

Factors Impacting Functional Status in Veterans of Recent Conflicts With PTSD

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Veterans with posttraumatic stress disorder (PTSD) underwent a systematic evaluation to determine which factors were associated with the degree of functional status. Demographic information, self-report scales, and symptom ratings performed by trained evaluators were investigated in multiple regression models to determine their contribution to functional status. Ninety-six participants were included in the model assessing degree of functional status. Depressive symptoms, a depressive disorder diagnosis, and to a lesser extent, the Clinician-Administered PTSD Scale were selected in the final model that best predicted the degree of functional status. Depressive symptoms significantly affect the function of veterans with PTSD.

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Posttraumatic stress disorder (PTSD) is a major military and civilian public health problem. The National Comorbidity Survey reported a lifetime prevalence rate of 7.8% for PTSD in a national sample.^{1,2} The National Vietnam Veterans Readjustment study reported that 31% of male veterans and 27% of female veterans met full criteria for a DSM-IV-TR diagnosis of PTSD during their lifetime (N=3,016), and 15% of men and 9% of women met full criteria for PTSD at the time of the study.³ With respect to veterans who were deployed to Iraq or Afghanistan, 15.6%–17.1% of those who deployed to Iraq met screening criteria for PTSD, major depression, or general anxiety disorder upon return, whereas 11.2% of those deployed to Afghanistan screened positively for one of these three diagnoses upon return.⁴

In addition to being a common sequela of deployment to combat regions, PTSD often results in significant distress⁵ and functional impairment.⁶ These functional impairments can result in difficulty with employment,⁷ family disruption,⁸ maintaining housing,⁹ and poor quality of life.^{10,11} Given the severity of functional impairment, more work is required to better understand which factors are most closely associated with functional impairment. For the purpose of our study, we defined functional impairment as difficulties with family relationships, work, friendships and socialization, parenting, education, self-care, and romantic relationships with a spouse or partner.⁶ Although considerable work has been done in identifying predictors of PTSD symptoms^{12–14} and treatment outcomes,¹⁵ less work has focused on predictors of function in patients with PTSD.

This analysis was performed using the baseline data of treatment-seeking participants enrolled in a randomized

controlled trial of repetitive transcranial magnetic stimulation (rTMS) to augment cognitive processing therapy (CPT) in veterans with PTSD. Evaluations of function and symptoms were performed at baseline for participants that qualified for the study. This trial recruited veterans who had served in Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) and were suffering from PTSD symptoms as a result. All participants received CPT,¹⁶ an evidence-based psychotherapy treatment for PTSD. The trial tested whether adding rTMS just before CPT significantly augmented the response to CPT. The veterans could choose to have a brief summary of their evaluation and outcome scores sent to their primary provider if they desired, but study data were independent of Veterans Affairs and disability determination. Because this was a unique data set of veterans, we used the baseline evaluation to test for which factors were most strongly associated with functional status. The hypothesis was that specific clinical or demographic factors would predict the degree of functional impairment in veterans with PTSD.

METHODS

Participants

As part of a Department of Defense-funded study for assessing rTMS augmentation of CPT for PTSD, veterans from OEF, OIF, and OND with current symptoms of PTSD were recruited from the community to participate in the clinical trial (ClinicalTrials.gov NCT01391832). Briefly, the clinical trial involved random selection of veterans with PTSD to active versus sham 1-Hz rTMS to the right

