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Deployment, Combat, and Risk of Multiple Physical Symptoms in the US Military: A Prospective Cohort Study

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ABSTRACT

Purpose: Multiple physical symptoms (MPS) have historically been observed following deployment to a combat zone and are often disabling in nature. This study examined longitudinal trends in MPS status and its relationship to deployment in US military service members.

Methods: Using longitudinal data from panel 1 participants in the Millennium Cohort Study ($n = 76,924$), MPS status was assessed at 3 time points (2001–2008) using the 15-item Patient Health Questionnaire. Probability of reporting MPS was analyzed using mixed-effects multinomial logit regression, with time and deployment experience as main explanatory variables.

Results: After adjustment for demographic, military, and health characteristics, service members who deployed with combat were significantly more likely to report MPS at each time point compared with those not deployed (odds ratio [OR] and 95% confidence interval [CI] for wave 1 = 1.49 (1.47, 1.52), wave 2 = 1.73 (1.69, 1.78), wave 3 = 2.08 (2.03, 2.12)), and those who deployed without combat (OR and CI for wave 1 = 2.66 (2.59, 2.74), wave 2 = 1.81 (1.75, 1.87); wave 3 = 1.68 (1.63, 1.74)).

Conclusions: Longitudinal trends indicate that the probability of reporting MPS has increased consistently over time only for those deployed, regardless of combat experience.

Keywords: signs and symptoms, military medicine, military personnel, veterans health, cohort studies

Abbreviations: DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition*; MPS, multiple physical symptoms; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; PCL-C, PTSD Checklist–Civilian Version; PHQ, Patient Health Questionnaire; PTSD, posttraumatic stress disorder.

Physical symptom complaints account for more than half of all outpatient encounters in general medical practice [1,2] and are associated with significantly higher health care utilization and costs [3,4], comorbidity [5,6], health status impairment and disability [7-9], and mortality [10]. As in civilian general practice, physical symptoms are commonly reported by patients seeking care in the US Military Health System. According to 2012 surveillance of all active component service members, “symptoms, signs, and other ill-defined conditions” diagnoses represent a leading category for medical encounters and number of individuals affected [11,12]. Given the high occurrence in the Military Health System and the demonstrated relationship to negative health outcomes, physical symptoms represent an important health priority for the US military to promote force fitness and retention.

Historically, multiple physical symptoms (MPS) have been observed following deployment to a combat zone, typically in constellations of poorly defined somatic complaints [13-16]. Following the 1991 Gulf War, a significant proportion of service members reported unexplained postwar symptoms, characterized popularly as Gulf War syndrome and later described more rigorously as chronic multisymptom illness [17-20]. However, for reasons yet to be identified, the association between deployment and MPS has been inconsistent [21-27].

After nearly 15 years of conflict in Iraq and Afghanistan, careful and systematic efforts to understand MPS and their relationship to deployment over time among military personnel are sparse. The purpose of this study was to examine the relationship of deployment and combat exposure to subsequent MPS in a longitudinal sample of active duty, Reserve, and National Guard personnel from all branches of the US military.

METHODS

Study population

The Millennium Cohort Study, the largest longitudinal military study, was launched in 2001 to assess the long-term health effects of military service [28,29]. The population for the current study included the first panel of participants (panel 1) of the Millennium Cohort Study, a probability-based sample of all US military personnel serving as of October 2000, with oversampling for women, members of the Reserve or National Guard, and those who had previously deployed to Southwest Asia, Bosnia, or Kosovo. Data from the first 3 waves of Millennium Cohort data collection were utilized: wave 1 (July 2001–June 2003), wave 2 (June 2004–February 2006), and wave 3 (June 2007–December 2008).

Primary outcome variable: MPS status

MPS status was assessed using the 15-item Patient Health Questionnaire (PHQ; see Figure 1) [30,31]. The first 13 items are rated on a 0 to 2 scale for the past month; the remaining 2 items, sleeping trouble and fatigue, are rated on a 0 to 3 scale for the past 2 weeks and were adapted to the 0 to 2 response scale using the validated approach of Kroenke and colleagues [31,32]. Using Millennium Cohort data the Somatoform Disorders subscale (which composes 13 of the 15 items from the PHQ-15) was found to have satisfactory internal consistency (Cronbach's $\alpha = 0.76$) [33]. This method yields total scores ranging from 0 to 30 for women and 0 to 28 for men. In the current study, we derived MPS status (positive or negative) based on a cut point score of ≥ 10 , which represents a moderate to high level of somatic symptom severity [31].

