Posttraumatic Stress Symptomatology Is Associated With Unexplained Illness Attributed to Persian Gulf War Military Service

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Objective: Controversy exists concerning unexplained illness in Persian Gulf War veterans, especially regarding the contribution of psychological trauma. We sought to determine if war zone trauma or posttraumatic stress symptomatology (PTSS) are associated with illnesses reported by Gulf War veterans that were documented by medical examination but not attributable to a medical diagnosis. **Methods:** A total of 1119 (55% response rate) of 2022 randomly sampled veterans of the United States Persian Gulf War were screened and 237 cases and 113 controls were identified by medical examination for a case-control study comparing Persian Gulf War military veterans with or without medically documented, but unexplained, symptoms. Multivariate logistic regression and cross-validation analyses examined self-report measures of demographics, subjective physical symptoms and functioning, psychiatric symptoms, stressors, war zone trauma, and PTSS, to identify correlates of case-control status. **Results:** Posttraumatic stress symptomatology and somatic complaints were independently associated with case status, as were (although less consistently) war zone trauma and depression. Age, education, and self-reported health, stress-related somatization, pain, energy/fatigue, illness-related functional impairment, recent stressors, and anxiety were univariate (but not multivariate) correlates of case status. **Conclusions:** PTSS related to war zone trauma warrants additional prospective research study and attention in clinical screening and assessment as a potential contributor to the often debilitating physical health problems experienced by Persian Gulf War veterans. **Key words:** adults, combat exposure, etiology, Gulf War, posttraumatic stress, somatic symptoms.

PTSS = posttraumatic stress symptomatology; PTSD = posttraumatic stress disorder; PEHRC = Portland (Oregon) Environmental Hazards Research Center; SCL-90-R GSI = Symptom Checklist 90-Revised Global Severity Index; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; MMPI-2 Hs and Hy = Minnesota Multiphasic Personality Inventory-2 Hypochondriasis and Hysteria subscales; LES-NI = Life Experiences Scale-Negative Impact; SF-36 = 36-item Short Form Health Survey of the Medical Outcomes Study; SASSI-2 = Substance Abuse Subtle Screening Inventory-2; CES-R = Combat Exposure Scale Revised; Miss-PTSD = Mississippi Scale for PTSD; OR = odds ratio; CI = confidence interval.

An unexpectedly high prevalence of medical and psychiatric conditions of uncertain etiology and diagnosis has been reported among the 693,826 military personnel who served in the Persian Gulf war zone between August 1990 and July 1991 (1). Approximately 15,000 Operation Desert Storm military personnel who served in the Persian Gulf were found by Department of Veterans Affairs physicians to exhibit persistent but diagnostically unexplained physical symptoms with onset during or after Persian Gulf military service (2), as were another approximately 13,000 veterans evaluated by the Department of Defense Comprehensive Clinical Evaluation Program (3). Compared with military personnel who were on active duty during the Persian Gulf War but were not stationed in the war zone, Persian Gulf war zone veterans show a significantly higher prevalence of symptoms of physical illness (ie, chronic fatigue, bronchitis, and asthma), cognitive impairment, and psychological distress (ie, depression, anxiety, and PTSD), as well as poorer overall health and greater health-related physical and psychosocial functional impairment (4–9).

At least one in seven, and perhaps as many as one in three, Persian Gulf War veterans suffers from diverse and persistent medical and psychiatric symptoms (10–12). Clinical examinations often reveal complex and wide-ranging complaints (1–3), suggesting that psychological as well as biological factors warrant investigation to better understand the nature and etiology of unexplained health problems and to identify veterans at risk (3–5, 13). Exposure to neurotoxicants in the Persian Gulf has been linked to Persian Gulf War veterans' medical problems (5, 14). Psychological stressors and disorders, including war zone trauma and PTSD, also have been implicated as potential causal or contributory factors in Gulf War veterans' unexplained illnesses (4, 11, 13, 15–21), although these factors do not seem to entirely account for the reported physical health problems (20, 21).

