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Comparison of the Functional Health Limitations of Veterans Deployed to Iraq or Afghanistan to Veterans Deployed to Desert Shield/Storm With Chronic Fatigue Syndrome

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ABSTRACT

The majority of studies to examine the levels of physical symptoms after Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) deployment have found that veterans experience high levels of physical symptoms after deployment. What is not known is whether the physical symptoms experienced by OEF/OIF veterans meet criteria for chronic fatigue syndrome (CFS), as was seen after Operation Desert Shield/Operation Desert Storm. This determination would require a medical evaluation to rule out medical conditions that may explain the symptoms. Further, it is not well known if the physical symptoms experienced by OEF/OIF veterans are causing significant functional impairment. We compared OEF/OIF veterans with CFS to Desert Shield/Storm veterans with CFS seen at a postdeployment Veterans Affairs (VA) clinic soon after their respective deployments. We found 17.6% of OEF/OIF veterans met criteria for CFS. Compared to Desert Shield/Desert Storm veterans with CFS, the OEF/OIF veterans with CFS demonstrated poorer mental health function and similar physical health function.

KEYWORDS

Quality of life; function; veterans; chronic fatigue syndrome; Iraq; military; Gulf War illness; physical symptoms; mental health; post-traumatic stress disorder; PTSD

Introduction

The United States deployed more than 2.5 million service members to Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). There is initial evidence that some OEF/OIF veterans are experiencing widespread physical symptoms (e.g., back pain, headaches, nausea) (Iverson, Pogoda, Gradus, & Street, 2013; McAndrew, Teichman, Osinubi, Jasien, & Quigley, 2012; Quigley et al., 2012), a concern also raised by the Institute of Medicine (2013). The experience of increased physical symptoms after combat is consistent with reports after previous wars. Hyams, Wignall, and Roswell (1996) found an increase in reporting of physical symptoms after every war since the U.S. Civil War. Jones et al. (2002) found increases in physical symptoms after every war since the Boer War.

Increases in physical symptoms were particularly notable after Operation Desert Shield/Operation Desert Storm. Returning veterans experienced debilitating fatigue, pain, and cognitive dysfunction. These symptoms correspond closely to chronic fatigue syndrome (CFS) in nonveterans (Fukuda et al., 1994). CFS, a poorly understood illness, can be defined by persistent chronic fatigue of at least six months duration, which is accompanied by four additional symptoms. CFS is diagnosed only after all other medical conditions that could be causing the presenting symptom complex have been excluded (Fukuda et al., 1994). The rate of CFS among civilians is less than 1% (Jason et al., 1999; Reyes et al., 2003) and as high as 2.6% in primary care (Bates et al., 1993; Buchwald et al., 1995; Wessely, Chalder, Hirsch, Wallace, & Wright, 1997). In comparison, the rates of CFS among Operation Desert Shield/Operation Desert Storm veterans is 2.1% to 5.6% (Kang, Natelson, Mahan, Lee, & Murphy, 2003; McCauley et al., 2002). Desert Shield/Desert Storm veterans with CFS-like conditions have significant functional impairments (Blanchard et al., 2006). Further, the cause of this increase in physical

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symptoms remains contested, and there are few effective treatments.

To date, no study has examined CFS specifically among OEF/OIF veterans, but a number of studies have found evidence that veterans self-report increased physical symptoms after OEF/OIF deployment. Hoge, Terhakopian, Castro, Messer, and Engel (2007) found among non-treatment-seeking OEF/OIF veterans that 6.5% of soldiers without post-traumatic stress disorder (PTSD) reported severe levels of physical symptoms, and 11.5% of soldiers with PTSD reported severe levels of physical symptoms. McAndrew, Helmer, Phillips, Chandler, Ray, and Quigley (2016) found that one year after deployment to OEF/OIF, in a sample of 319 soldiers, almost 60% self-reported significant levels of widespread symptoms (11% of which reported severe symptoms). Symptoms were defined using the Centers for Disease Control and Prevention's (CDC) definition of chronic multisymptom illness (CMI) (Fukuda et al., 1998). CMI is an umbrella term for significant multisystem physical symptoms—one which has fewer exclusion criteria than CFS. The largest study to examine rates of physical symptoms reported after OEF/OIF was the Millennium Cohort Study, an epidemiological study of 73,078 OEF/OIF military personnel (Smith et al., 2014). The Millennium Cohort Study examined OEF/OIF military personnel who deployed, OEF/OIF military personnel who did not deploy, and Operation Desert Shield/Operation Desert Storm veterans who deployed. They found that, compared to OEF/OIF military personnel who did not deploy, deployment to OEF/OIF resulted in a 1.7 times increase in likelihood of having self-reported significant, widespread symptoms. (This was defined using an approximation of the CDC definition for CMI.) Approximately 26% of OEF/OIF military personnel who deployed met criteria for clinically significant widespread symptoms after deployment. OEF/OIF military personnel who deployed reported fewer physical symptoms compared to Operation Desert Shield/Operation Desert Storm veterans.