Main explanatory variable: Deployment group

Deployment in support of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) was derived from Department of Defense personnel files obtained from the Defense Manpower Data Center and based on receiving imminent danger pay, hardship duty pay, or combat zone tax exclusion benefits. Participants were classified as having recent deployment if records indicated at least 1 day of deployment in support of OIF/OEF in the 3-year interval prior to each respective wave survey date. Among those deployed, combat-related experience was based on at least 1 affirmative response to questions about witnessing death, trauma, injuries, prisoners of war, or refugees in the last 3 years. The main explanatory deployment group variable classified individuals as 1) not deployed, 2) deployed without combat experience, or 3) deployed with combat experience. Deployment group was defined as a time-varying characteristic measured at each wave with an observation window of 3 years prior to the respective wave.

Covariates

Demographic and military-specific data were obtained at baseline from electronic personnel files maintained by the Defense Manpower Data Center and included sex, date of birth, race/ethnicity, military rank, service component, and service branch.

Depression was assessed as a time-dependent variable using the 9 depression items of the PHQ [30,34] and a question that asked participants if they had ever (baseline) or in the last 3 years (wave 2 and 3) been diagnosed with depression by a health professional. The PHQ items were scored using an algorithm that corresponds to the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV) [35] depression diagnosis criteria. For each wave,

participants who screened positive for depression on the PHQ items or reported a depression diagnosis were classified as having depression.

Posttraumatic stress disorder (PTSD) was assessed as a time-dependent variable using the 17-item PTSD Checklist–Civilian Version (PCL-C) [36] and a question that asked participants if they had ever (baseline) or in the last 3 years (waves 2 and 3) been diagnosed with PTSD by a health professional. The PCL-C items were scored using an algorithm that corresponds to the DSM-IV PTSD diagnosis criteria [35]. For each wave, participants who screened positive on the PCL-C or reported a PTSD diagnosis were classified as having PTSD.

Panic or other anxiety syndromes was assessed as a time-dependent variable using 15 panic items and 6 generalized anxiety items from the PHQ. For each wave, responses were classified as a positive screen if they met PHQ-defined criteria for panic and/or other anxiety [30,37].

A count of participants' reported physical conditions was assessed as a time-dependent continuous variable derived from self-report of ever (baseline) or in the last 3 years (waves 2 and 3) being diagnosed with any of 24 serious or chronic physical conditions [38].

Statistical analysis

Descriptive analyses were conducted to compare demographic and behavioral characteristics between the 3 outcome categories (MPS positive, MPS negative, or attrition [death or dropout between 2 successive waves]). Unadjusted analyses, including chi-square tests, were used to calculate measures of association of MPS with deployment, occupational, demographic, and behavioral characteristics.

In light of existing theories on deployment and mental health, we specified a set of control variables in the regression analysis to adjust for possible confounding effects in

describing longitudinal trajectories of MPS, including 5 sociodemographic control factors (age, sex, race/ethnicity, pay grade, and service branch) and 4 time-varying health variables (depression, PTSD, anxiety/panic, and number of physical conditions); all control variables were rescaled to be centered at sample means for analytic convenience. Prior deployment and cumulative duration of deployment were both considered as potential predictors on the association of interest (i.e., MPS and deployment); however, these variables did not have any additive effect on MPS when the present control variables are considered, and thus were removed from the model. A combination of time and time $\times$ time, the so-called quadratic polynomial time function, as well as time $\times$ deployment interaction were considered for capturing the changing pattern of the longitudinal trajectories in MPS. Because the outcome variable consisted of 3 nominal levels, a mixed-effects multinomial logit regression model was performed using the probability of falling in a given MPS category, with time and deployment experience as the main explanatory variables. Given 3 response levels, we applied the mixed-effects multinomial logit model on 2 logit components, using time, deployment group, and other covariates as the independent variables. Using the adaptive Gaussian quadrature, both the fixed and random effects for the mixed-effects multinomial logit model were estimated. The impact of missing cases on MPS status was adequately handled by applying the empirical Bayesian approach in longitudinal data analysis [39]. With respect to dropouts at waves 2 and 3, mixed-effects modeling techniques are robust to missing data in derivation of parameter estimates [40].

The conditional odds ratio was computed from these models using the predicted probabilities involved in the 2 odds terms, rather than directly from the antilog transformation of the corresponding regression coefficient. The statistical procedures for computing the predicted

probabilities, the conditional odds ratios, and their respective standard errors, are described in Liu and Engel [40].

