It is illegal to post this copyrighted PDF on any website. Course and Predictors of Postdeployment Fatigue: A Prospective Cohort Study in the Dutch Armed Forces

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ABSTRACT

Objective: The purpose of this study was to examine course and predictors of fatigue in military personnel deployed to Afghanistan.

Methods: A total of 906 soldiers in the Dutch Armed Forces who participated in a 4-month mission to Afghanistan were included in this study. Assessment took place prior to and 1, 6, 12, and 24 months after deployment. Data were collected between 2005 and 2011. The fatigue severity subscale of the Checklist Individual Strength was used to indicate the level of fatigue during the previous 2 weeks. Mixed models and logistic regression analysis were used to predict course and prevalence of fatigue after deployment. Predictors of postdeployment fatigue were assessed prior to deployment.

Results: The mean level of fatigue increased significantly following deployment (B=0.58, P=.007). In total, 274 soldiers (30.2%) were severely fatigued at least once after deployment and 130 (14.3%) soldiers had recurrent levels of severe fatigue. Only a minority of the veterans with severe fatigue could be classified as having posttraumatic stress disorder (PTSD, per *DSM-IV-TR* criteria) or potential medical problems. Significant predeployment predictors of less favorable courses of fatigue after deployment were higher levels of fatigue (B=0.46, $P \le .001$), emotional abuse during childhood (B=0.99, $P \le .001$), and harm avoidance (B=0.27, P=.012). These predeployment factors also predicted severe fatigue after deployment.

Conclusions: Severe fatigue is a substantial problem in Afghanistan War veterans that does not seem to resolve over time. In a majority of cases, the symptoms cannot be attributed to medical problems or PTSD, whereas predeployment differences in psychosocial factors partially explain course and prevalence of postdeployment fatigue. These findings support assumptions that a complex interplay of various factors might be responsible for the symptoms.

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*Corresponding author: Hans Knoop, PhD, Expert Center for Chronic Fatigue, Radboud University Medical Center, PO Box 9101, 6500 HB Nijmegen, the Netherlands (hans.knoop@amc.uva.nl). Debilitating health complaints of unknown origin have been reported by military personnel following deployment. The US Committee on Gulf War and Health estimates that about one quarter to one third of all veterans from the 1991 Gulf War suffer from persistent and unexplained complaints such as fatigue, pain, and associated symptoms that are also characteristic of symptom-based conditions such as chronic fatigue syndrome and irritable bowel syndrome.¹ According to a systematic review² of the literature, current symptoms of fatigue (eg, tiredness, the need to rest, a lack of energy) seem to be a particularly prevalent problem reported by about 10%–60% of the veterans from the Gulf War depending on the respective sample and assessment of fatigue.

Only limited data exist about the relevance of fatiguerelated symptoms in veterans who were deployed to one of the current wars, and virtually none of the existing studies has collected prospective data starting prior to deployment to adequately reflect the variability in symptoms across time.^{3,4} This fact has also seriously limited the potential to identify risk factors for the development of fatigue-related symptoms since retrospective reports can bias conclusions about the actual importance of these factors.^{4,5} More insight into the predictors of postdeployment fatigue based on comprehensive longitudinal data would therefore significantly enhance our understanding of the etiology of these symptoms and might thereby help to resolve some of the controversies that are present in this area of research.^{1,4,6}

One of these controversies is whether psychosocial factors contribute to the development of postdeployment fatigue. If this were the case, it would support models which assume that an interplay of multiple factors is responsible for the complaints, as opposed to models that tend to attribute the complaints to a specific causal agent (eg, a virus or exposure to toxic substances) and would also have implications for the management of the symptoms. Research in nonmilitary populations has shown that factors such as childhood trauma, certain personality traits, and preexisting symptoms can predispose individuals to developing medically unexplained fatigue.⁷⁻¹⁰ There is also preliminary research in military populations¹¹⁻¹³ which has suggested that the same factors may serve as vulnerabilities for the development of fatigue-related symptoms in veterans.

