outcome of this condition varies according to a number of factors, including comorbidity.[4] Often co-occurring with PTSD are problems related to depression, generalized anxiety, and impairment in neuropsychological functioning.[5] The impairments in neuropsychological performance are often associated with a mild traumatic brain injury (mTBI), but can occur independently.[6]

Although many treatments exist for PTSD, one of the few that has so far been evaluated in active-duty service members is virtual reality graded exposure therapy (VR-GET). VR-GET is a form of exposure therapy in which a patient takes on fears related to his or her trauma in a controlled, simulated environment generated using virtual reality (VR). VR-GET differs somewhat from other forms of VR exposure therapy, such as that used previously for PTSD to treat Vietnam veterans.[7] Rather than adding VR to a traditional session of prolonged exposure,[8] VR-GET combines graded VR exposure with physiologic monitoring and skills training. This is designed to allow a participant to confront and tolerate simulated memories and fears more fully within the VR environment. One advantage to the VR-GET approach is that it may allow a patient who is unable to talk about a combat experience to learn skills that can be applied to a number of anxiety-provoking situations. In particular, patients are trained to recognize and control excessive autonomic arousal and cognitive reactivity. This is intended to allow them to confront difficult memories, intrusive thoughts, and feelings more fully during therapy, and to be more fully engaged in their daily activities. As with other approaches to exposure

[1]Directorate for Mental Health, Naval Medical Center San Diego, San Diego, California.
[2]Naval Center for Combat & Operational Stress Control, San Diego, California.
[3]National Centers for PTSD, Honolulu, Hawaii.
[4]Virtual Reality Medical Center, San Diego, California.
*Deceased.

therapy for PTSD,[9] VR-GET encourages engagement with, rather than avoidance of, trauma-related triggers. Previous studies suggest that VR-GET is a safe means of decreasing PTSD symptoms in individuals with PTSD related to service in Iraq or Afghanistan. This was demonstrated in a single-group pilot study[10] and in a small randomized controlled trial[11] in which PTSD symptoms decreased to a greater extent in VR-GET than in treatment as usual.

In evaluating any treatment for PTSD, it is important to understand not just the impact on the PTSD symptoms but also on other psychological comorbidities. Previous work has suggested that VR exposure therapy as a whole may have beneficial impacts on depression and generalized anxiety.[12] To our knowledge, however, there is no study to date regarding the efficacy of VR-GET on neuropsychological functions. Understanding if a treatment such as VR-GET can improve a wide variety of symptoms is important not just for the effectiveness of the treatment itself but also the extent to which commonly comorbid conditions reflect a similar, underlying pathology. Many symptoms such as alteration of mental status (e.g., being dazed or confused), changes in memory, concentration, and irritability that are usually attributed to mTBI can also be explained by psychological trauma.[13] By no means is this the only—or even the predominant—view.[14] If persistent postconcussive symptoms can be best explained by psychological trauma,[15,16] then presumably treatments that improve PTSD and depression should result in improvements in neurocognitive functioning as well.

In developing and testing VR-GET to treat PTSD, a portion of the participants in the open-label and randomized trial were evaluated for changes in comorbid psychopathology and neuropsychological functioning. Specifically, participants were assessed with self-report measures of depression and generalized anxiety, and were tested with a version of the software that the military routinely uses to screen for symptoms after mTBI. This is called the Automated Neuropsychological Assessment Metric (ANAM). We used a variant of this called the ANAM Readiness Evaluation System (ARES). ARES is a library of computerized tests and test batteries designed for a broad spectrum of research and clinical applications,[17] and can be run in a number of variations and on different computer platforms. In this case, participants were evaluated with a palm operating system (OS) hand-held computer, that is, a personal digital assistant (PDA) that assessed simple reaction time, reaction time when performing a procedural task, and performance on four versions of the Stroop test.[18,19] The intention of the neuropsychological testing provided by ARES is not to diagnose a particular pathology or dysfunctional region of the brain. Cognitive testing of the sort reported here is intended instead to demonstrate overall cognitive functioning in response to treatment.