Data management and statistical analyses were performed using SPSS statistical software, version 20 (IBM, Armonk, NY), and SAS software, version 9.3 (SAS Institute Inc., Cary, NC).

RESULTS

Of the 76,924 eligible participants who completed the wave 1 survey, 54,954 (71%) completed the wave 2 follow-up survey and 54,728 (71%) completed the wave 3 follow-up survey. Observations (each participant was supposed to have 3 observations) were excluded from the analysis if MPS status was indeterminable (i.e., they did not provide complete PHQ-15 responses; $n = 986$ for wave 1, 972 for wave 2, and 746 for wave 3). An additional 4 participants lacked any useable data in fitting the longitudinal model and were thus excluded at baseline, resulting in a total of 75,934, 53,982, and 53,982 observations available for analysis at each respective wave. Characteristics of the Millennium Cohort participants at baseline (wave 1) are presented in Table 1. Of the participants included in the descriptive analysis, 8.7%, 9.9%, and 12.5% were characterized as having MPS at waves 1, 2, and 3, respectively.

In the application of the mixed-effects multinomial logit model, individuals who deployed but whose combat experience status was indeterminable (i.e., they did not provide responses to respective exposure questions; waves 1 ($n = 46$), 2 ($n = 241$), and 3 ($n = 135$), respectively) were included in the deployed without combat group after multiple analyses indicated that there was no difference in the analytic results between this method and exclusion. The inclusion of time $\times$ time and time $\times$ deployment interactions did not contribute significantly

to the model fit, and thus were removed. The remaining variables from Table 1 and the random effects were all very strongly statistically significant in the mixed-effects multinomial logit model and included as covariates in subsequent models.

Figure 2 displays the probabilities of MPS by deployment group over the 3 waves. For those not deployed, the probability of MPS, or MPS prevalence at each wave, is not distinctly associated with time since it stabilizes at about 7%. For those deployed with combat experience, the probability of MPS at baseline is about 10%, considerably higher than for the other 2 groups, and then it increases steadily to about 11% in 2004 and about 13% in 2007. The pattern for those deployed without combat is similar to those who deployed with combat, though at a much lower level. More specifically, MPS prevalence for this deployment group increases from 4% in 2001 to about 7% in 2004 and further to about 8% in 2007.

Table 2 presents the conditional MPS odds ratios and their respective 95% confidence intervals for 3 deployment groups at each wave. The adjusted odds ratios for the 3 deployment groups at the 3 waves are all statistically significant. The conditional odds ratios for those deployed with combat experience versus each of the other 2 deployment groups are all well above unity (range 1.5 – 2.7), demonstrating consistent and robust elevated risk of developing MPS in those deployed with combat experience. The largest odds ratio (odds ratio [OR] = 2.7) is found at baseline (wave 1), suggesting a 2.7 times increase in the individual odds of having MPS for a person deployed with combat experience compared with those who deployed without combat experience, other covariates being constant at average conditions. Between those deployed without combat and those not deployed, the pattern is less consistent. At the first 2 time points, the MPS conditional odds ratios are smaller than unity, thus highlighting lower individual odds of having MPS among those deployed without combat (OR = 0.56 at wave 1 and 0.96 at

wave 2); at the third time point, however, the pattern is reversed, with higher odds among those deployed without combat (OR = 1.23).

DISCUSSION

Using data from the largest and most extensive longitudinal epidemiologic military health survey conducted to date, these analyses demonstrate a consistent and robust longitudinal association between service members' reports of combat experience during deployment and the occurrence of MPS. Interestingly, deployment without combat experience was not consistently associated with an increase in risk of MPS, suggesting the most important risk factor was combat exposure. In addition to higher odds of MPS among the combat-deployed group, we also found that the probability of MPS increased over time for both combat and non-combat-deployed groups, a trend that was not observed among nondeployed personnel. While we did not examine number of deployments or cumulative duration of deployment in this study, increases over time may indicate that the sustained conflicts may be giving rise to more complaints of physical symptoms among those who deploy. It is certainly conceivable that analyses including later (i.e., post-2007) waves of data from this cohort will demonstrate an increased risk of MPS for non-combat deployment as well, given the longitudinal trend of probabilities observed in the current analysis.