The purpose of the present study was 2-fold. At first, we were interested in the course of fatigue severity in military personnel deployed to Afghanistan to present prevalence data about the relevance of fatigue-related symptoms from one of the current war areas. These data will expand on a

Wiborg et al It is illegal to post this copyrighted PDF on any website. routine medical examination prior to deployment. Typical

- **Clinical Points**
- Symptoms of fatigue in veterans may be easily trivialized as being simply due to other potential pathology or as being necessarily transient in nature.
- When veterans complain about severe fatigue, their symptoms should be carefully evaluated over time so that decisions about adequate management strategies can be made.

previous report by Reijnen et al.¹⁴ We hypothesized that we would find substantial rates of current symptoms of fatigue within the range of previous studies, showing that fatigue is a relevant problem in veterans from the current wars as well. In this context, we also hypothesized that these symptoms cannot simply be attributed to potential medical problems or posttraumatic stress disorder (PTSD). Both assumptions are commonly expressed in controversies about the etiology of these symptoms.^{4,6}

The second objective was to predict the course of postdeployment fatigue severity and identify soldiers at risk for experiencing symptoms of fatigue after deployment. On the basis of previous findings,^{7,10-13} we focused on baseline levels of fatigue, anxiety, and depression as well as experiences of childhood trauma and the personality trait harm avoidance (as an indicator of negative emotionality) as potential predictors of postdeployment fatigue. We hypothesized that these psychosocial risk factors would significantly predict the course of symptoms up to 2 years after deployment, thereby supporting the assumption that the symptoms are likely to be produced by an interplay of multiple factors rather than a specific causal agent.^{4,6} To minimize potential bias, all risk factors for postdeployment fatigue were assessed prior to deployment and were adjusted for deployment-related stress.

METHODS

Participants and Procedure

Data were collected between 2005 and 2011 in the context of a large prospective cohort study of risk factors for the development of deployment-related symptoms in the Dutch Armed Forces.¹⁴ The study was approved by the ethics committee of the University Medical Center Utrecht, the Netherlands. A volunteer sample of 1,032 soldiers signed written informed consent forms after receiving oral and written information about the study. Of this cohort, 1,025 soldiers (99.3%) participated in the first assessment (approximately 2 months prior to deployment), 842 (81.6%) in the second assessment (1 month after deployment), 774 (75.0%) in the third assessment (6 months after deployment), 572 (55.4%) in the fourth assessment (12 months after deployment), and 566 (54.8%) in the fifth assessment (24 months after deployment). In contrast to the first 3 assessments, the last 2 assessments were conducted by mail, and nonresponders were approached up to 5 times by (electronic) mail and telephone. All participants passed routine medical examination prior to deployment. Typical duties during deployment consisted of combat patrols, clearing or searching buildings, participation in demining operations, and traveling across enemy territory.

Twenty-five soldiers were not deployed and therefore were excluded from the present study. One hundred one additional participants were excluded because they completed none of the 4 assessments of postdeployment fatigue. In the 906 included participants, the amount of missing data was between 0% and 22% with respect to the baseline variables, including stress during deployment assessed 1 month after return from Afghanistan. An exception was the baseline assessment of PTSD with a rate of 31%, which was due to the fact that a part of the cohort had already completed baseline assessment when this measure was introduced to the study. The rates of missing data in postdeployment fatigue severity, PTSD, and use of medication in these participants were between 10% and 17% 1 month after deployment, between 19% and 20% 6 months after deployment, and between 38% and 42% 12 and 24 months after deployment. Strategies for the imputation of missing data are discussed later in this section.

Instruments

The fatigue severity subscale of the Checklist Individual Strength (CIS)¹⁵ was used to indicate the level of fatigue during the previous 2 weeks. This subscale consists of 8 items ("I feel tired"/"Physically I feel exhausted"/"I feel fit"/"I feel powerless"/"I am rested"/"Physically I feel I am in bad form"/"I tire easily"/"Physically I feel I am in an excellent condition") that are scored on a 7-point Likert scale. Sum scores vary between 8, no fatigue, and 56, severe fatigue. The CIS is a reliable and valid instrument for the assessment of fatigue severity and is sensitive to change.¹⁵ We used a cutoff score of 35 or higher to indicate severe fatigue. This cutoff score has frequently been used as a criterion to indicate problematic levels of fatigue in clinical studies.^{16,17}

The revised Dutch version of the Symptom Checklist-90 $(SCL-90)^{18}$ was used to assess symptoms of anxiety and depression. The scales consist of 10 and 16 items, respectively, that are scored on a 5-point Likert scale. Higher sum scores indicate higher levels of anxiety and depression. The Self-Rating Inventory for Posttraumatic Stress Disorder $(SRIP)^{19}$ was used to measure PTSD symptoms. The inventory consists of 22 items that are assessed using a 4-point Likert scale. These items reflect content of clusters B, C, and D of the *DSM-IV-TR*²⁰ criteria for PTSD (ie, reexperiencing, avoidance/numbing, arousal). A cutoff score of 38 was used to classify soldiers as having PTSD. This cutoff score showed best sensitivity and specificity with respect to clinician-administered diagnoses of PTSD according to *DSM-IV* criteria in a previous study.²¹