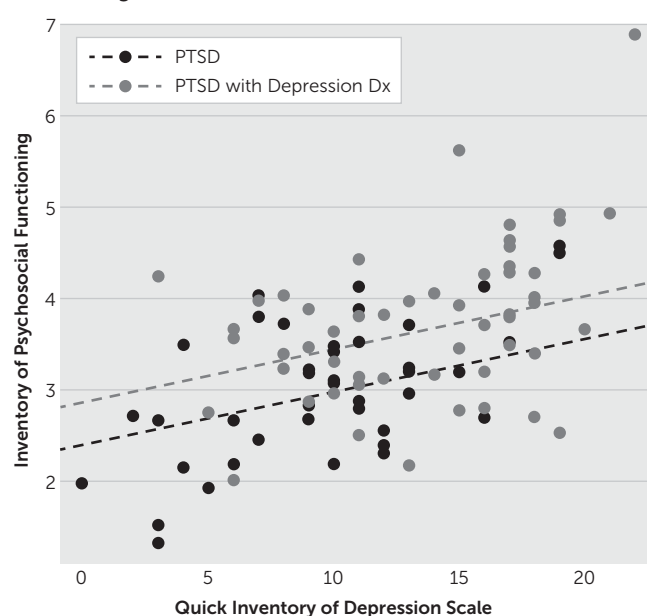
TABLE 1. Demographics^a

Demographic	Value
Age, years	31.66±6.54 (21–51)
Education, years	14.49±2.16 (12–20)
Years of active duty	6.16±4.28 (0.50–24.71)
Gender	
Male	88
Female	8
Race	
Caucasian	59
Hispanic	17
Other	20
Clinical	
Inventory of Psychosocial Functioning	3.424±0.88 (1.32–6.89)
Clinician-Administered PTSD Scale	74.78±21.98 (25–123)
Quick Inventory of Depression Scale	11.80±4.92 (0–22)
Full Combat Exposure Scale	20.73±7.58 (5.0–33.0)
Adverse Childhood Experiences	2.79±2.40 (0–9)
Mood disorder diagnosis	
Major depressive disorder	54 (56%)
Depressive disorder NOS	2 (2%)
Dysthymic	15 (15%)
Anxiety disorder diagnosis	
Generalized anxiety disorder	6 (6%)
Panic disorder with agoraphobia	2 (2%)
Panic disorder without agoraphobia	1 (1%)
TBI	
No TBI	30 (31%)
TBI with no LOC or symptoms lasting >15 minutes	17 (18%)
TBI with no LOC but symptoms lasting >15 minutes	7 (7%)
TBI with LOC	42 (44%)

^a Data are presented as mean±SD (range) or N (%). LOC, loss of consciousness; TBI, traumatic brain injury.

prefrontal cortex just before CPT to determine whether rTMS could augment the treatment effect of CPT. In addition, before treatment, as well as when treatments were completed, participants underwent magnetic resonance neuroimaging and EEG evaluations. Participants were recruited from the community, focusing on military installations, Veteran Affairs hospitals, veteran centers, local universities and colleges with veteran enrollment, and various nonprofit veteran-associated service organizations. Interested participants contacted the study team and were interviewed by telephone. Study coordinators provided information to the veteran and performed a brief screen of eligibility. Those who were interested in participating and met basic qualifications were brought in for a formal evaluation. The data for this study were acquired from February 2012 to February 2015.

Before any procedures or evaluation at the first visit, the study was reviewed with the participants in detail and all questions were answered. Written informed consent was obtained from all participants. This study was approved by the institutional review boards (IRBs) of the University of Texas Southwestern Medical Center (IRB of record) and

FIGURE 1. Relationship Between Depressive Symptoms and Functioning in Veterans With PTSD

the University of Texas at Dallas, as well as the Army Human Research Protection Office. Participants included male and female veterans of OIF/OEF/OND between 18 and 60 years old who had a current diagnosis of combat-related PTSD. Participants were recruited, screened, and included in the study in an unbiased fashion with regard to race, ethnicity, or gender. The data from the initial visit were used in this analysis to assess factors associated with functional status. Participants were permitted to continue their medications, including psychiatric medications, unless contraindicated for safety reasons. Veterans were excluded for a history of the psychiatric comorbidities of eating disorders, psychotic symptoms, and current (<3 months) substance dependence, primarily for concerns of potentially confounding the results. Other exclusionary conditions for primarily safety reasons included a history of a significant neurological/medical disorder (including seizure), traumatic brain injury (TBI) (moderate or severe), brain tumors, stroke, blood vessel abnormalities in the brain, dementia, Parkinson's disease, Huntington's chorea, multiple sclerosis, cardiac pacemaker, implanted medication pumps of any sort that would increase the risk for rTMS, history of significant heart disease (e.g., history of myocardial infarction, tachyarrhythmia, congestive heart failure, or valvular disease), or any metal objects in or near the head (most dental work was permitted) that could not be safely removed for TMS treatments. TBI was screened by both history and review for significant lesions indicative of TBI on the participant's structural MRI scan obtained during the neuroimaging session. Veterans with greater than mild TBI (i.e., loss of consciousness >30 minutes, posttraumatic amnesia >1 day, penetrating trauma, or evidence of structural injury on MRI) were excluded. Women who were pregnant or breastfeeding