The findings from this study are consistent with a recent examination of chronic multisymptom illness in Millennium Cohort Study participants [23], but they contradict a second study by Quartana et al. [24] of US soldiers deployed to Iraq that found only an indirect relationship between combat and MPS through PTSD, depression, and insomnia. The current findings that increased MPS reporting was associated with combat experience even after

adjusting for psychological morbidity may reflect sample differences (e.g., population-based vs. only Army, average deployment length), methodological differences (e.g., length of follow-up window, MPS classification), and sample size (<600 vs. approximately 75,000). These results stand in contrast to the early Iraq and Afghanistan war findings among British and Danish military personnel, in which conflict participation was not associated with subsequent physical symptoms [21,22]. This may be attributable to the higher levels of combat exposure among the US deployed troops, a finding noted in similar comparisons of PTSD rates between US and UK militaries [41]. Our study findings would suggest that generally lower levels of combat exposure during OIF/OEF deployments could lead to little or no elevation in conflict-related MPS in these troops. This proposition is supported by a 2014 study that directly compared the health outcomes of US and UK military personnel deployed to Iraq in 2007–2008 and found no difference in MPS reporting when stratified by combat exposure level [42].

The longitudinal increases in probabilities of developing MPS associated with non-combat and combat deployment found in this study may appear small, but they have significant implications when applied across an entire military population of over 2.2 million active duty, Reserve, and National Guard members [43]. Several studies have shown that MPS is associated with significant increases in morbidity, mortality, and health care use [3-10], suggesting that the increase in MPS observed among deployed individuals may not only have adverse long-term effects on service member health and well-being, but also on the entire force readiness and later the civilian work force as these individuals separate from military service. Indeed, despite the rigorous health criteria required for entrance into the military, there is evidence that veterans and military service members are experiencing physical health declines faster than age-adjusted population norms in the years following deployment [44].

Given the long history of postwar physical symptom syndromes among war veterans and the common and disabling nature of physical symptoms in general, the Military Health System should consider care models that can maximize functioning in service members who return from combat and develop these symptoms. Many experts have recommended shifting the clinical paradigm away from focusing solely on etiologic cause and toward encouraging providers to consider a biopsychosocial approach to symptom-focused management [45-47]. Models such as stepped care and collaborative care have been shown to be effective in this respect [48-51]. An emphasis on early identification of symptoms and engagement in care following deployment may also minimize declines in physical health associated with delay in visiting a treatment clinic [44].

A potential limitation of the current study is that the population consists of a sample of respondents to the Millennium Cohort questionnaire and may not be representative of the entire military population. However, investigation of several key potential biases in the Millennium Cohort has found the Cohort to be mostly representative, specifically with respect to health care use prior to study enrollment among responders compared with nonresponders, with reliable reporting of data by study participants [33,52-55]. Additionally, a previous study examining weighting for nonresponse among panel 1 members of this cohort indicated that prevalence rates of key outcomes are comparable to results of unweighted analysis [56]. A second limitation of this study is that we cannot be certain of the temporal relationship between deployment and symptoms, given that MPS status can change in the three-year interim between waves. Third, we cannot ascertain whether MPS can be attributed to an underlying condition (i.e., whether they are “medically unexplained”), although our statistical model did adjust for a range of serious and chronic physical conditions.

Despite these limitations, there are many strengths of this study. The large sample size of this study allows for robust analyses of MPS. This study was one of the first to prospectively analyze MPS in relation to the recent operations in Iraq and Afghanistan among US military personnel, allowing elucidation of the temporal sequence. This cohort consists of participants from all military services and includes active duty, Reserve, and National Guard members, as well as service members who have left the military. Methodologically, this analysis is the first study to focus on military personnel that derives the predicted probabilities, conditional effects, and conditional odds ratios from an integrated statistical framework.

CONCLUSIONS

The findings of this study indicate that combat deployment to Iraq and Afghanistan is associated with an increased risk of developing MPS in US service members compared with non-combat deployment or nondeployment. Additionally, longitudinal trends demonstrate a consistent increase in probabilities of developing MPS over time for those deployed, regardless of combat experience. This study offers a glimpse into the relationship between deployment and MPS; future systematic efforts to understand MPS among military personnel will provide useful data for developing health policies and programs, especially for those who seek care with deployment-related health concerns. Intensified efforts to understand MPS in the military may also foster trust between service members and the government agencies that provide benefits and health care for them.