The short version of the Cloninger Temperament and Character Inventory (TCI)^{22,23} was used to assess harm avoidance. This scale consists of 15 items that are scored dichotomously (yes/no). These items reflect different aspects of anticipatory worry, fear of uncertainty, shyness, and fatigability. These constructs can be examined separately

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Table 1. Baseline characteristics of the Sample (14–500)			
Variable	Value		
Age, y	28.7 (9.0)		
Male, n (%)	827 (91.3)		
Higher education, n (%)	210 (23.2)		
Currently in relationship, n (%)	562 (62.0)		
Officer rank, including NCO, n (%)	365 (40.3)		
Previously deployed, n (%)	433 (47.8)		
SCL-90			
Anxiety score	11.0 (1.8)		
Depression score	18.0 (3.1)		
PTSD symptoms (SRIP score)	26.9 (5.3)		
Fatigue severity (CIS score)	17.6 (9.0)		
ETI			
Physical abuse score	0.9 (1.3)		
Emotional abuse score	0.5 (1.1)		
Sexual abuse score	0.1 (0.6)		
Harm avoidance (TCI)	3.2 (2.9)		

^aValues are mean (SD) unless otherwise indicated.

Abbreviations: CIS = Checklist Individual Strength, ETI = Early Trauma Inventory, NCO = noncommissioned officer, PTSD = posttraumatic stress disorder, SCL-90 = Symptom Checklist-90, SRIP = Self-Rating Inventory for Posttraumatic Stress Disorder, TCI = Cloninger Temperament and Character Inventory.

in the long version of the TCI, but this strategy has been discouraged in the context of the short version of the TCI due to psychometric problems.²³ We conducted a preliminary analysis of the psychometric properties of the harm avoidance scale using principal component analysis to ensure that an association between this personality trait and fatigue severity (assessed with the CIS) was not mainly due to a dominance of the items that refer to fatigue, rest, or energy. This analysis revealed that the 5 items with such content had the lowest loadings (ie, ≤ 0.43) of all 15 harm avoidance items.

The physical, emotional, and sexual abuse subscales of the short version of the Early Trauma Inventory (ETI)²⁴ were used to measure childhood trauma. These subscales have 5 items each with the exception of sexual abuse, which has 6 items. All items are assessed dichotomously (yes/no). The sum score of each subscale reflects the number of events that occurred before the age of 18 years. A checklist with 19 dichotomous items (yes/no) was used to measure deployment-related stress such as witnessing incoming enemy fire or other people getting injured or killed and perceiving personal risk due to war-related actions, accidents, or threats.¹⁴ Additional questions were included about demographic characteristics (age, gender, relationship, education, and military rank), use of medication, and previous deployment. Ordinal response categories for relationship, education, and military rank were dichotomized to facilitate further analysis. Use of medication included dichotomous (yes/no) assessment of current intake of any medication (including nonprescription medicines). We used this variable to indicate potential medical problems.

We included repeated assessment (from before to 24 months after deployment) of fatigue severity (CIS), PTSD symptoms (SRIP), and use of medication as well as baseline (ie, predeployment) assessment of anxiety (SCL-90), depression (SCL-90), childhood trauma (ETI), harm avoidance (TCI), and the demographic variables age, gender, relationship, education, military rank, and previous deployment in this

Table 2. Course and Prevalence of Fatigue During the Study (N = 906)

Variable	Level of Fatigue, Mean (SD)ª	Severely Fatigued (CIS score≥35), n (%)		
Total course				
Prior to deployment	17.6 (9.0)	54 (6.0)		
After deployment				
1 mo	19.7 (10.4)	104 (11.5)		
6 mo	19.6 (10.7)	109 (12.0)		
12 mo	20.1 (11.3)	137 (15.1)		
24 mo	20.6 (11.5)	133 (14.7)		
After deployment				
At least 1 assessment		274 (30.2)		
More than 1 assessment		130 (14.3)		
^a Level of fatigue is equal to the sum score of the 8 items on the CIS that are scored on a 7-point Likert scale				

Abbreviation: CIS = Checklist Individual Strength.