The majority of studies to examine the levels of physical symptoms after OEF/OIF deployment have shown high levels of physical symptoms after deployment. What is not known is whether the physical symptoms experienced by OEF/OIF veterans meet criteria for CFS, as was seen after Desert Shield/Desert Storm. This determination would require a medical evaluation to rule out other medical conditions that could explain the symptoms. Further, it is not well known if the physical symptoms experienced by OEF/OIF veterans are causing significant functional impairment. Our goal was to answer these questions by comparing the functional impairment of OEF/OIF veterans with CFS and without CFS who presented at a specialty clinic to Desert Shield/Storm veterans with CFS who presented soon after their deployment.

Methods

The research design was a cross-sectional chart review composed of self-report data, clinician evaluations, and laboratory results. This research was approved by the New Jersey Department of Veterans Affairs Institutional Review Board and Research and Development Committee, and participants either signed a consent form or we received a waiver of consent prior to including participants' data.

Participants

OEF/OIF veteran outpatient participants ($N = 675$) were enrolled at a U.S. Department of Veterans Affairs tertiary clinic between 2001 and 2010. This clinic provides comprehensive clinical assessments to address postdeployment health concerns with a focus on medically unexplained symptoms. Veterans could be referred from their provider or self-referred. OEF/OIF veterans were assessed on average two years after OEF/OIF deployment.

A comparison cohort of Operation Desert Shield/Operation Desert Storm veteran participants ($N = 200$) was enrolled at a VA postdeployment center that was in operation between 1994 and 2000 and had a primary mission to study health consequences of deployment during the Desert Shield/Desert Storm. The Desert Shield/Desert Storm veteran cohort was recruited through letters sent to individuals on the Department of Veterans Affairs Persian Gulf Registry and via local fliers and advertisements. Desert Shield/Desert Storm veterans were assessed on average six years after their combat deployment.

Definition of CFS and physical symptoms

In both veteran cohorts, CFS was diagnosed using the 1994 case definition (Fukuda et al., 1994). CFS is defined by persistent chronic fatigue of new onset and at least six months duration in addition to at least four out of eight other symptoms that include short-term memory or concentration problems, sore throat, tender lymph nodes, muscle pain, multijoint pain, headaches, unrefreshing sleep, and fatigue after exercise. An individual is not diagnosed with CFS if clinical evaluation reveals medical or psychiatric conditions that can explain the fatiguing illness, such as sleep apnea, anemia, major depressive disorder with psychotic features, bipolar disorder, severe obesity, or use of certain medications (for full definition and exclusion criteria, see Fukuda et al., 1998; Pollet et al., 1998). Head injury resulting in unconsciousness of at least 30 minutes was also excluded.

In both veteran cohorts, CFS symptoms were ascertained through the same self-report questionnaire designed to assess the criteria required to meet the 1994 case definition of CFS. The questionnaire asks about the time of onset and severity of the eight noted symptoms. This questionnaire has been used in previous studies to capture self-report of CFS and has been used clinically to screen for CFS (e.g., Kang et al., 2003; Lange et al., 2013). The self-report questionnaire also asked about diagnoses and medications that would exclude veterans from a diagnosis of CFS. Next, veterans in both cohorts received a comprehensive medical examination administered by a physician complete with laboratory testing. The medical examination was used to probe for medical, psychiatric, and laboratory results that could explain the veteran's symptoms; these veterans were excluded from additional analyses. Neither alcohol nor substance abuse was used to exclude cases in either sample.