In this study, the overall effectiveness of VR-GET was assessed. The primary outcome—the effect on PTSD—was previously published.[11] However, we also measured comorbidities, including depression, anxiety, and neuropsychological functioning. These conditions are often comorbid, and some have suggested that they all are part of a larger syndrome.[14] It would be expected that if PTSD, depression, anxiety, and cognitive symptoms are all expressions of the same underlying pathology, then a treatment that has been shown to improve PTSD would also result in improvements in all measures. Furthermore, it would be anticipated that the magnitude of symptoms and of improvements would be related. We set out to test this hypothesis in participants that had been treated for combat PTSD with VR-GET. Specifically, we first examined how severity of the various measures correlated with each other, looking at the situation both before and after treatment. We then examined if the scores for these measures of PTSD, depression, anxiety and neuropsychological function improved with treatment. Finally, we examined if the magnitude of the improvement was similar or different between the different measures.

Methods

Study participants

Participants were drawn from two previously described[10,11] trials of VR-GET for combat-related PTSD. Although a total of 28 subjects completed VR-GET, not all received neuropsychological testing. Participants were allowed to decline neuropsychological testing, and in some cases, the neuropsychological testing computer was not available. Only those who had completed neuropsychological testing and self-report measures of PTSD, depression, and generalized anxiety were included here ($n = 15$). Of note, this sample size was not determined by power analysis. Rather, the included population was a convenience sample taken from a study powered for the primary outcome—improvement in PTSD symptoms. Also, only subjects who participated in the active condition, and not controls, were included. There were no significant differences in demographics between those included here and the larger population who may have declined or not received the additional measures. All participants were active-duty service members with PTSD related to service in Iraq or Afghanistan. All the PTSD cases were chronic. Many had failed previous treatment, but due to difficulties in establishing the exact nature of the treatment received, we did not track the exact percentage who failed evidence-based intervention. Regardless of previous intervention, little spontaneous improvement would be expected in such chronic patients. In previous work, only one in nine of control subjects improved significantly with treatment as usual.[11] Presence or absence of mTBI was determined via the Defense Veterans Brain Injury Center mTBI screener.[20] Subjects were not selected or excluded based on diagnoses of depression, anxiety, or mTBI. Subjects were excluded if they were actively suicidal, homicidal, psychotic, or alcohol dependent without at least being in early remission. All participants gave written informed consent to treatment and assessment. Demographics concerning those participants are given in Table 1.

VR equipment

The VR hardware and software are described in detail elsewhere.[21] Briefly, the hardware consisted of two networked computers: one rendered the visual and auditory displays to the patient through VR goggles with built-in headphones, and a second system had a control panel and menu that the therapist used to add arousal elements into the VRGET environment (e.g., various combat events and

Table 1. Demographics and Baseline Neuropsychological Measures of the Study Sample ($N=15$)

Variable	*Min*	*Max*	*Average*
Age	25	49	34.07
Gender (% male)	n/a	n/a	93.3%
Branch (% in Navy)	n/a	n/a	100%
TBI (% positive)	n/a	n/a	40%
PCL-M (T1)	38	78	59.73
BAI (T1)	3	40	21.47
PHQ-9 (T1)	4	25	15.33
C-Stroop (T1)	0.01	0.07	0.0394
I-Stroop (T1)	0.01	0.05	0.0306
N-Stroop (T1)	0.01	0.06	0.0380
E-Stroop (T1)	0.01	0.05	0.0268
SRTT (T1)	0.02	0.08	0.0608
PRTT (T1)	0.03	0.06	0.0493

n/a, not applicable; TBI, traumatic brain injury; PCL-M, PTSD Checklist, Military version; T1, baseline scores; BAI, Beck Anxiety Inventory; PHQ-9, Patient Health Questionnaire; C-Stroop, the congruent Stroop; I-Stroop, incongruent Stroop; N-stroop, neutral Stroop; E-Stroop, emotional Stroop; SRTT, simple reaction time test; PRTT, procedural reaction time test.

combat background sounds, vehicle sounds, sounds of people conversing, etc.). A third computer was used to run the physiological monitoring (i.e., skin conductance, finger temperature, respiration rate, heart rate, and feedback system; J & J Engineering, Inc., Poulsho, WA). The computer graphic images and the spatial audio were computed in real time as the patient experienced and explored each environment. All environments were immersive (i.e., the patient experienced only the computer-generated audio and visual stimuli while ''real world stimuli'' were shut out). Therapist communications with the patient were via prearranged signals/hand pressure on the patient's left shoulder.