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Haley and colleagues (22) attributed neurotoxic causation to the psychological aspects of putative Gulf War syndromes. Haley (23) concluded that, due to problems of measurement error, the prevalence of PTSD is effectively nil among Gulf War veterans. However, the studies critiqued by Haley (23) assessed PTSD using validated questionnaire cut scores, and reported current PTSD prevalence estimates of 2% to 17% among Persian Gulf military veterans (4, 12, 15–18, 24, 25). These prevalence estimates are comparable with or greater than levels reported for current PTSD (26; 1.2% to 2.7%) and lifetime PTSD (27; 5% to 10%) in recent epidemiologic studies of adults in the United States. More recently, Wolfe et al. (21) used structured clinical research interviews to document elevated rates of PTSD and major depressive disorder among Persian Gulf military veterans compared with non–Gulf-deployed veteran controls. They also reported a "small but significant" association between PTSD diagnosis and self-reported illness symptoms (21). Wolfe et al. (21) and others (20, 28) are skeptical about the contribution of posttraumatic stress to unexplained physical health problems of Gulf War veterans. However, in samples of male World War II and Korean military veterans (29–31) and Dutch resistance fighters (32), and of midlife Vietnam-era male (33–37) and female (37, 38) military veterans, a PTSD diagnosis or PTSS severity correlated with self-reported health problems.

Thus, it seems premature to rule psychological trauma and posttraumatic stress either in or out as a contributor to the health problems of thousands of Gulf War veterans. One possibility is that PTSS, rather than the full diagnostic syndrome of PTSD, may influence physical health problems (13). PTSS has been shown to be associated with substantial psychosocial impairment even in the absence of full PTSD (26). More specifically, PTSS has been linked to adverse physical health outcomes (28, 31) and physical health-related functional impairment (29, 30, 35, 36). We attempted to determine on a cross-sectional basis if PTSS are associated with Persian Gulf War veterans' medically documented but unexplained symptoms independent of other potential correlates of physical health problems. We used data from a case-control study comparing military veterans of the Persian Gulf war with or without documented but medically unexplained illness symptoms attributable to Persian Gulf service. Our analyses accounted for demographic correlates (ie, education level and age), substance abuse, stressful events, psychiatric symptoms, physical health factors (ie, global health perception, energy/fatigue, pain, and somatic preoccupation) and health-related functional impairment. A cross-validation strategy was used to identify robust correlates of unexplained illness symptoms.

METHODS

Participants

Potential study participants were identified from a Department of Defense database provided to the Portland (Oregon) Environmental Hazards Research Center (PEHRC). This information listed all United States military veterans deployed to the Persian Gulf during the time period of August 1, 1990 through July 31, 1991 who recorded Oregon or Washington as their home state at the time of deployment and had a current address in either state. Veterans were ineligible if they had participated in the Department of Veterans Affairs National Survey of Persian Gulf War veterans, had enrolled in the National Registry for Gulf War veterans, or had participated in PEHRC pretesting (see below). A total of 2022 veterans were randomly selected from the 8603 eligible veterans from Oregon or southwest Washington.

Survey questionnaires were mailed between November 1995 and June 1997. The mailing included a complete written description of the project. All participants provided written, informed consent in a protocol approved by the Institutional Review Boards of the Department of Veterans Affairs, Portland Oregon Medical Center and the Oregon Health Sciences University. The initial goal was to identify veterans who either were asymptomatic (potential controls) or reported at least one of the following symptoms (potential cases): 1) cognitive or psychological changes including memory loss, confusion, concentration difficulties, mood swings, or somnolence; 2) gastrointestinal distress; 3) fatigue; 4) muscle or joint pain; and 5) skin or mucous membrane lesions. The fatigue classification required endorsement of unexplained fatigue plus four or more of the other index symptoms. Table 1 summarizes specific symptom items for each category. To be a potential case, the respondent had to affirm that symptoms: a) were present during the past 3 months; b) were persistent (ie, 1 month or longer); and c) began during or after Persian Gulf service.