Health function

We used the self-report Medical Outcomes Study (MOS) Short Form-36 (SF-36) to assess functional status. The SF-36 compares favorably with other functional measures (Jones et al., 2001; Kazis et al., 2002). The measure has eight subscales and composite physical and mental health scores. Scores range from 0 to 100 with a mean of 50 and a standard deviation of 10. Higher scores denote better functioning. OEF/OIF veterans were assessed with the Veterans Rand-36 (VR-36), whereas Desert Shield/Desert Storm veterans were assessed with the SF-36 Version 1. The VR-36 differs from SF-36 in that it uses a 5-point response for seven of the items (used to score the role physical and role emotional subscales) as opposed to the dichotomous response choice used in the SF-36 Version 1. Kazis and colleagues (2004) compared the VR-36 to the SF-36 Version 1 in a survey of 2,162 veterans and determined that the modified items have the same interpretation as the original items. The VR-36 was developed from the MOS RAND SF-36. The SF-36 is a registered trademark of the Medical Outcomes Trust. The 1998 norms were used to score both versions to facilitate comparisons across cohorts. For ease of discussion, the remainder of this article refers to these measures simply as the SF-36.

PTSD

The 17-item PTSD Checklist (PCL) was used to measure PTSD symptom severity in the OEF/OIF cohort (Weathers, Litz, Herman, Huska, & Keane, 1993). The PCL asks participants to rate on a 5-point scale from 1 (*Not at all*) to 5 (*Extremely*) how much the symptom/statement has bothered them over the past month. We used a cutoff of 50, which has been shown to have a sensitivity of .82 and a specificity of .84 compared to a structured clinical interview (Weathers et al., 1993).

The 35-item Mississippi Scale for Combat-Related PTSD (M-PTSD) was used as a measure of PTSD symptoms in the Desert Shield/Desert Storm cohort (Hyer, Davis, Boudewyns, & Woods, 1991). The M-PTSD asks respondents to rate how true each question is for them on a 5-point Likert scale (e.g., "Before I entered the military I had more close friends than I have now"). We used a cutoff of 107, which has been found to have a diagnostic accuracy of 90%, sensitivity of 93%, and specificity of 89% compared to a structured clinical interview. PCL and M-PTSD scores are correlated at .68 to .86 in veteran populations (Orsillo, 2001).

Statistical analysis

Statistical analyses were conducted using PASW Version 18.0. We examined prevalence of CFS, physical symptoms, PTSD, and functional status in the cohorts and used *t* tests to explore demographic differences between OEF/OIF veterans with CFS and OEF/OIF veterans without CFS, and between OEF/OIF veterans with CFS and Desert Shield/Desert Storm veterans with CFS. Next, a series of logistic regression analyses was conducted to compare rates of physical symptoms between OEF/OIF veterans with and without CFS and the rates of physical symptoms between Desert Shield/Desert Storm veterans with CFS and OEF/OIF veterans with CFS. We reported the rates of physical symptoms for each group in Table 1 and the results of the logistic regression analyses comparing Desert Shield/Desert Storm veterans with CFS to OEF/OIF veterans with CFS in Table 1.

We used one multivariate analysis of covariance (MANCOVA) to compare physical and mental functional status of OEF/OIF veterans with CFS to Desert Shield/Desert Storm veterans with CFS. A MANCOVA can have multiple dependent variables. We included each of the SF-36 subscales and the two composite scales (10 total) as the dependent variables. We initially controlled for age, sex, education, PTSD, race, and ethnicity. Only PTSD and age contributed significantly to the model. Therefore, we controlled only for PTSD and age in subsequent analyses.

We used one MANCOVA to compare physical and mental functional status of OEF/OIF veterans with CFS to OEF/OIF veterans with CFS. We included each of the SF-36 subscales and the two composite scales (10 total) as the dependent variables. We initially controlled for age, sex, education, PTSD, race, and ethnicity. Only PTSD and age contributed significantly to the model. Therefore, we

Table 1. Prevalence of CFS Symptoms in OEF/OIF Veterans With and Without CFS and GW Veterans With CFS.

	OEF/OIF No CFS ($N = 416$)[a]	OEF/OIF CFS ($N = 119$)	GW CFS ($N = 100$)	OR*	95% CI*	*p* Value*
Concentration	69.2%	97.5%	100%	—	—	n.s.
Joint pain	61.6%	95.0%	95.0%	—	—	n.s.
Fatigue after exercise	38.3%	87.8%	99.0%	12.3	1.5–98.1	.02
Poor sleep	71.6%	100.0%	100.0%	—	—	n.s.
Fever	25.4%	52.5%	65.0%	2.0	1.0–3.6	.04
Swollen glands	14.3%	40.2%	71.0%	5.6	2.7–11.3	< .001
Sore throat	33.5%	61.2%	78.0%	3.0	1.5–6.2	.002
Headaches	47.3%	85.6%	98.0%	17.4	2.2–137.2	.007
Muscle pain	55.1%	95.0%	96.0%	—	—	n.s.
Weakness	36.4%	78.2%	91.0%	3.1	1.3–7.7	.01