Treatment

Participants received VR-GET as previously described.[11] The therapy manual is available on the Web (www.navypsych.com). Briefly, treatment consisted of weekly to biweekly sessions with a psychologist. In the open-label, treatment development study, participants had a fixed number of sessions (5, 10, 15, or 20), whereas in the randomized trial, treatment time was fixed at 10 weeks, and VR-GET treatment stopped at the end of this period regardless of how many sessions had been completed. In the early sessions, participants were interviewed concerning the nature of their trauma, and were taught meditation and attention control techniques by the psychologist. Then they engaged in a VR simulation of Iraq or Afghanistan. Participants interacted with the VR environment using a head-mounted display that showed three-dimensional images of ''video game quality.'' During both the training and the exposure in the VR, the psychologist monitored the participants' ability to relax and engage using physiological monitoring. This monitoring included heart rate, breathing, skin conductance, skin temperature, and variables derived from these. The psychologist and participants collaborated to determine the day's content in the VR, and the psychologist controlled the content during the actual sessions. Typically, scenarios became gradually more challenging as therapy progressed, and in later sessions, participants were also encouraged to engage by talking about their trauma. At the end of each session, participants cognitively processed their experiences with the psychologist. Sessions typically lasted 90 minutes. Participants had to be stable on psychiatric medication prior to treatment, but medication changes were allowed during the protocol if the prescribing physician felt this was appropriate. Participants could continue group therapy while on VR-GET, but they were asked to give up other individual psychotherapy during treatment.

Measurement of improvement

All participants tested were given self-report questionnaires both before and after treatment with VR-GET.

PTSD symptom severity was measured using the PTSD Checklist, Military version (PCL-M). The PCL-M is a self-report scale in which a patient rates the severity of the 17 DSM-IV symptoms of PTSD on a scale from 1 = ''no symptoms'' to 5 = ''extreme problems'' over the past month. Scores on the PCL-M range from 17 to 85. It is a well-accepted measure of PTSD,[22] and correlates with other measures of PTSD such as the Clinician Administered PTSD Scale (CAPS).[11]

The Patient Health Questionnaire (PHQ-9) was used as the measure of depressive symptoms. The PHQ-9 is a self-report measure asking frequency of symptoms corresponding to the nine DSM-IV symptoms for major depressive disorder over the past 2 weeks. The PHQ-9 is part of the Primary Care Evaluation of Mental Disorders (PRIME-MD) and has been well validated in assessing depressive symptoms.[23]

The Beck Anxiety Inventory (BAI) was used as the measure of anxiety and to quantify anxiety symptoms. The BAI is a well-validated, extensively used,[24] self-report measure developed to assess anxiety symptoms as separate from those of depression.[25]

Neuropsychological function was assessed using ARES. ARES is a cognitive testing system designed for operation on a hand-held Palm OS.[18] ARES is designed for assessment of injuries, such as concussion due to blast exposure. This battery includes simple reaction time test (SRTT), procedural reaction time test (PRTT), and four versions of the Stroop test: the congruent Stroop (C-Stroop), incongruent Stroop (I-Stroop), neutral Stroop (N-stroop), and emotional Stroop (E-Stroop). SRTT presents a simple stimulus on the screen (e.g., an asterisk), which prompts the participant to tap the screen as quickly as possible. This test provides a measure of pure reaction time and to partial out the effects of motor response speed from actual cognitive processing time. PRTT presents the numbers 2, 3, 4, or 5 rapidly on the screen. When the 2 or 3 appears, the subjects taps on a block labeled 2, 3. The subject is instructed to tap on the block that is labeled 4, 5 when the 4 or 5 is flashed on the screen. This test is forced paced. It is a good measure of mental flexibility and sustained concentration, and as a whole is considered a cognitive vigilance task. It is reasonably sensitive to mTBI.[26] There are previously established norms for both SRTT and PRTT in military populations.[16] The Stroop test is a well-studied measure that tests the ability to identify the color of different words. In the C-Stroop, the word and the color of the word are the same, for example the word red in the color

Table 2. Correlation Coefficients (*R*) Between Severity of PTSD, Anxiety, Depression, and Measures of Neuropsychological Function Before Treatment

	PCL-M (T1)	*BAI (T1)*	*PHQ (T1)*	*C-Stroop (T1)*	*I-Stroop (T1)*	*N-Stroop (T1)*	*E-Stroop (T1)*	*SRTT (T1)*	*PRTT (T1)*
PCL-M	1	0.432	0.410	−0.379	−0.104	−0.288	−0.516*	−0.218	−0.183
BAI		1	0.634*	−0.182	−0.005	−0.152	−0.343	0.253	0.006
PHQ			1	−0.552*	−0.323	−0.431	−0.487	−0.072	−0.407