Symbol: ... = not applicable.

study. The checklist for deployment-related stress was completed 1 month after return from Afghanistan.

Statistical Analyses

We used linear mixed models analysis to predict the course of postdeployment fatigue severity as a continuous dependent variable. In this statistical approach, postdeployment fatigue severity was included as repeated measure from 1 to 24 months after deployment at the within-subject level of the model. The repeated measures were nested within individual soldiers at the between-subjects level of the model. The intercept was included as random factor. We computed a model with predeployment predictors, deployment-related stress, and time after deployment as fixed effects at the between-subjects level of the model as our main model. Logistic regression analysis was used to identify risk factors for episodes of severe fatigue after deployment and to compare medical problems and PTSD classification between severely fatigued and not severely fatigued soldiers.

We handled missing data using multiple imputation with 10 imputations (fully conditional specification) according to the predictive mean matching method. We imputed missing scale scores based on a model that included all variables of the present study. In the mixed models approach, missing postdeployment repeated measures data were handled using maximum likelihood estimations. Multiple imputation and maximum likelihood estimations have been shown to be robust methods for handling missing data even when the data are not missing completely at random.^{25,26} IBM SPSS Statistics 21 was used for all computations with a threshold for significance of $P \le .05$.

RESULTS

In Table 1, we present baseline characteristics of the sample assessed prior to deployment. We also assessed the level of deployment related stress 1 month after return from Afghanistan and found a mean score of 4.5 (SD = 3.3). An overview of the course and clinical patterns of fatigue severity is presented in Table 2. The largest increase in the mean

Wiborg et al **It is illegal to post this copyrighted PDF on any website.** Table 3. Comparison of Use of Medication and Reports of PTSD Between Severely Fatiguéd and

Table 3. Comparison of Use of Medication and Reports of PTSD Between Severely Fatigue Not Severely Fatigued Soldiers

	Any Medication, n/Total n (%)		PTSD (SRIP score ≥ 38), n/Total n (%)	
Time of Assessment	Severely Fatigued	Not Severely Fatigued	Severely Fatigued	Not Severely Fatigued
Prior to deployment	10/54 (18.5)	91/852 (10.7)	11/54 (20.4)	31/852 (3.6)***
After deployment				
1 mo	17/104 (16.3)	90/802 (11.2)	25/104 (24.0)	52/802 (6.5)***
6 mo	23/109 (21.1)	98/797 (12.3)*	31/109 (28.4)	44/797 (5.5)***
12 mo	27/137 (19.7)	97/769 (12.6)	40/137 (29.2)	24/769 (3.1)***
24 mo	31/133 (23.3)	94/773 (12.2)**	30/133 (22.6)	26/773 (3.4)***
*D~ OF **D~ O1 ***	R < 001			

 $*P \le .05. **P \le .01. ***P \le .001.$

Abbreviations: PTSD = posttraumatic stress disorder, SRIP = Self-Rating Inventory for Posttraumatic Stress Disorder.

Table 4. Prediction of the Longitudinal Course of Postdeployment Fatigue Severity (repeated measures) Based on the Predeployment Assessment of Predictors Using Linear Mixed Models (N = 906)^a

Predictor	B (SD)	Р
Time after deployment	0.58 (0.21)	.007
Age	0.00 (0.05)	.934
Male gender	-0.19 (0.92)	.837
Currently in relationship	-0.44 (0.59)	.451
Higher education	-0.35 (0.71)	.626
Officer rank, including NCO	0.61 (0.84)	.465
Previously deployed	0.31 (0.62)	.616
Anxiety (SCL-90)	0.64 (0.22)	.769
Depression (SCL-90)	0.25 (0.14)	.077
Fatigue severity (CIS)	0.46 (0.04)	≤.001
Physical abuse (ETI)	-0.42 (0.22)	.063
Emotional abuse (ETI)	0.99 (0.29)	≤.001
Sexual abuse (ETI)	0.47 (0.49)	.334
Harm avoidance (TCI)	0.27 (0.11)	.012

^aAll predictors adjusted for reports about stress during deployment.