Note. GW = Operation Desert Shield/Operation Desert Storm; CFS = chronic fatigue syndrome; OEF/OIF = Operation Enduring Freedom/Operation Iraqi Freedom; OR = odds ratio; CI = confidence interval.
*Reported statistical comparison was only between OEF/OIF and GW veterans with CFS, and was adjusted for age, sex, and PTSD.
[a]OEF/OIF veterans with CFS reported greater prevalence of all symptoms as compared to OEF/OIF veterans with no CFS ($p < .05$).

controlled only for PTSD and age in subsequent analyses. There was no overlap in assessment time since deployment between the Desert Shield/Desert Storm veterans and OEF/OIF veterans; therefore, assessment time since deployment was not used as a control variable in any of the analyses as it "defined" the two groups (all Desert Shield/Desert Storm veterans were approximately six years postdeployment, and all OEF/OIF veterans were approximately two years postdeployment).

Results

Demographics

We first examined the frequency of CFS among OEF/OIF veterans in our sample. In all, 4% of OEF/OIF veterans did not have complete data and so could not be classified; 34% of OEF/OIF veterans screened positive for CFS. Of these,16.3% were excluded from further analysis as they were using a medication or had a medical or psychiatric illness that could explain their symptoms (Fukuda et al., 1994). Therefore, 17.6% of OEF/OIF veterans in our sample met criteria for CFS.

Table 2. Demographic Characteristics.

Demographics	OEF/OIF No CFS ($n = 416$)	OEF/OIF CFS ($n = 119$)	GW CFS ($n = 100$)
Age, *M* (*SD*)	31.2 (9.2)	32.4 (9.5)	33.8 (8.2)
Years since deployment, *M* (*SD*)	1.6 (1.7)	2.1 (1.4) [a]	6.0 (.94) [b]
Male, %	87.3	82.4	70.0 [b]
Years of education, *M* (*SD*)	13.4 (1.7)	13.4 (1.8)	13.5 (1.7)
White, %	33.3	36.1	66.0 [b]
Black, %	20.9	17.6	20.0
Latino/a, %	31.0	31.9	7.0 [b]
Other, %	8.9	9.2	6.0

Note. GW = Operation Desert Shield/Operation Desert Storm; CFS = chronic fatigue syndrome; OEF/OIF = Operation Enduring Freedom/Operation Iraqi Freedom.
[a]Statistically significant difference between OEF/OIF No CFS and OEF/OIF CFS ($p < .05$).
[b]Statistically significant difference between OEF/OIF CFS and GW CFS ($p < .05$).

We compared demographic characteristics of OEF/OIF veterans with and without CFS using *t* tests. The only significant difference found was OEF/OIF veterans with CFS were assessed longer after deployment. We next compared demographic characteristics of OEF/OIF veterans with CFS to our sample of Desert Shield/Desert Storm veterans with CFS, again using *t* tests. Compared to OEF/OIF veterans with CFS, our sample of Desert Shield/Desert Storm veterans was assessed later postdeployment, was more likely to be female, was more likely to self-identify as White, and was less likely to identify as Latino. There were no significant differences in education or age (see Table 2).

PTSD

We examined the rates of PTSD among OEF/OIF veterans with CFS, OEF/OIF veterans without CFS, and Desert Shield/Desert Storm veterans with CFS. Among OEF/OIF veterans without CFS, 23% had probable PTSD; among OEF/OIF veterans with CFS, 65% had probable PTSD; and among Desert Shield/Desert Storm veterans with CFS, 43% had probable PTSD.

Symptoms

A series of logistic regression analyses was conducted to compare rates of physical symptoms between OEF/OIF veterans with and without CFS. By definition, OEF/OIF veterans who screened positive for CFS had a higher prevalence of all reported symptoms than those without CFS. We then compared rates of symptoms in OEF/OIF veterans with CFS to Desert Shield/Desert Storm veterans with CFS (see Table 1). Desert Shield/Desert Storm veterans with CFS were more

Table 3. MANCOVA Comparing Functioning of OEF/OIF Veterans With CFS to OEF/OIF Veterans Without CFS Controlling for Age and Probable PTSD.*

SF-36 Subscale	OEF/OIF No CFS ($N = 416$)	OEF/OIF CFS ($N = 119$)	F
PCS	48.7	39.4	61.3
PF	48.9	37.9	67.4
RP	47.9	35.0	68.1
BP	45.5	35.1	43.6
GH	46.0	34.0	72.3
MCS	42.7	26.7	47.1
VT	46.5	34.2	57.0
SF	41.6	26.5	60.8
RE	45.3	28.8	46.6
MH	43.4	28.7	61.3