*Correlation significant ($\alpha = 0.05$; two-tailed).

red. In the I-Stroop, the color and the word are different, for example the word red colored in green. Correctly identifying a color in the C-Stroop is helped by both color identification and reading ability, whereas performance in the I-Stroop requires not just the ability to recognize the pigment but also the ability to suppress the textual information. The C-Stroop and I-Stroop tests are sensitive for neuropsychological impairment, particularly in areas of attention, language, sensorimotor function, and executive function.[27,28] Functional imaging studies have indicated that anterior cingulate cortex and dorsolateral prefrontal cortex are involved in responding to these tasks. More recently, another variation of the Stroop test has been developed that helps identify PTSD—the E-stroop. The E-Stroop uses emotionally charged words (e.g., ''IED'') that is relevant to a particular type of trauma, in this case, war in Iraq or Afghanistan. For an individual with PTSD, the emotional nature of the word causes a distraction that may result in a slower reaction time or an error in identifying the color of the word. The E-Stroop has been shown to correlate with PTSD Symptoms[29] but has not previously been used as an outcome measure when measuring improvement in PTSD. In the N-stroop, the participant matches the color of the letters of the words without emotional valence (e.g., ''morp''). This tests the ability to recognize the color of the word.

In these neuropsychological tests, impairment can manifest either in a delayed reaction time to complete the task or in an error in response. To simplify scoring, both aspects are gathered together by computing ''throughput,'' which measures correct responses per median correct response time. Higher throughputs indicate better (less impaired) performance.

Data analysis

Data were gathered from a database, and descriptive statistics were calculated. Using SPSS v18 (SPSS, Inc., Chicago, IL), paired pre/post *t* test analysis was done to find out which of the measures improved with VR-GET treatment. Relationship between the measures at baseline (before VR-GET) and at postassessment (after VR-GET), as well as a change score (before VR-GET minus after VR-GET treatment), was done using bivariate Pearson correlation. Scores are reported before treatment (T1) and after treatment (T2). Also, change scores (T1 minus T2) are reported.

Results

Demographics and baseline scores of the study sample

Demographics and baseline neuropsychological functioning of the study sample measured as ''throughput'' scores and baseline PCL-M, BAI, and PHQ-9 are given in Table 1. As would be expected for a sample seeking treatment for PTSD, participants exhibited severe symptoms of PTSD as assessed by the PCL-M. Also present, on average, were moderately severe symptoms of depression as assessed by the PHQ-9 and moderate symptoms of anxiety as assessed by the BAI. Normative values are not established for the Stroop tests, thus it is not possible to analyze whether these baseline scores showed impairment.

Relationships between measures before treatment

Correlation coefficients between the variables measured at baseline are given in Table 2. Significant correlations are flagged with an asterisk. Severity of PTSD was not significantly correlated with either severity of depression ($p = 0.129$) or severity of anxiety ($p = 0.108$). This lack of significance is most likely due to small sample size. PTSD symptom severity was significantly ($p = 0.049$) correlated with throughput on the E-Stroop test, but was not significantly ($p > 0.05$) correlated with throughput for SRTT, PRTT, the C-Stroop, the I-Stroop, or the N-Stroop tests. Generalized anxiety severity scores were not significantly correlated with any of the neuropsychological measures. Depression scores were significantly correlated with anxiety scores ($p = 0.011$). Also, depression severity was significantly

Table 3. Correlation Coefficients (*R*) Between Severity of PTSD, Anxiety, Depression, and Measures of Neuropsychological Function After Treatment

	PCL-M (T2)	*BAI (T2)*	*PHQ-9 (T2)*	*C-Stroop (T2)*	*I-Stroop (T2)*	*N-Stroop (T2)*	*E-Stroop (T2)*	*SRTT (T2)*	*PRTT (T2)*
PCL-M (T2)	1	0.500	0.341	−0.529*	−0.452	−0.594*	−0.742**	−0.278	−0.332
BAI (T2)		1	0.391	0.139	−0.125	−0.194	−0.403	−0.178	−0.040
PHQ (T2)			1	−0.449	−0.348	−0.326	−0.405	−0.190	−0.408

T2, scores after treatment with VR-GET.
*Correlation significant ($\alpha = 0.05$; two-tailed); **correlation significant ($\alpha = 0.01$; two-tailed).