TABLE 2. Backward/Forward Stepwise Variable Selection for Predicting Degree of Functional Disability (IPF) Based on the BIC^a

Initial Steps 1–13				Final Steps 200–215			
Variable	Addition (+)/ Removal (–)	df	BIC	Variable	Addition (+)/ Removal (–)	df	BIC
Race	–	6	0.55	None			–55.34
TBI	–	3	12.59	CAPS	–	1	–55.25
Number of times deployed	–	1	21.57	Substance use	+	1	–53.08
Total years of active duty	–	1	21.65	CBE	+	1	–52.56
Age	–	1	21.77	DepDx:CAPS	+	1	–52.09
ACE:DepDx	–	1	21.93	ACE	+	1	–51.92
DepDx:FCE	–	1	22.69	DepDx	–	1	–51.74
CBE	–	1	22.91	QIDS	–	1	–51.42
DepDx:QIDS	–	1	22.99	Gender	+	1	–51.21
Gender	–	1	23.07	FCE	+	1	–51.13
Substance use	–	1	23.54	Number of times deployed	+	1	–51.11
None	–		26.08	Age	+	1	–50.94
DepDx:CAPS	–	1	26.27	Total years of active duty	+	1	–50.86
				DepDx:QIDS	+	1	–50.83
				TBI	+	3	–42.69
				Race	+	6	–30.79

^a Variable candidates were as follows: TBI, substance use, combat-related traumatic events, age, gender, race, number of times deployed, total years of active duty, adverse childhood experiences, depressive disorder diagnosis, FCE score, QIDS score, CAPS score, and interactions of each quantitative predictor with each of gender, race, and depressive disorder diagnosis. ACE, Adverse Childhood Experiences Questionnaire; BIC, Bayesian information criterion; CAPS, Clinician-Administered PTSD Scale; CBE, combat-related traumatic event; DepDx, Depressive Disorder Diagnosis; FCE, Full Combat Exposure Scale; IPF, Inventory of Psychosocial Functioning; QIDS, Quick Inventory of Depressive Symptomatology–Self-Report; TBI, traumatic brain injury.

were excluded. Non-English speakers were also excluded because some of the screening forms, questionnaires, and tests were only available in English. Veterans were also excluded if they were unable or unwilling to stop taking a prescription medication or illegal substances that significantly lowered the seizure threshold. Participants could not start any new psychological treatment for PTSD while being in the study.

Procedures

At the initial visit, participants provided baseline data, including filling out forms and being clinically evaluated by trained evaluators. Veterans also provided a urine sample for drug testing and pregnancy testing if applicable. If the participant was fatigued by the evaluation, he or she could finish the evaluation on a subsequent day.

Self-administered scales and information obtained were as follows. Demographic information including age, gender, race, education in years, and years of active duty was obtained. Participants filled out the following questionnaires: Transcranial Magnetic Stimulation Adult Safety Screen (TASS),¹⁷ MRI Safety Screening Form, Inventory of Psychosocial Functioning (IPF),⁶ Quick Inventory of Depressive Symptomatology–Self-Report (QIDS),¹⁸ Full Combat Exposure Scale (FCES),⁴ and Adverse Childhood Experience Questionnaire (ACE).¹⁹ The TASS and MRI Safety Screening Form were administered to ensure the

patient's safety in undergoing TMS and MRI, respectively. The QIDS assessed the severity of depressive symptoms using a 0–3 scale on each of the 16 items. Higher scores indicated greater endorsement of depressive symptoms. The ACE score consisted of 10 questions utilized to assess the participant's degree of exposure to different categories of trauma during the first 18 years of life. Higher scores indicated greater exposure. The FCES consisted of 34 questions to measure the participant's degree of exposure to combat-related traumatic events with higher scores indicating greater exposure. The IPF, an 80-item self-report measure that assessed functional impairment experienced by active-duty service members and veterans during the past 30 days, was scored on a 7-point scale ranging from 1 (“never”)

to 7 (“always”). The IPF provided a total score for each of seven subscales (romantic relationships with a spouse or partner, family relationships, work, friendships and socializing, parenting, education, and self-care functioning), and an overall functional impairment score was computed by calculating the mean of the scores for each completed (i.e., applicable) subscale. Thus, the IPF measures broad areas of functioning, including social and occupational functioning, in addition to self-care. Again, higher scores indicated a greater degree of impairment.