The PEHRC received 1119 completed questionnaires of 2022 mailed to eligible participants—a 55% response rate. Three hundred twenty veterans were deemed ineligible because they had participated in telephone interviews or completed a short-exposure questionnaire ($N = 155$) for other studies; had moved out-of-state ($N = 36$) or refused additional contact ($N = 25$); were Vietnam veterans ($N = 26$); had symptoms predating the Gulf war ($N = 17$); had exclusionary diagnoses ($N = 32$); or for other personal reasons such as an accident, work requirements, or a death in the family ($N = 29$). Exclusion diagnoses included: hepatitis, cancer, diabetes, HIV, epilepsy, schizophrenia, malaria, narcolepsy, tuberculosis, and myasthenia gravis. An additional 356 eligible respondents were eliminated from further study participation because they could not be located ($N = 69$), refused further contact ($N = 163$), or agreed to examination but canceled their appointments ($N = 124$). A total of 443 participants participated in comprehensive examinations. Veterans were recruited for the case-control study if they returned the survey questionnaire, were not veterans of the Vietnam conflict, could travel to the testing center, and did not report an exclusionary diagnosis on the survey health history. Veterans who provided consent for further contact (via the protocol reviewed and approved by the Institutional Review Boards), were contacted by telephone to verify the symptom(s) and to review their self-reported medical history for a diagnosis that could credibly explain each symptom reported (eg, head trauma, and/or diabetes). As with the screening questionnaire, veterans in this phone screening whose symptoms

TABLE 1. Categories of Unexplained Illness and Qualifying Symptoms for Each Category

Cognitive/Psychological	Gastrointestinal	Fatigue	Muscle/Joint	Skin/Mucous
Difficulty in speech	Upset stomach	Unexplained fatigue	Back pain	Red irritated eyes
Insomnia	Frequent diarrhea	Chills or fevers	Persistent muscle aches/pains	Eyebrow hair loss
Changes in memory	Bloody diarrhea	Headaches	Painful joints	Tumor or cyst
Difficulty in concentration	Abdominal cramping	Unrefreshing sleep	Swollen joints	Acne
Mood swings		Tender glands	Joint stiffness	Mouth sores
Depression		Memory changes	Pain after exertion	Skin rash or blisters
Anxiety		Difficulty concentrating		
Difficulty learning		Sore throat		
		Painful joints		
		Unexplained weakness		
		Fatigue after exercise		
		Persistent muscle aches		

could be accounted for by a medical diagnosis were excluded to limit study "cases" to veterans with unexplained symptoms. Eligible participants were evaluated at the PEHRC, and they did not differ from nonparticipants in age, ethnicity, gender, or branch of military service. Data were complete for all demographics except ethnicity (not reported by 22% of cases and 19% of controls).

A clinical examination was conducted with each symptomatic and asymptomatic study participant by one of three physicians (two neurologists, one rheumatologist) blind initially to potential case or control status. The examination confirmed the presence, persistence, and onset of self-reported symptoms during or after their Persian Gulf military service, and ruled in or out medical diagnoses. All participants reporting muscle and/or joint pain were evaluated by the rheumatologist as potential fibromyalgia cases. The clinical protocol included a detailed standardized history of symptoms, a physical examination, and complete neurological and rheumatological examinations. Psychological and neurobehavioral tests were conducted, followed by laboratory tests for infectious diseases, blood chemistry (including thyroid function), and urinalysis. The clinical protocol was conducted in accordance with Department of Veterans Affairs and Oregon Health Sciences University guidelines for protection of human subjects. Symptom reliability was established by comparing initial questionnaire responses to the results of a) the subsequent telephone interview, and b) the direct clinical examination.