Note. PCS = physical composite score; MCS = mental composite score; PF = physical function; RP = role physical; BP = bodily pain; GH = general health; VT = vitality; SF = social function; RE = role emotional; MH = mental health; MANCOVA = multivariate analysis of covariance; PTSD = post-traumatic stress disorder.
*For all comparisons. $p < .001$.

likely to report fatigue after exercise, fever, swollen glands, sore throat, headaches, and weakness. There were no significant differences in concentration, joint pain, poor sleep, or muscle pain.

Physical and mental health functioning

We completed one MANCOVA to determine differences in physical and mental health functioning among OEF/OIF veterans with and without CFS. As expected, OEF/OIF veterans with CFS reported worse functioning on all scales of the SF-36 as compared to OEF/OIF veterans without CFS (see Table 3). OEF/OIF veterans with CFS scored greater than one standard deviation below the mean on all scales of the SF-36, while OEF/OIF veterans without CFS scored within one standard deviation of the mean on all scales of the SF-36.

We performed a final MANCOVA to determine differences in physical and mental health functioning between OEF/OIF veterans with CFS and Desert Shield/Desert Storm veterans with CFS. On average, OEF/OIF veterans with CFS reported significantly poorer functioning on the mental composite scale, and on the social function, role emotional, and mental health subscales. Desert Shield/Desert Storm veterans reported significantly poorer functioning on the physical composite scale and the general health function subscale. There were no differences in the physical function, role physical, body pain, or vitality subscales (see Figure 1). Both Desert Shield/Desert Storm and OEF/OIF veterans with CFS scored greater than one standard deviation below the mean on all scales of the SF-36.

Discussion

As early as the U.S. Civil War, returning soldiers were described as having an "irritable heart" and reported to suffer from fatigue (Da Costa, 1871). In a review of U.S. conflicts from the Civil War to Desert Shield/Desert Storm, fatigue has been reported as a consistent problem in returning veterans (Hyams et al., 1996). Examination of physical symptoms among OEF/OIF veterans is still in its infancy, and to our knowledge this is the first study to examine CFS. We found that CFS was high (17.6%) in our population

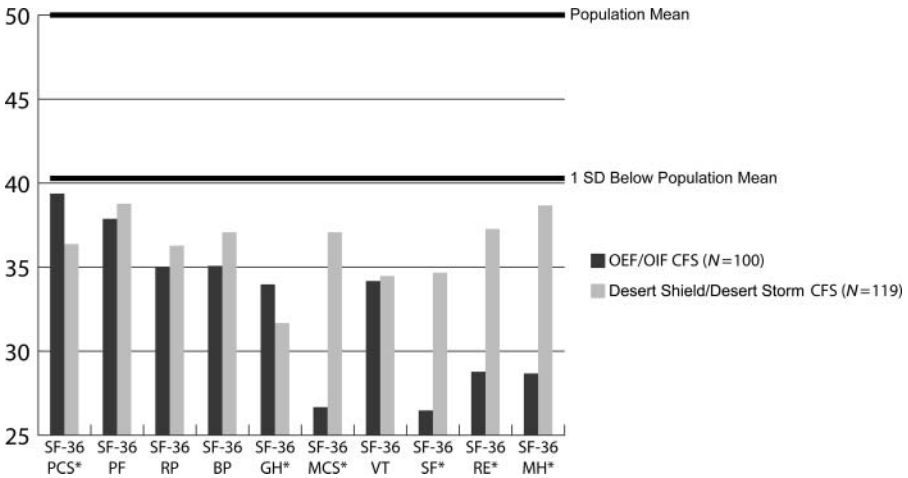

Figure 1. Comparison of functioning between OEF/OIF veterans with CFS to Operation Desert Shield/Operation Desert Storm veterans with CFS. Adjusted SF-36 scores controlling for age and PTSD (higher scores indicate better functioning). PCS = physical composite score; MCS = mental composite score; PF = physical function; RP = role physical; BP = bodily pain; GH = general health; VT = vitality; SF = social function; RE = role emotional; MH = mental health; CFS = chronic fatigue syndrome; PTSD = post-traumatic stress disorder; OEF/OIF = Operation Enduring Freedom/Operation Iraqi Freedom. *Significant difference between the groups.

of OEF/OIF veterans seeking treatment at a postdeployment clinic. Furthermore, OEF/OIF veterans with CFS had physical health functional impairments comparable to Desert Shield/Desert Storm veterans with CFS, but they had significantly worse mental health functioning.