Abbreviations: CIS = Checklist Individual Strength, ETI = Early Trauma

Inventory, NCO = noncommissioned officer, SCL-90 = Symptom Checklist-90, TCI = Cloninger Temperament and Character Inventory.

level of fatigue severity and the number of cases of severe fatigue can be found between the predeployment assessment and the assessment 1 month after deployment. During this period, there was almost a doubling in terms of the number of individuals with severe fatigue. This number increased further during the 6- and 12-month follow-up assessments. From 12 to 24 months' follow-up, there was a slight decrease in the number of cases of severe fatigue. The mean level of fatigue severity increased continually after deployment. In total, 274 soldiers (30.2%) were severely fatigued at least once after deployment. One hundred thirty soldiers (14.3%) were severely fatigued more than once after deployment. We did not find a consistent pattern of statistically significantly greater use of medication in severely fatigued soldiers as opposed to not severely fatigued soldiers across the study period (Table 3). However, there were significantly more reports of PTSD in severely fatigued soldiers than in not severely fatigued soldiers at all 5 assessments.

We present results from the mixed models approach in Table 4. In this analysis, we predicted the course of fatigue severity after deployment. We found that the level of postdeployment fatigue increased significantly over time. Significant predictors of less favorable courses of fatigue severity after deployment were higher predeployment levels of fatigue severity, harm avoidance, and emotional abuse Table 5. Predicting Episodes of Severe Fatigue After Deployment Based on the Predeployment Assessment of Predictors Using Multiple Binary Logistic Regression Analysis (N = 906)^a

Predictor	At Least 1 Episode OR (95% CI)	More Than 1 Episode OR (95% Cl)
Age	1.02 (0.99–1.05)	1.02 (0.97-1.06)
Male gender	0.75 (0.42-1.36)	0.70 (0.32-1.53)
Currently in relationship	0.93 (0.62-1.39)	0.79 (0.44-1.41)
Higher education	1.01 (0.62–1.65)	1.05 (0.60-1.82)
Officer rank, including NCO	0.85 (0.49–1.49)	1.13 (0.53–2.39)
Previously deployed	1.22 (0.81–1.82)	1.45 (0.80-2.62)
Anxiety (SCL-90)	1.05 (0.90-1.24)	1.00 (0.81-1.23)
Depression (SCL-90)	1.04 (0.95–1.14)	1.08 (0.94-1.24)
Fatigue severity (CIS)	1.09 (1.06–1.12)***	1.09 (1.06-1.12)***
Physical abuse (ETI)	0.94 (0.80-1.09)	0.87 (0.69–1.10)
Emotional abuse (ETI)	1.16 (0.94–1.42)	1.29 (1.02–1.64)*
Sexual abuse (ETI)	1.38 (0.98–1.95)	1.28 (0.85–1.92)
Harm avoidance (TCI)	1.10 (1.02–1.19)*	1.08 (0.98–1.19)

^aAll predictors adjusted for reports about stress during deployment. $*P \le .05$. $***P \le .001$.

Abbreviations: CIS = Checklist Individual Strength, ETI = Early Trauma Inventory, NCO = noncommissioned officer, SCL-90 = Symptom Checklist 00, TCI = Checklist On TCI = Checklist 00, TCI

Checklist-90, TCI = Cloninger Temperament and Character Inventory.

during childhood. The model was adjusted for reports of deployment-related stress assessed 1 month after return from Afghanistan. This variable also yielded significance (P=.008). These effects remained significant when we repeated our mixed models analysis, this time without additional imputation techniques (ie, multiple imputation). The only exception was the *P* value of the variable emotional abuse during childhood, which increased beyond the threshold for statistical significance of this study (P=.088)and which is likely to be caused by a decrease in power due to the smaller sample size. We also repeated our mixed models approach, this time adding postdeployment assessment of potential medical problems and PTSD as repeated measures at the within-subject level of the model to adjust our main model for these potentially influential variables. We found that all predictors remained significant in this analysis while the new variables were also significantly and positively associated with postdeployment levels of fatigue severity (data not shown).

Results from the multiple binary logistic regression analysis are presented in Table 5. Risk factors for at least 1 episode of severe fatigue after deployment were higher predeployment levels of fatigue and harm avoidance. Risk factors for more than 1 episode of severe fatigue after deployment were higher predeployment levels of fatigue and **It is illegal to post this copy** emotional abuse during childhood. We adjusted our analyses for deployment-related stress, which significantly predicted at least 1 episode (P=.030) but not more than 1 episode of severe fatigue after deployment (P=.142). Adjustments for postdeployment factors were not made. In contrast to mixed models, logistic regression analysis is not capable of handling longitudinal data adequately.