After clinical testing, approximately 20% of potential cases were referred to a specialist (eg, dermatology) for diagnostic review. A six-member case-determination panel representing neurology, rheumatology, internal medicine, neuropsychology, and epidemiology reviewed each potential case to identify any diagnostic explanation for target physical illness symptoms and make a final determinations of case-control status. With one exception, panel members were blind to participants' histories of environmental or trauma exposure in the Persian Gulf. The exception was an internal medicine physician who had treated a small number of the study participants before entering the study. All cases were discussed anonymously using only research identification numbers and findings only from study examinations, so that even these patients were not recognizable by history. As an additional precaution against the chance of bias, we checked and determined that no case-control determination was made with this physician casting the deciding vote.

Specific exclusionary medical diagnoses were considered for each class of unexplained illness symptoms. For example, for "Muscle/Joint symptoms," exclusionary criteria included a diagnosis of diabetes mellitus or a "history of injury/surgery and current pain *only in the area of previous injury or surgery*." If any of the 19 specific disorders and sources of known medical causation was identified on examination or in the case review, the individual was excluded from the study. The 19 exclusionary criteria were: mechanical back pain, myofacial pain, bursitis/tendonitis, diabetes, patellar-femoral syndrome, osteoarthritis, postsurgery/trauma pain, hormonal therapy/cancer, alcoholism, shiftwork, overuse syndrome, gastroesophageal reflux, dietary gas/bloating, tinea, eczema, atopic dermatitis, acne/folliculitis, and skin tag/cyst.

As a result, 237 participants with complete study data were classified as study cases with persistent-illness symptoms that were not attributable to a specific disease condition that had an onset since Persian Gulf military service. A control sample of 112 participants with complete study data had no persistent medical symptomatology in any of the five index categories. Four potential case participants and one potential control were excluded from study analyses due to missing data on one or more of the measures. Cases included 92 with muscle/joint symptoms, 100 with fatigue symptoms, 25 with gastrointestinal symptoms, 4 with dermatologic symptoms, and 207 with cognitive symptoms. The modal case included cognitive and one or both of the muscle/joint or fatigue conditions ($N = 119$). Most cases met at least one physical rule-in: only $N = 89$ cases had *only* cognitive symptoms.

Study Measures

We administered a 4-hour battery of 19 tests to assess psychological status and neurobehavioral function. The psychological tests were presented by a computerized Health Screening System (39) that enables participants to transition smoothly through multiple questionnaires at their own pace with explicit test instructions and minimal need for examiner oversight or instruction. Nine widely used tests with psychometrically demonstrated reliability and validity were used, all showing strong temporal stability in the computerized format in a 1-week retest study with a noncombat normative sample ($r \geq .75$; 40).

1. The SCL-90-R, a 90-item questionnaire assessing psychiatric symptoms, with a GSI computed as the total of all items (41).

2. The Beck Depression Inventory (BDI; 42), a 21-item questionnaire with forced-choice ratings of the presence and current severity of depressive attitudes, behaviors, and symptoms.

3. The BAI (43), a 21-item questionnaire parallel in format to the BDI that assesses the presence and severity of subjective, somatic, or panic-related symptoms of anxiety.

4. The MMPI-2 (44), a 370-item measure of psychopathology severity, from which the Hs (hypochondriasis) and Hy (Hysteria)

subscales were used as indicators of intensity of somatic symptoms and stress-related somatization, respectively.

5. The LES (45), a 57-item self-report questionnaire identifying and rating the impact of subtraumatic life events that may be psychosocial stressors (eg, significant job change and/or divorce), which yields a score for the negative impact of stressor exposure (LES-NI).

6. The SF-36, a 36-item questionnaire that assessed functional (somatic) impairment and symptoms due to medical health problems (46). Five subscales were included in study: General Health (SF-36-GH); Vitality (SF-36-V); Bodily Pain (SF-36-P); Health Transition (SF-36-HT); and Mental Health (SF-36-MH).