The finding of high rates of CFS among OEF/OIF veterans is consistent with previous studies that show OEF/OIF veterans are self-reporting significant physical symptoms after deployment (Hoge et al., 2007; McAndrew et al., 2012; Quigley et al., 2012; Smith et al., 2014). The current study addressed limitations in previous studies by using a clinician-administered medical examination. Many conditions can cause increases in physical symptoms. This study is the first to find that some OEF/OIF veterans are experiencing multiple physical symptoms that are not better explained by other conditions. We found the prevalence of OEF/OIF veterans with CFS in a postdeployment clinic to be 17%. Previous studies have used different definitions to capture these chronic physical symptoms (e.g., chronic multisymptom illness) and not all have adequately excluded for potential comorbid medical conditions. Further research is needed to better understand the prevalence of widespread physical symptoms that are not caused by another medical condition outside of a treatment-seeking context.

We also examined the functional impairment of veterans with CFS seen at a VA clinic. We found that the level of functional impairment is greater than one standard deviation below the mean. On average, the level of functional impairment may be similar to or worse than the level of functional impairment found among individuals with other significant chronic illnesses, such as cancer (Sprangers et al., 2000). Further, we found the level of functional impairment of OEF/OIF veterans with CFS is similar to the level of Desert Shield/Desert Storm veterans with CFS. Desert Shield/Desert Storm veterans continue to have CFS and associated disability 25 years after the end of the war with few efficacious treatments. Our results are consistent with one other study to examine the functional impairment among OEF/OIF veterans with chronic physical symptoms. McAndrew et al. (2016) examined the level of functional impairment among OEF/OIF veterans not seeking treatment and found those who screened positive for severe chronic multisymptom illness also had functional impairment that was greater than one standard deviation below the mean. Together, these studies suggest that some veterans returning from OEF/OIF are experiencing debilitating physical symptoms.

In contrast to the relatively few studies on CFS or multiple physical symptoms in OEF/OIF veterans, many reports have been published on the "signature illness" of OEF/OIF, PTSD, and mild traumatic brain injury (e.g., Ramchand et al., 2010). This may be due to physical symptoms being attributed to PTSD or mild traumatic brain injury by clinicians and/or veterans. Although the higher rates of PTSD likely contribute to the poorer physical functioning for veterans from the current conflict, controlling for PTSD did not fully account for the impairment in physical functioning, suggesting that PTSD is not the only variable contributing to this finding. Further, a growing literature suggests that the misattribution of symptoms to mild traumatic brain injury may be common (Uomoto & Williams, 2009) and may cause diagnostic confusion (Hoge, Goldberg, & Castro, 2009).

The strength of this study was our unique ability to compare a noncontemporaneous sample of OEF/OIF and Desert Shield/Desert Storm veterans both assessed soon after their deployment; however, our study was not without limitations. These include a relatively small sample of veterans seeking treatment at a VA tertiary care clinic. Like all studies of clinical samples, the rate of CFS found in this study would not be the same rate as found in a nationally representative sample. Another limitation was the differences between our samples, including referrals, inclusion and exclusion criteria, different clinicians, years postdeployment, and measurement of PTSD and health function. It is impressive that with these differences we found striking similarities between the samples in regard to physical health function. Further, our data suggest a potentially understudied problem among OEF/OIF veterans deserving of additional study. This study was not designed to examine the cause of CFS in either Desert Shield/Desert Storm veterans or OEF/OIF veterans. We did find a difference in the pattern of symptoms between the cohorts. Veterans from Desert Shield/Desert Storm reported a greater prevalence of symptoms often seen in infectious or acute illness (sore throat, swollen glands, and fatigue after exercise) whereas OEF/OIF veterans had worse mental health function.

In conclusion, our data suggest that OEF/OIF veterans seeking specialized postdeployment care are experiencing a high rate (17.6%) of chronic fatigue syndrome that is not accounted for by another medical or psychiatric condition. In addition, our study found both OEF/OIF veterans with CFS and Desert Shield/Desert Storm veterans with CFS have similar levels of physical functional impairment. It is clear that with more than 2 million soldiers sent to the Afghanistan and Iraq theaters, these levels of functional impairment will require additional clinical and research resources to better understand both the sources of poor functioning and how to intervene to rehabilitate the functioning of these veterans.

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