Table 4. Scores Before and After Treatment with VR-GET

	Pretreatment (SD)	*Post-treatment* (SD)	t	p
PCL-M	59.73 (12.753)	45.40 (14.574)	4.401	0.001*
BAI	21.47 (10.176)	14.67 (8.958)	2.238	0.042*
PHQ-9	15.33 (5.576)	12.60 (5.962)	1.543	0.145
C-Stroop	0.0394 (0.0128)	0.0404 (0.0108)	−0.613	0.550
I-Stroop	0.0306 (0.1181)	0.0334 (0.0111)	−1.840	0.087
N-Stroop	0.0380 (0.0119)	0.0364 (0.0127)	1.020	0.325
E-Stroop	0.0268 (0.0115)	0.0309 (0.0126)	−2.185	0.046*
SRTT	0.0608 (0.0178)	0.0609 (0.0154)	−0.025	0.981
PRTT	0.0493 (0.0095)	0.0497 (0.0117)	−0.246	0.809

*Difference significant ($\alpha = 0.05$; two-tailed); PCL-M, BAI, and PHQ-9 are scores. Stroop, SRTT, and PRTT are throughputs.

correlated with throughput on the C-Stroop ($p = 0.033$), but was not significantly ($p > 0.05$) correlated with any other neuropsychological measures.

Relationships between measures after treatment

Correlation coefficients between the variables measured after treatment is given in Table 3. Significant correlations are flagged with an asterisk. Severity of PTSD did not significantly correlate with severity of depression, and approached, but did not reach, significance for correlation with anxiety symptoms ($p = 0.058$). The severity of residual PTSD symptom severity was significantly correlated with throughput on the C-Stroop test ($p = 0.043$), the N-Stroop test ($p = 0.019$), and the E-Stroop test ($p = 0.002$). The correlation between residual PTSD symptom severity and the I-Stroop test maintained a trend but did not reach significance ($p = 0.091$). Generalized anxiety severity scores were not significantly correlated with any of the neuropsychological measures. Depression scores were not significantly correlated with any of the neuropsychological measures. In short, residual PTSD symptoms correlated with a broader range of neuropsychological function, compared to pretreatment scores, when PTSD was only significantly correlated with the E-Stroop.

Changes in symptoms with treatment

Pretreatment scores, post-treatment scores, and significance of change, as assessed by paired *t* tests, are given in Table 4. As shown, treatment via VR-GET was associated with significant improvements in PTSD and anxiety but not in depression. The only measure of neuropsychological function that improved significantly with treatment was performance on the E-Stroop, which is itself presumably a reflection of PTSD severity.

Relationships between magnitude of change on various measures

The relationships between the change in scores (score at T1 minus the score at T2) are shown in Table 5. This correlation was examined to help determine if all aspects of psychiatric function improved similarly in treatment, or if improvements in one area were unrelated to improvements in another. The correlation coefficients between the change scores are also given in Table 5. The change in the number of points decreased on the PTSD scale was significantly ($p = 0.039$) related to the change in the decrease on the scales for anxiety ($p = 0.04$) and the scale for depression ($p = 0.013$), but was not significantly related to the change in any measure of neuropsychological function, including the E-Stroop test. Similarly, change in anxiety did not correlate significantly ($p > 0.05$) with the change in any neuropsychological measure. The change score for depression was significantly related to change score for anxiety ($p = 0.003$) and change score for PTSD ($p = 0.013$). However, change in depression did not correlate significantly ($p > 0.05$) with the change in any neuropsychological measure.

Discussion

This study examined changes in comorbid anxiety, depression, and neuropsychological functioning in individuals who were treated for combat-related PTSD with VR-GET. It also investigated the relationship between those comorbidities, and if a treatment aimed at PTSD would result in improvements in all conditions. The overall question as to if all these conditions do really represent a unitary syndrome is an extensive topic, covered elsewhere,[30] and beyond the scope of this paper. However, in general, the idea that all conditions respond to the same intervention would support the hypothesis of a unitary syndrome, whereas divergent responses would argue that different conditions are simply comorbid.