7. The SASSI-2, a 62-item questionnaire that, when combined with 14 items assessing specific alcohol and drug use, measures risk of alcohol and drug abuse, including subtle attributes of abuse and denial (47). The dichotomous classification of substance abuse (ie, abuse/nonabuse; SASSI2-CAT) was used in the study analyses.

8. The CES-R, a 50-item questionnaire assessing war zone exposure to violence, wounding/death of others, threat of severe injury/death, leadership failures, physical and sexual abusive violence, and POW captivity. Two existing measures, the CES (48) developed for male Vietnam War veterans and the Women's War-time Exposure Scale-Revised (49), were adapted to provide a complete but nonduplicative survey with uniform response options. Some items were changed and new items were included to reflect the presence/absence of certain conditions specific to the Persian Gulf conflict (eg, "How often did you see dead or dying animals?").

9. The Miss-PTSD, a 35-item self-report questionnaire of military-related PTSS (50). We used the original Miss-PTSD rather than an Operation Desert Storm revision (14) because of its wider use and better psychometric validation (51) with Persian Gulf War veterans (23).

Statistical Analyses

Univariate logistic regression analyses were conducted initially to identify potential variables for subsequent multivariate analyses and to determine if war zone trauma exposure and PTSS were associated with case status on an unadjusted basis. Subsequently, all variables with an unadjusted odds ratio statistically significant at the $p < .05$ level were entered into a stepwise multivariate logistic regression model. The number for cases of 237 was sufficient to achieve a case/measure ratio greater than 10:1 when all 14 Health Screening System scores and six demographic variables were entered into a multivariate model. Entry of independent variables into the multivariate logistic model was conducted through a forward stepwise procedure based on chi-squared (X^2) tests of the significance of log likelihood ratios. OR and 95% CI for each variable were calculated after adjusting for the contributions of all other variables, and the utility (ie, sensitivity, specificity, and positive and negative predictive power) of the final model was calculated.

To test the classificatory accuracy and stability of the resultant model, the sample was divided into two randomly selected halves. A stepwise multivariate solution was obtained with identical variables for each half sample separately. Variable contributions were evaluated by OR and 95% CI calculations, and classificatory accuracy by identification of true "hits" and false "misses" followed by calculation of positive and negative predictive power. The resulting model for each half sample was then applied to the other half sample, resulting in two parallel cross-validation iterations.

RESULTS

To ensure that the study findings were not primarily because of overlap between the PTSS symptoms and cognitive/psychological criteria symptoms, we conducted separate analyses excluding participants who were classified as cases, solely based on cognitive or psychological symptoms ($N = 89$). Results of these analyses did not differ in pattern or strength from results based on the full sample, therefore, only results from the full-sample analyses are reported.

Univariate Regression Analyses

Two of six demographic variables were associated significantly ($p < .05$) with case status in unadjusted univariate logistic regression analyses: younger age, $X^2[1, N = 349] = 7.48$, OR = 0.96, 95% CI, 0.93–0.99, and lower education level, $X^2[1, N = 349] = 10.74$, OR = 0.82, 95% CI, 0.73–0.93 (Tables 2 and 3). Gender, ethnicity, marital status, and income were unrelated to case or control status.

Thirteen of 14 psychological variables were significantly associated with case (vs. control) status in unadjusted univariate logistic regression analyses (Table 3). Cases reported statistically significantly higher levels of: a) somatic distress and preoccupation (higher MMPI-2 Hs and Hy scores); b) health problems, fatigue and pain, and deterioration in physical health in the past year (lower SF-36-GH, V, P, CH subscale scores); c) global (ie, SCL-90-R GSI; SF-36-MH subscale) and specific (ie, BDI depression and/or BAI anxiety) psychiatric distress, d) negative impact from recent life events; and e) war zone trauma exposure (ie, CES-R) and PTSS (ie, Miss-PTSD).