Clinician-administered scales were as follows. The Clinician-Administered PTSD Scale (CAPS)²⁰ and Structured Clinical Interview for DSM-IV (axis I disorders)–Patient Version (SCID)²¹ were administered by either a licensed psychologist or licensed professional counselor. The SCID was used to provide diagnostic classifications for patients with axis I psychiatric disorders based on DSM-IV-TR criteria. Although a diagnosis of current PTSD was obtained from the CAPS, the SCID was used to assess for the presence of comorbid disorders that may exclude a patient from the study. The CAPS was developed at the National Center for PTSD and has become the “gold standard” for assessing PTSD in individuals >15 years old. The CAPS consisted of 30 interview questions that targeted DSM-IV-TR criteria for PTSD. These items assessed core PTSD symptoms and related issues, as follows: re-experiencing symptoms, avoidance and numbing symptoms, hyperarousal symptoms,

trauma-related guilt, dissociation, subjective distress, functional impairment, onset, duration, symptom severity, symptom improvement, and response validity. The evaluation provided a measure of symptom severity and sufficient criteria to determine whether a current or lifetime diagnosis of PTSD was valid.

Data Analysis

The variables of PTSD severity (CAPS), combat exposure (FCES), depression (QIDS), diagnosis of a depressive disorder, childhood adversity (ACE), TBI, substance use, number of combat-related traumatic events, age, gender, race, education in years, number of times deployed, years of active duty, and interactions of each quantitative predictor with each of gender, race, and diagnosis of a depressive disorder were investigated in multiple regression models to determine their contribution to the degree of functional impairment as measured by the IPF. A variable selection routine was utilized, which incorporated combinations of forward addition and backward elimination of variables until there was no further improvement in model diagnostics. The Bayesian information criterion (BIC) was the chosen statistic for the determination of the best model.

RESULTS

Of 513 veterans who were screened by telephone, 187 presented for formal evaluation. Participants were not brought in for further evaluation if they did not meet inclusion criteria during the telephone screen. Of these individuals, 154 underwent formal screening and 107 completed the baseline assessments. Reasons for exclusion included current alcohol or drug dependence, medications that increased the risk for seizure with TMS, previous severe head injury, not meeting full criteria for PTSD, and not having a combat-related trauma. There were 11 participants with incomplete data, including no IPF score. This resulted in 96 participants available for further evaluation of function (IPF) (Table 1). The majority of veterans were men ($N=88$ of 96), with all having served in Afghanistan, Iraq, or both. The average age was 31.6 ± 6.54 years (age range=21–51 years). The average number of years of education was 14.49 ± 2.16 years (range=12–20 years), and the average number of years of active duty was 6.16 ± 4.28 years (range=0.5–24.71 years). Of the 96 participants with PTSD, 59 (61%) also had a diagnosis of a mood disorder.

For the model investigating predictors of functional status, the depression measure (QIDS), a depressive disorder diagnosis, and the CAPS were selected in the final model that best predicted the degree of functional status (IPF) ($F_{(3,92)}=20.4$, $p<0.0001$, adjusted $R^2=0.379$). The greater the depressive symptoms experienced by the veteran, the greater the degree of functional impairment ($t_{(92)}=2.92$, $p<0.0001$). Moreover, those with a diagnosis of a depressive disorder had a mean IPF score 0.47 units higher than those

TABLE 3. Regression Analysis of Final Model Determined by Minimum BIC for Predicting Degree of Functional Status^a

Variable	B	SE	t	95% CI for B		p Value
Depressive disorder diagnosis	0.47 ^b	0.16	2.86	0.14	0.79	0.005
QIDS	0.06 ^c	0.02	2.92	0.02	0.10	<0.0001
CAPS	0.01 ^c	0.01	2.12	0.00	0.02	0.035

^a Adjusted $R^2=0.38$. BIC, Bayesian information criterion; CAPS, Clinician-Administered PTSD Scale; IPF, Inventory of Psychosocial Functioning; PTSD, post-traumatic stress disorder; QIDS, Quick Inventory of Depression Scale.