Of the 28 subjects who completed the active condition, VR-GET, only 15 received neuropsychological testing because the computer was not available, or the participants

Table 5. Correlation Coefficients (*R*) Between Change in Severity of PTSD, Anxiety, Depression, and Change in Measures of Neuropsychological Function Over the Course of Treatment

	PCL-M (T1 − T2)	*BAI (T1 − T2)*	*PHQ-9 (T1 − T2)*	*C-Stroop (T1 − T2)*	*I-Stroop (T1 − T2)*	*N-Stroop (T1 − T2)*	*E-Stroop (T1 − T2)*	*SRTT (T1 − T2)*	*PRTT (T1 − T2)*
PCL-M (T1–T2)	1	0.538*	0.626*	−0.154	0.100	−0.015	−0.234	−0.081	0.319
BAI (T1 − T2)		1	0.716**	−0.182	0.396	0.169	−0.192	0.178	0.209
PHQ-9 (T1 − T2)			1	−0.113	0.419	0.132	−0.169	0.256	0.437

T1, baseline scores; T2, scores after treatment.
*Correlation significant ($\alpha = 0.05$; two-tailed); **correlation significant ($\alpha = 0.01$; two-tailed).

declined testing or did not fill in the assessment questionnaires. There were no significant differences in demographics between those included here and those who may have declined the testing or additional measures. Our sample represents a treatment seeking population with chronic PTSD, and who are possibly resistant to standard PTSD treatment.

The sample population had significant problems with anxiety, depression, slow reaction times, and slow cognitive processing. The impairments in reaction time and cognitive processing could not be attributed to mTBI alone, since only six subjects reported having had a prior mTBI. However, prior to treatment, the severity of impairment in reaction time also did not correlate significantly with the severity of PTSD, anxiety, or depression. The relationship between PTSD severity and neuropsychological impairment could only be detected in the emotional Stroop test, which is a measure specifically designed to distract individuals with words related to their PTSD.[31–33] After treatment, the relationship between remaining PTSD symptoms was significantly correlated with a broader array of neuropsychological impairment, specifically with performance on the neutral and congruent Stroop tests. One possible explanation is that residual symptoms might indicate a broader category of neuropsychological impairment that is unrelated to PTSD. Alternately, our sample size may have been too small to detect relationships between PTSD and a broad range of neuropsychological impairment consistently.

As was previously shown using different measures of PTSD symptom severity,[11] treatment with VR-GET was associated with a significant reduction in PTSD severity. Although the sample studied here did not include a control group, previous studies have suggested that this improvement is greater than seen in those receiving usual treatment and, at a minimum, does not just reflect a placebo effect or the passage of time.[11] With the addition of these results, we now have three different measures of PTSD, including clinician-administered scales (CAPS),[34] self-report measures (the PCL-M), and a relatively specific neuropsychological measures (the E-Stroop test), all of which show that VR-GET improves PTSD.

Treatment with VR-GET was also associated with significant reductions in anxiety severity, with the magnitude of the improvement in anxiety significantly correlated with the improvement in self-reported symptoms of PTSD. Interestingly, however, the magnitude of the improvement in self-reported PTSD symptoms did not correlate with the magnitude of improvement on the E-Stroop test. The most likely explanation for this is that our sample size was too small to detect such correlations. It is also possible that the E-Stroop test is measuring some aspect of PTSD that is somehow different from what is picked up in self-report measures of PTSD or anxiety. Other studies have suggested that self-report scales may undervalue the magnitude of improvement with treatment.[35] This study does not specifically support or refute that finding, but it does support the idea that different measures of PTSD that correlate well at baseline may potentially show different degrees of improvement.

Although symptoms of PTSD improved with VR-GET treatment, symptoms of depression, simple reaction times, procedural reaction times, and non-PTSD-specific versions of the Stroop test did not. Use of other therapies has been associated with more broad-based improvements. For example, selective serotonin reuptake inhibitors have been used to treat PTSD,[36] depression,[37] and generalized anxiety,[38] and have been reported to have some effectiveness in treating mTBI.[39] Even other VR therapies have been shown to improve depression along with PTSD and anxiety.[12] This has led many to believe that these supposedly separate conditions are all really part of a singular, underlying syndrome.[40]

The fact that the treatment improvements observed here were specific to PTSD and anxiety argues that there is some validity to the idea of classifying PTSD as something other than just a part of a larger spectrum of psychological impairment. This does not mean that there is no relationship between PTSD and other areas of neuropsychological function, or even that VR-GET has no utility in treating other symptoms. Larger studies will be needed to determine if the treatment modality has efficacy in other areas. It does indicate, however, that some treatments, such as VR-GET, may be better for specifically treating PTSD. A one-size fits-all approach to treating those with combat-related psychological issues is not likely to be successful, but rather specific treatments will likely be needed that match an individual's specific problems.