TABLE 2. Demographic and Military Service Characteristics of Participants Classified as Unexplained Illness Cases vs. Asymptomatic Controls

	Cases $n = 237$	Controls $n = 112$
Mean age (SD)	31.8 (6.69)	34.2 (9.31)
Mean education (SD)	13.3 (1.73)	14.0 (2.2)
Race (%)		
White	91.3	92.3
Black	2.7	1.1
Hispanic	3.3	4.4
Native American	0.5	1.1
Asian/Pacific Islander	2.1	1.1
Gender (%)		
Female	17.4	15.0
Male	82.6	85.0
Military service (%)		
Navy	21.6	36.3
Air Force	5.0	8.0
Marines	19.1	16.8
Army	42.3	28.3
National Guard	9.5	10.6

TABLE 3. Univariate Logistic Regression Tests for Differences Between Unexplained Illness Cases vs. Asymptomatic Controls

Measure	Cases M (SD) n = 237	Control M (SD) n = 112	*p*-Value	Odds ratio	95% CI
Age	31.8 (6.69)	34.2 (9.3)	.006	.96	(.93–.99)
Education	13.3 (1.7)	14.0 (2.2)	.0013	.82	(.73–.93)
SF-36-GH	57.5 (21.3)	83.5 (14.8)	<.0001	.93	(.91–.94)
SF-36-V	40.3 (19.6)	67.9 (17.4)	<.0001	.93	(.91–.94)
SF-36-P	61.0 (20.8)	79.6 (17.5)	<.0001	.95	(.94–.97)
SF-36-CH	44.9 (19.6)	53.6 (17.4)	.0002	.98	(.97–.99)
SF-36-MH	64.1 (18.9)	82.2 (13.4)	<.0001	.93	(.92–.95)
MMPI2-Hs	66.3 (13.5)	49.1 (8.5)	<.0001	1.15	(1.11–1.18)
MMPI2-Hy	60.9 (13.2)	48.2 (8.5)	<.0001	1.12	(1.09–1.16)
BDI	12.4 (7.4)	3.7 (4.2)	<.0001	1.36	(1.27–1.46)
BAI	10.6 (7.5)	3.0 (3.3)	<.0001	1.40	(1.29–1.53)
SCL-90R-GSI	90.84 (55.30)	47.65 (44.67)	<.0001	1.02	(1.01–1.02)
SASSI2	1.80 (.40)	1.90 (.33)	.08	0.56	(0.30–1.07)
LES-NI	1.5 (.73)	1.1 (.87)	<.0001	0.48	(.36–.65)
CES-R	76.4 (19.2)	63.2 (12.9)	<.0001	1.05	(1.04–1.07)
Miss-PTSD	73.0 (17.0)	53.7 (9.9)	<.0001	1.13	(1.11–1.16)

Multivariate Regression Analyses

In a multivariate logistic regression model, four variables were identified as correlates of case status (Table 4). Two of the four variables reflect somatic distress, either directly (ie, MMPI-2-Hs) or indirectly (ie, BDI)—subsequent analyses (not reported here) indicated that the contribution of BDI to the model was determined largely by physical fatigue items within the scale. The other multivariate correlates were the Miss-PTSD and CES-R. The final multivariate model produced a significant fit, $X^2[16, N = 349] = 222.85$, $p < .0001$. The model's utility was reflected in an overall correct classification of 86% of participants, with greater success in identifying cases (0.90 sensitivity, 0.89 positive predictive power) than controls (0.77 specificity, 0.79 negative predictive power).