^b Conditional mean difference between groups with a depressive disorder diagnosis.

^c The unstandardized regression coefficient.

without a depressive disorder diagnosis, adjusted for QIDS and CAPS ($t_{(92)}=2.86$, $p=0.005$). Finally, CAPS contributed positively to IPF prediction, although its influence in the presence of QIDS and a depressive disorder diagnosis was relatively marginal ($t_{(92)}=2.12$, $p=0.035$) (Figure 1, Table 2, and Table 3).

DISCUSSION

In treatment-seeking veterans with PTSD, depressive symptoms are a major contributor to functional impairment and are potentially the most important factor. In this study (which was independent of compensation for disability determination), depression, a diagnosis of depression, and symptoms of PTSD were the only factors to survive significance from the variables assessed in predicting the level of psychosocial function. Of these factors, the strongest predictor of functional status was clearly depressive symptoms, because these were associated with the largest Wald statistics and the largest decrease in BIC during model selection. This has important implications for the assessment and management of patients with PTSD. Clearly, depressive symptoms are strongly linked with the severity of PTSD symptoms and resulting functional impairment; thus, depression should be carefully evaluated and treated in patients with PTSD. This is especially important because studies that examine only symptoms of PTSD, as it is traditionally defined (e.g., CAPS), may be missing important components that are contributing to patient functional impairment. In addition, Conner et al.²² demonstrated that depressive symptoms had the largest influence on the association between PTSD and suicide. Similarly, Ramsawh et al.²³ reported that although PTSD and depressive symptoms were independently associated with suicidality, the combination resulted in a significantly increased risk. Future studies of PTSD should assess depressive and functional measures as well as traditional symptoms of PTSD.

These results also lead to another important question. Are depressive symptoms an independent illness, comorbidity, or simply a marker of severity for PTSD? A significant body of work has attempted to address this question.^{24–26} Although our data do not enable us to directly test this distinction, our results provide some interesting information with respect to function. Of the participants with PTSD in our sample, more than one-half also had a SCID-confirmed

diagnosis of a mood disorder. This is consistent with epidemiological data of much larger data sets.²⁷ Figure 1 seems to demonstrate that it is the degree of mood symptoms, rather than the presence or absence of a mood disorder, that drives the functional impairment. Thus, regardless of a diagnosis of a mood disorder, depressive symptoms in PTSD should be monitored and addressed. Future work is required to determine whether these are separate illnesses or simply symptoms indicative of severity of PTSD.

This study was initiated while the standard for assessing severity of PTSD symptoms was the CAPS based on DSM-IV criteria. In DSM-5, however, the criteria for PTSD have changed to include symptoms of negative alterations in cognition and mood associated with the traumatic events. There is considerable overlap with these symptoms and the symptoms of depression. Future work is required to clarify whether these findings could be replicated using the new criteria for PTSD. Regardless of which rating scale the symptoms are assigned, the role that depressive symptoms play in the functional impairment of patients suffering from PTSD is still considerable.

The interpretation of these results requires several caveats. The sample studied included predominantly male participants and only included veterans from a particular era of combat. In addition, the participants were restricted to patients that were recruited for a study of rTMS along with CPT outside of the Department of Veterans Affairs medical system. Our sample included a small percentage of participants with other comorbid anxiety disorders, which may have been attributable to the nature of the study for which they were recruited. Because of safety concerns, the sample was limited to participants who could be safely enrolled in the study, which included eliminating patients with conditions such as moderate to severe TBI. As such, further work is required to assess these factors in other samples of participants. In addition, this study focused on several areas of function (including social, occupational, and self-care) and not specifically on health-related quality of life or a more constrained view of function such as activities of daily living. In contrast with our results, Pagotto et al.²⁸ found that PTSD symptom severity was the strongest predictor of health-related quality-of-life decrements, even in the presence of other psychiatric comorbidities. These illnesses may differentially affect different aspects of quality of life. Finally, our assessment of function (the IPF) was based on a self-rated scale. Further work is required to determine whether these results can be replicated with independent assessments of function.

In conclusion, depressive symptoms are important contributors of functional impairment in veterans with PTSD from combat. Future work is required to better understand the biology behind these symptoms, with the target to improve the outcomes of patients with PTSD.

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