DISCUSSION

The purpose of the present study was to examine the course of fatigue severity and identify predeployment predictors of severe fatigue in military personnel deployed to Afghanistan. We found an increase in the mean level of fatigue severity during the course of the study. Our linear mixed models analysis revealed that the increase in fatigue severity after deployment was statistically significant. At each postdeployment assessment, between 11% and 15% of all soldiers reported severe fatigue. In total, almost onethird of all soldiers were severely fatigued at least once after deployment. Although there was fluctuation in the level of fatigue over time, 14% of all soldiers had recurrent levels of severe fatigue after deployment. These rates are generally consistent with reports from Gulf War populations, although our cross-sectional rates tend to be at the lower end of the range of prevalence rates compared with the Gulf War studies that were included in the systematic review by Thomas et al.² This finding is in agreement with a meta-analysis by the same authors, in which they found that Gulf War veterans were in fact about 3 to 4 times more likely to suffer from current fatigue than veterans from other conflicts such as the Bosnian War.² Rates similar to those of our study were also found in Dutch veterans who had participated in a mission to Cambodia.²⁷ Although we do not have additional data on the quality of life of the fatigued veterans, studies from military and nonmilitary populations have found substantial disabilities in daily activities of patients with high levels of fatigue severity, including physical dysfunction and inability to participate in work-related activities.^{12,28,29} Yet, more work is needed to examine the course of disabilities in fatigued veterans across time to better evaluate the severity of the complaints and guide cost-effective management.

Additional analysis revealed that predeployment levels of fatigue and harm avoidance were potent predictors of the course of fatigue severity up to 2 years following deployment. This finding is in accordance with previous studies from military populations that demonstrated an association between postdeployment levels of fatigue across time and cross-sectional differences in negative emotionality between fatigued and nonfatigued veterans.^{11–13} We used the concept of harm avoidance as an indicator of negative emotionality that reflects aspects of anticipatory worry, fear of uncertainty, shyness, and fatigability. All items related to fatigue, rest, and energy had the lowest loadings on the total factor according to our data, which suggests that the association between harm avoidance and postdeployment fatigue in this study is not merely due to the fatigue-related items of the concept. In contrast to previous studies,¹³ we did not find that levels of depression and anxiety or any of the demographic variables were able to predict the course of fatigue over time. Instead, we found that certain aspects of childhood trauma were significantly associated with the course of fatigue severity, which is in contrast to findings by Fiedler et al¹³ but is in line with previous research in nonmilitary populations.⁷ All inconsistent findings stem from studies that did not examine predeployment predictors of postdeployment fatigue. We therefore suggest that these differences are due to the fact that predeployment predictors are different from predictors that were assessed following deployment.

It is a general limitation of our study that we had no access to detailed information about the medical status of participants to validate the medically unexplained character of the complaints. However, we did not find that severely fatigued soldiers consistently had a statistically significantly higher use of medication than not severely fatigued soldiers. It should be noted in this context that the intake of any medication (including nonprescription medicines) is likely to overestimate the number of soldiers with potential medical problems. Also, only a significant minority of soldiers with fatigue were actually classified as suffering from PTSD according to our clinical cutoff score. These findings are in line with previous research showing that even rigorous somatic and psychiatric examination can reveal plausible explanations for the physical complaints in only a minority of veterans with unexplained symptoms.^{4,5,30,31} In addition to other limitations, a substantial amount of data was missing, which may have biased the findings of this study. To minimize this risk of potential bias, we implemented robust imputation strategies that are widely accepted.^{25,26} Furthermore, we did not include a random control group without deployment to Afghanistan, which limits our ability to establish a causal relationship between deployment and the complaints that were analyzed in this study. It should also be noted that deployment-related stress was assessed 1 month after deployment and that this variable was based on self-report, which may have biased the assessment of this factor.

We also have no data about traumatic brain injuries (TBIs) in the veterans of our sample to examine the effects of such injuries on fatigue-related symptoms. This would be an interesting aspect for upcoming studies to examine. Other studies have shown that fatigue is a frequent complaint of patients with mild TBI in nonmilitary samples.^{32,33} Since the symptoms of fatigue were not usually specific to the types of brain injury reported in those studies, we suggest that TBI may have served as a trigger for the development of fatigue-related symptoms (such as a passed virus infection in other patients), while other factors may contribute to the persistence of the symptoms. According to previous findings in nonmilitary samples, these perpetuating factors include patients' perception of the symptoms as well as behavioral strategies to cope with the symptoms, which can be targeted successfully in cognitive-behavioral interventions.^{8,9,34} Some studies have suggested that a selection of these

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It is illegal to post this copyrighted PDF on any website, cognitive-behavioral factors may also be relevant to the accounted for the course of fatigue after deployment. In perpetuation of postdeployment fatigue.^{11,12} More research is needed to better understand the factors that can be successfully modified to alleviate fatigue-related symptoms in veterans. Major strengths of the study include repeated assessment of fatigue severity from before to 2 years after deployment to adequately reflect fluctuation of the complaints across time and the assessment of risk factors prior to deployment to Afghanistan to minimize potential bias of these factors.