Subsequent cross-validation analyses with two randomly selected half samples confirmed the model's power while identifying two replicable correlates of case status: The MMPI Hs (OR[95% CI] = 1.16[1.09–1.24], $p < .0001$, and 1.10[1.05–1.15], $p = .0002$); and the Miss-PTSD (OR[95% CI] = 1.06[1.0–1.13], $p = .0599$, and 1.08[1.03–1.13], $p = .0012$). A final multivariate model for each half-sample produced a significant fit, $X^2[16, N = 174] = 123.4$, $p < .0001$, and $X^2[16, N = 175] = 97.3$, $p < .0001$, respectively. Each model's utility was comparable with that achieved with the full sample, achieving overall correct classification rates of 83% and 87% for the initial classification model when that model was cross-validated on the other subsample. The utility statistics for each subsample's initial model and for the cross-validation of each model were comparable with those for the full sample. Classification rates for the subsamples were 0.87 and 0.92 for sensitivity, 0.88 and 0.89 for positive predictive power, 0.73 and 0.83 for specificity, and 0.75 and 0.77 for negative predictive power.

TABLE 4. Significant Findings From a Multivariate Logistic Regression Test of Differences Between Unexplained Illness Cases vs. Asymptomatic Controls

Variable	Odds Ratio (95% CI)	SE	*p*-Value
MMPI2-Hs	1.12 (1.08–1.16)	.019	<.001
BDI	1.16 (1.05–1.27)	.049	.003
CES-R	1.03 (1.01–1.06)	.012	.007
Miss-PTSD	1.06 (1.02–1.11)	.021	.004

DISCUSSION

Findings from a previous report with these data sets suggested that psychological factors play a role in Persian Gulf veterans' unexplained illnesses (52). The present analyses showed that posttraumatic symptomatology was a robust correlate of Gulf War unexplained illness, independent of the effects of somatic or psychiatric distress, health impairment, and subtraumatic stress. War zone trauma also was associated with unexplained illness, but in comparison with PTSS was a less robust correlate in cross-validation analyses. Physical health problems have been shown to be associated with war trauma exposure in Persian Gulf War (19) and earlier era (28–30, 34–37, 53) veterans. Given the results of prior studies showing that PTSS mediates trauma's effect on health outcomes with other

military samples (30, 35), additional research should test whether PTSS mediates the relationship between trauma exposure and physical health problems in Persian Gulf War veterans.

Haley (23) argues that PTSD in Persian Gulf veterans is a clinical or statistical artifact. Like most studies cited by Haley, we found that PTSS levels were generally too low to qualify for a full PTSD diagnosis: our sample's Miss-PTSD score distribution ranged from 37 to 135, with scores generally well below the levels found with PTSD-diagnosed or psychiatric treatment seeking Vietnam veterans (ie, 70–175; 36). Thus, it seems unlikely that full syndromal PTSD accounts for Persian Gulf veterans' illnesses (20, 21). However, our findings suggest that the posttraumatic symptoms are associated with Persian Gulf veterans' unexplained illnesses, and that this association cannot be explained by the effects of psychiatric symptoms, physical health symptoms, functional impairment, or recent life stressors.

PTSD often is comorbid with other psychiatric disorders (27, 36), therefore, the effect attributed to trauma or PTSS might be due to other psychiatric disorders (3, 21) or to psychiatric symptoms (54, 55)—both of which tend to be associated with physical health complaints and treatment-refractory physical illness. We found that both global and specific indices of psychiatric distress were related to case status only on an unadjusted univariate basis, with one exception—depression. Depression often is comorbid with PTSD (27, 36), and has been linked to trauma exposure in women (56). On closer examination, however, we found that it was the BDI's symptoms of fatigue, and not affective symptoms per se, which accounted for its contribution. Similarly, Wolfe et al. (21) found that depression, although prevalent in Gulf War veterans, did not account for health symptoms. Thus, converging findings suggest that it is PTSS and not other psychiatric symptomatology that plays a role in Gulf War veterans' health problems.