Acknowledgments

The authors wish to thank Margery Farnsworth for editorial assistance. Portions of this paper were previously presented as an abstract and poster at the American Psychological Association Annual Convention, August 2–5, 2012, Orlando, FL.

Author Disclosure Statement

Drs. Mark and Brenda Wiederhold are part owners of, and Drs. Wood, Webb-Murphy, and Spira have previously been employed by, the Virtual Reality Medical Center, which develops and sells the Virtual Reality System described in this work. Dr. Reeves is the developer of the Automated Neuropsychological Assessment Metrics (ANAM), and its variant, the ANAM Readiness Evaluation System (ARES). Funding for this study was provided by Office of Naval Research.

The views expressed in this article are those of the authors and do not necessarily reflect the opinions of The Navy, The Department of Defense, or any other governmental agency.

References

1. Strengthening our military families: meeting America's commitment. www.defense.gov/home/features/2011/0111_initiative/strengthening_our_military_january_2011.pdf (accessed Nov. 6, 2011).
2. Sundin J, Fear NT, Iversen A, et al. PTSD after deployment to Iraq: conflicting rates, conflicting claims. Psychological Medicine 2010; 40:367–382.
3. Tanielian T, Jaycox LH. (2008) *Invisible wounds of war: psychological and cognitive injuries, their consequences, and services to assist recovery.* Oxford University Press, Santa Monica, CA, Rand Corporation Monographs.
4. Hoge CW, Castro CA, Messer SC, et al. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. New England Journal of Medicine 2004; 351: 13–22.