In conclusion, our findings suggest that fatigue is a substantial problem in Afghanistan veterans. According to our data, this problem does not seem to resolve over time. It also cannot be attributed to medical problems or PTSD in a majority of cases. Instead, predeployment differences in fatigue severity, childhood trauma, and harm avoidance sum, these findings provide support for the assumption that a complex interplay of different factors might be responsible for the symptoms as opposed to theories that attribute the symptoms to a specific causal agent. To the best of our knowledge, this is the first longitudinal study with a focus on psychosocial risk factors that was able to identify predeployment predictors for severe fatigue in Afghanistan veterans. Upcoming studies could validate these findings and include other potentially influential biological variables, such as central sensitization mechanisms³⁵ and proinflammatory cytokine signaling processes,³⁶ to further complement our understanding of how veterans develop fatigue after deployment and to inform effective prevention and management strategies for these complaints.

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REFERENCES

- 1. Committee on Gulf War and Health. Treatment for Chronic Multisymptom Illness, Board on the Health of Select Populations, Institute of Medicine—Gulf War and Health: Treatment for Chronic Multisymptom Illness. Washington, DC: National Academies Press; 2013.
- 2. Thomas HV, Stimpson NJ, Weightman AL, et al. Systematic review of multi-symptom conditions in Gulf War veterans. Psychol Med. 2006;36(6):735-747.
- 3. Coughlin SS, McNeil RB, Provenzale DT, et al. Method issues in epidemiological studies of medically unexplained symptom-based conditions in veterans. J Mil Veterans Health. 2013;21(2):4-10.
- 4. Iversen A, Chalder T, Wessely S. Gulf War Illness: lessons from medically unexplained symptoms. Clin Psychol Rev. 2007:27(7):842-854
- 5. Murphy D, Hotopf M, Wessely S. Multiple vaccinations, health, and recall bias within UK armed forces deployed to Iraq: cohort study. BMJ. 2008;337:a220.
- 6. Engel CC, Jaffer A, Adkins J, et al. Can we prevent a second "Gulf War syndrome"? population-based healthcare for chronic idiopathic pain and fatigue after war. Adv Psychosom Med. 2004;25:102-122.
- 7. Borsini A, Hepgul N, Mondelli V, et al. Childhood stressors in the development of fatigue syndromes: a review of the past 20 years of research. Psychol Med. 2014;44(9):1809-1823.
- 8. Lievesley K, Rimes KA, Chalder T. A review of the predisposing, precipitating and perpetuating factors in Chronic Fatigue Syndrome in children and adolescents. Clin Psychol Rev. 2014;34(3):233-248
- 9. Prins JB, van der Meer JWM, Bleijenberg G.

Chronic fatique syndrome. Lancet. 2006;367(9507):346-355.