Somatization is a controversial explanation for unexplained physical illness (57–59). Somatic distress could be a byproduct of psychological distress, but it is equally possible that both somatic and psychiatric distress are byproducts of primarily physiogenic illnesses. Veterans and their healthcare providers do not want Persian Gulf War veterans' physical symptoms to be mistakenly attributed to psychogenic causes (2, 21), because this could lead to the stigmatizing of ill veterans as "psychiatric somatizers" who react poorly to stress. This could result in a tragic failure to detect and treat possible neurotoxicant-related pathophysiology (23). Our findings do not support somatization as an explanation for unexplained health problems. We found that a psychogenic vulnerability to physical symptoms because of stress (ie, MMPI Hy) was not a robust correlate of case status. We also found that case status was not robustly associated with subjective health complaints on the SF-36. The only index of somatic distress that was strongly associated with case status was the MMPI Hs, which reflects the understandable discomfort of experiencing physical symptoms independent of stress reactivity (44).

Two demographic variables emerged as correlates of case status. Education was inversely related to case status, consistent with previous studies (19, 21, 35, 37). Unlike previous studies (28, 60, 61), we found that older age was a protective factor mitigating against unexplained physical illness. The finding on age was not particularly robust, and in our sample, may be explained because the age range did not include the cohort of older adults (ie, >55) for whom age increasingly is associated with declining health (35), as well as by the positive correlation between age and education. Neither education nor age contributed significantly to the multivariate model.

Our findings do not address directly the issue of biological causal factors for Persian Gulf veterans' medically documented but unexplained symptoms. Instead, we found that psychological factors specifically related to trauma play a role in what also may be valid biological concerns. Although it is possible that "the excess of symptoms in deployed veterans could be due to a wide range of...medical or psychiatric etiologies" (23) other than trauma and PTSS, we ruled out several specific alternative hypotheses. Moreover, concerning other potential medical etiologies, the detailed clinical examinations and an expert panel review of examination findings made it possible to rule out known medical diagnostic causes. Future research on the pathophysiology of unexplained illness attributed to Persian Gulf military service may reveal medical factors not yet recognized. However, it still seems advisable to evaluate PTSS and war zone trauma exposure as potential contributory factors given their documented links to medical illness (33) and illness-related functional impairment (29–31, 35, 36, 39, 62). Several psychobiological mechanisms may account for a linkage between PTSS, and physical illness: neuroendocrine or immunologic dysregulation, biological sensitization, and pathophysiological adaptations to traumatic stress at the structural or cellular levels in the peripheral and central nervous systems or the brain (33).

Several methodological precautions were taken, including controlling for selection biases with a population-based case-control design (4), with a sufficient sample size (23) to limit both type I (ie, false-positive)

and type II (ie, false-negative) error and a three-stage analytic strategy that further reduced the risk of type I error by filtering findings using univariate, multivariate, and cross-validational procedures. Nevertheless, several limitations should be borne in mind. Retrospective assessment of war trauma may be inaccurate, eg, an artifact of PTSS or psychiatric symptomatology (23). Objective documentation of trauma exposure is as difficult, yet also as essential, as is that for chemical exposure (9, 62, 63). Our use of a cross-sectional rather than longitudinal design does not allow us to address the questions of etiology or prospective risk. The representation of participants of nonwhite ethnicity, while comparable to that of other large Persian Gulf War cohorts (5, 13) and representative of the ethnocultural mix of veterans at the study site, is lower than that of the overall national cohort. Although the sample included a mix of officers and enlisted personnel, our analyses did not include military rank as a variable. Prospective studies with more diverse samples and a fuller specification of variables are needed to address these limitations.

To conclude, our findings indicate that the severity of PTSS reported by Persian Gulf War veterans was robustly associated with the presence of persistent somatic problems that could be medically documented but not diagnostically explained. We focused on PTSS because it is more common in this population and subsyndromal PTSD has been shown to be a risk for physical health problems (19–24, 29). Although the exact nature of the links between PTSS and unexplained somatic problems remains to be determined in prospective studies, screening and assessment of traumatic exposure and PTSS seem to be important elements in the care of patients who report the kinds of disturbing and difficult to explain symptoms like those suffered by thousands of Persian Gulf veterans.

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