5. Barrett DH, Green ML, Morris R, et al. Cognitive functioning and posttraumatic stress disorder. American Journal of Psychiatry 1996; 153:1492–1494.
6. Vincent AS, Roebuck-Spencer T, Lopez MS, et al. Effects of military deployment on cognitive functioning. Military Medicine 2012; 177:248–255.
7. Rothbaum BO, Hodges LF, Ready D, et al. Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. Journal of Clinical Psychiatry 2001; 62: 617–622.
8. Foa EB. Prolonged exposure therapy: past, present, and future. Depression and Anxiety 2011; 28:1043–1047.
9. Foa EB, Hembree E, Rothbaum BO. (2007) *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences therapist guide*. Oxford: Oxford University Press.
10. Wood DP, Webb-Murphy J, McLay RN, et al. Reality graded exposure therapy with physiological monitoring for the treatment of combat related post traumatic stress disorder: a pilot study. Studies in Health Technology & Informatica 2011; 163:696–702.
11. McLay RN, Wood DP, Webb-Murphy JA, et al. A randomized, controlled trial of virtual reality-graded exposure therapy for post-traumatic stress disorder in active duty service members with combat-related post-traumatic stress disorder. CyberPsychology, Behavior, & Social Networking 2011; 14:223–229.
12. Rizzo AA, Difede J, Rothbaum BO, et al. VR PTSD exposure therapy results with active duty OIF/OEF combatants. Studies in Health Technology & Informatics 2009; 142:277–282.
13. Hoge CW, McGurk D, Thomas JL, et al. Mild traumatic brain injury in U.S. Soldiers returning from Iraq. New Englang Journal of Medicine 2008; 358:453–463.
14. Vasterling JJ, Brailey K, Constans JI, et al. Attention and memory dysfunction in posttraumatic stress disorder. Neuropsychology 1998; 12:125–133.
15. Reeves DL, Bleiberg J, Roebuck-Spencer T, et al. Reference values for performance on the Automated Neuropsychological Assessment Metrics V3.0 in an active duty military sample. Military Medicine 2006; 171:982–994.
16. Hoge CW, Goldberg HM, Castro CA. Care of war veterans with mild traumatic brain injury—flawed perspectives. New England Journal of Medicine 2009; 360:1588–1591.
17. Kane RL, Roebuck-Spencer T, Short P, et al. Identifying and monitoring cognitive deficits in clinical populations using Automated Neuropsychological Assessment Metrics (ANAM) tests. Arch Clin Neuropsychol. 2007;22 Suppl 1:S115-126.
18. Elsmore TF, Reeves DL, Reeves AN. The ARES test system for palm OS handheld computers. Archives of Clinical Neuropsychology 2007; 22:S135–144.
19. Reeves DL, Winter KP, Bleiberg J, et al. ANAM genogram: historical perspectives, description, and current endeavors. Archives of Clinical Neuropsychology 2007; 22: S15–37.
20. Schwab K, Baker G, Ivins B, et al. (2006) The Brief Traumatic Brain Injury Screen (BTBIS): investigating the validity of a self-report instrument for detecting traumatic brain injury (TBI) in troops returning from deployment in Afghanistan and Iraq. Neurology 2006; 66(Supp. 2):A235.
21. Wood DP, Murphy J, Center K, et al. Combat-related posttraumatic stress disorder: a case report using virtual reality exposure therapy with physiological monitoring. CyberPsychology & Behavior 2007; 10:309–315.
22. Weathers FW, Litz BT, Herman DS, et al. (1993) The PTSD Checklist (PCL): reliability, validity, and diagnostic utility. Annual Meeting of International Society for Traumatic Stress Studies, San Antonio, TX.
23. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. Journal of the American Medical Association 1999; 282:1737–1744.
24. Beck AT, Epstein N, Brown G, et al. An inventory for measuring clinical anxiety: psychometric properties. Journal of Consulting & Clinical Psychology 1988; 56:893–897.
25. Enns MW, Cox BJ, Parker JD, et al. Confirmatory factor analysis of the Beck Anxiety and Depression Inventories in patients with major depression. Journal of Affective Disorders 1998; 47:195–200.
26. Levinson DM, Reeves DL. Monitoring recovery from traumatic brain injury using automated neuropsychological assessment metrics (ANAM V1.0). Archives of Clinical Neuropsychology 1997; 12:155–166.
27. Ben-David BM, Nguyen LL, van Lieshout PH. Stroop effects in persons with traumatic brain injury: selective attention, speed of processing, or color-naming? A meta-analysis. Journal of the International Neuropsychological Society 2011; 17:354–363.
28. Bryan C, Hernandez AM. Magnitudes of decline on Automated Neuropsychological Assessment Metrics subtest scores relative to predeployment baseline performance among service members evaluated for traumatic brain injury in Iraq. Journal of Head Trauma Rehabilitation 2012; 27:45–54.
29. Cisler JM, Wolitzky-Taylor KB, Adams TG Jr, et al. The emotional Stroop task and posttraumatic stress disorder: a meta-analysis. Clinical Psychology Review 2011; 31:817–828.
30. Kennedy JE, Jaffee MS, Leskin GA, et al. Posttraumatic stress disorder and posttraumatic stress disorder-like symptoms and mild traumatic brain injury. Journal of Rehabilitation Research & Development 2007; 44:895–920.
31. Williams JM, Mathews A, MacLeod C. The emotional Stroop task and psychopathology. Psychological Bulletin 1996; 120:3–24.
32. Buckley TC, Blanchard EB, Neill WT. Information processing and PTSD: a review of the empirical literature. Clinical Psychology Review 2000; 20:1041–1065.
33. McNally RJ, Kaspi SP, Riemann BC, et al. Selective processing of threat cues in posttraumatic stress disorder. Journal of Abnormal Psychology 1990; 99:398–402.
34. Weathers FW, Keane TM, Davidson JR. Clinician-administered PTSD scale: a review of the first ten years of research. Depression & Anxiety 2001; 13:132–156.
35. Forbes D, Creamer M, Biddle D. The validity of the PTSD checklist as a measure of symptomatic change in combat-related PTSD. Behavior Research & Therapy 2001; 39: 977–986.
36. Stein DJ, Ipser J, McAnda N. Pharmacotherapy of posttraumatic stress disorder: a review of meta-analyses and treatment guidelines. CNS Spectrums 2009; 14:25–31.
37. Naudet F, Maria AS, Falissard B. Antidepressant response in major depressive disorder: a meta-regression comparison of randomized controlled trials and observational studies. PLoS One 2011; 6:e20811.

38. Baldwin DS, Ajel KI, Garner M. Pharmacological treatment of generalized anxiety disorder. Current Topics in Behavioral Neurosciences 2010; 2:453–467.
39. Fann JR, Hart T, Schomer KG. Treatment for depression after traumatic brain injury: a systematic review. Journal of Neurotrauma 2009; 26:2383–2402.
40. Miller MW, Wolf EJ, Harrington KM, et al. An evaluation of competing models for the structure of PTSD symptoms using external measures of comorbidity. Journal of Traumatic Stress 2010; 23:631–638.

Address correspondence to:
Dr. Robert McLay
Naval Medical Center San Diego
Directorate for Mental Health
34800 Bob Wilson Drive
San Diego, CA 92134

E-mail: Robert.McLay@med.navy.mil