- 10. Poeschla B, Strachan E, Dansie E, et al. Chronic fatigue and personality: a twin study of causal pathways and shared liabilities. Ann Behav Med. 2013;45(3):289-298.
- 11. Hotopf M, David A, Hull L, et al. Risk factors for continued illness among Gulf War veterans: a cohort study. Psychol Med. 2004;34(4):747-754.
- 12. De Vries M, Soetekouw PMMB, Van Der Meer JWM, et al. Natural course of symptoms in Cambodia veterans: a follow-up study. Psychol Med. 2001;31(2):331-338.
- 13. Fiedler N, Lange G, Tiersky L, et al. Stressors, personality traits, and coping of Gulf War veterans with chronic fatigue. J Psychosom Res. 2000:48(6):525-535.
- 14. Reijnen A, Rademaker AR, Vermetten E, et al. Prevalence of mental health symptoms in Dutch military personnel returning from deployment to Afghanistan: a 2-year longitudinal analysis. Eur Psychiatry. 2015;30(2):341-346.
- 15. Vercoulen JHMM, Swanink CMA, Fennis JFM, et al. Dimensional assessment of chronic fatigue syndrome. J Psychosom Res. 1994;38(5):383-392.
- 16. Wiborg JF, Wensing M, Tummers M, et al. Implementing evidence-based practice for patients with chronic fatigue syndrome. Clin Psychol Psychother. 2014;21(2):108-114.
- 17. Knoop H, Bleijenberg G, Gielissen MFM, et al. Is a full recovery possible after cognitive behavioural therapy for chronic fatigue syndrome? Psychother Psychosom. 2007:76(3):171-176
- 18. Arrindell WA, Ettema JHM. SCL-90; Handleiding Bij Een Multidimensionele Psychopathologie-Indicator. Lisse, Netherlands: Swets Test-Service: 1986.
- 19. Hovens JE, Bramsen I, van der Ploeg HM. Selfrating inventory for posttraumatic stress disorder: review of the psychometric properties of a new brief Dutch screening instrument. Percept Mot Skills. 2002;94(3 pt 1):996-1008.
- 20. American Psychiatric Association. Diagnostic and Statistical Manual for Mental Disorders Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association; 2000.
- 21. van Zelst WH, de Beurs E, Beekman AT, et al. Criterion validity of the self-rating inventory for posttraumatic stress disorder (SRIP) in the community of older adults. J Affect Disord. 2003;76(1-3):229-235.
- 22. Duijsens IJ, Spinhoven P, Verschuur MJ. Eurelings-Bontekoe, EHM De ontwikkeling van de Nederlandse Verkorte Temperament en

Karakter Vragenlijst (TCI-105). Ned Tijdschr Psychol. 1999;54:276-283.

- Farmer RF, Goldberg LR. A psychometric 23. evaluation of the revised Temperament and Character Inventory (TCI-R) and the TCI-140. Psychol Assess. 2008;20(3):281-291.
- 24. Bremner JD, Bolus R, Mayer EA. Psychometric properties of the Early Trauma Inventory-Self Report, J Nerv Ment Dis, 2007:195(3):211-218.
- 25. Twisk J, de Vente W. Attrition in longitudinal studies: how to deal with missing data. J Clin Epidemiol. 2002;55(4):329-337.
- 26. Peugh JL, Enders CK. Missing data in educational research: a review of reporting practices and suggestions for improvement. Rev Educ Res. 2004;74(4):525–556.
- 27. de Vries M. Soetekouw PMMB, Van Der Meer JW, et al. Fatigue in Cambodia veterans. QJM. 2000;93(5):283-289.
- 28. Huibers MJH, Kant IJ, Knottnerus JA, et al. Development of the chronic fatigue syndrome in severely fatigued employees: predictors of outcome in the Maastricht cohort study. I Enidemial Community Health 2004:58(10):877-882.
- Wiborg JF, van der Werf S, Prins JB, et al. Being 29. homebound with chronic fatigue syndrome: a multidimensional comparison with outpatients. Psychiatry Res. 2010;177(1-2):246-249
- 30. Lange G, Tiersky L, DeLuca J, et al. Psychiatric diagnoses in Gulf War veterans with fatiguing illness. Psychiatry Res. 1999;89(1):39-48.
- 31. Joseph SC; Comprehensive Clinical Evaluation Program Evaluation Team. A comprehensive clinical evaluation of 20,000 Persian Gulf War veterans. Mil Med. 1997;162(3):149-155.
- 32. Stulemeijer M, van der Werf S, Bleijenberg G, et al. Recovery from mild traumatic brain injury: a focus on fatigue. J Neurol. 2006:253(8):1041-1047.
- 33. Belmont A, Agar N, Hugeron C, et al. Fatigue and traumatic brain injury [in English, French]. Ann Readapt Med Phys. 2006;49(6):283-288, 370-374
- 34. Wiborg JF, Knoop H, Frank LE, et al. Towards an evidence-based treatment model for cognitive behavioral interventions focusing on chronic fatigue syndrome. J Psychosom Res. 2012;72(5):399-404.
- 35. Lewis JD, Wassermann EM, Chao W, et al. Central sensitization as a component of postdeployment syndrome. NeuroRehabilitation. 2012;31(4):367-372.
- van Zuiden M, Kavelaars A, Amarouchi K, et al. 36. IL-1ß reactivity and the development of severe fatigue after military deployment: a longitudinal study. J Neuroinflammation. 2012;9(1):205.

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