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Table 1. Characteristics of Millennium Cohort Participants by Multiple Physical Symptoms
Status at Baseline

	Baseline (Wave 1)		
	Total Sample (<i>n</i> = 75 938)	MPS Negative (<i>n</i> = 69 317)	MPS Positive (<i>n</i> = 6621)
	<i>N</i> (%) or <i>M</i> (SD)	<i>N</i> (%) or <i>M</i> (SD)	<i>N</i> (%) or <i>M</i> (SD)
Baseline age, years	33.76 (9.15)	33.88 (9.13)	32.46 (9.26)
Sex, male	55 659 (73.3)	52 216 (75.3)	3443 (52.0)
Race/ethnicity			
White, non-Hispanic	52 892 (69.7)	48 654 (70.2)	4238 (64.0)
Black, Non-Hispanic	10 388 (13.7)	9094 (13.1)	1294 (19.6)
Other	12 596 (16.6)	11 513 (13.1)	1085 (16.4)
Service branch			
Army	35 924 (47.3)	32 091 (46.3)	3833 (57.9)
Navy	13 257 (17.5)	12 198 (17.6)	1059 (16.0)
Marine Corps	3837 (5.1)	3494 (5.0)	343 (5.2)
Air Force	22 098 (29.1)	20 766 (30.0)	1332 (20.1)
Coast Guard	822 (1.1)	768 (1.1)	54 (0.8)
Military pay grade			
Enlisted	58 430 (76.9)	52 405 (75.6)	6025 (91.0)
Officer	17 508 (23.1)	16 912 (24.4)	596 (9.0)
Deployed to OIF/OEF			
No	71 787 (94.5)	65 404 (94.4)	6383 (96.4)
Yes	4151 (5.5)	3913 (5.6)	238 (3.6)
Number of physical conditions ^a	0.51 (1.67)	0.45 (1.64)	1.11 (1.83)
Depression ^b			
No	68 417 (90.9)	64 479 (93.8)	3938 (60.4)
Yes	6867 (9.1)	4285 (6.2)	2582 (39.6)
PTSD ^c			
No	69 881 (94.5)	65 491 (96.8)	4390 (69.4)
Yes	4082 (5.5)	2150 (3.2)	1932 (30.6)
Anxiety and/or panic ^d			
No	72 666 (97.1)	67 608 (98.9)	5058 (78.1)
Yes	2197 (2.9)	776 (1.1)	1421 (21.9)

Abbreviations: DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition*; OEF/OIF, Operation Enduring Freedom/Operation Iraqi Freedom; PHQ, Patient Health Questionnaire; PTSD, posttraumatic stress disorder.

^a Based on self-report of ever being diagnosed with any of 24 listed serious and chronic physical conditions (angina, asthma, Crohn's disease, coronary heart disease, chronic bronchitis, cirrhosis, cancer, diabetes, emphysema, heart attack, hepatitis A, hepatitis B, other hepatitis, significant hearing loss, hypertension, kidney failure requiring dialysis, lupus, multiple sclerosis, neuropathy-caused reduced sensation in hands or feet, pancreatitis, rheumatoid arthritis, stroke, ulcerative colitis or proctitis, stomach/duodenal/peptic ulcer); *n* = 75 768.

^b Based on the PHQ using standard diagnostic algorithm for depression and/or self-reported depression diagnosis by a health professional; *n* = 75 284.

^cBased on the PTSD Checklist–Civilian Version, using DSM-IV sensitive diagnostic criteria and/or self-reported PTSD diagnosis by a health professional; $n = 73\,963$.

^dBased on the PHQ using standard diagnostic algorithm for anxiety and/or panic disorder; $n = 74\,863$.

Table 2. Pairwise Conditional Odds Ratios and 95% Confidence Intervals of Multiple Physical Symptoms for Deployment Status at Three Time Points^{a,b}

Deployment Status	Wave 1		Wave 2		Wave 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Deployed with combat (ref = not deployed)	1.49	1.47, 1.52	1.73	1.69, 1.78	2.08	2.03, 2.12
Deployed without combat (ref = not deployed)	0.56	0.54, 0.58	0.96	0.95, 0.96	1.23	1.23, 1.24
Deployed with combat (ref = deployed without combat)	2.66	2.59, 2.74	1.81	1.75, 1.87	1.68	1.63, 1.74

Abbreviations: CI, confidence interval; OR, odds ratio.

^a All *P* values <0.05, two-sided.

^b Model was adjusted for the following demographic and health variables: age, sex, race/ethnicity, rank, service branch, depression, posttraumatic stress disorder, anxiety/panic, and number of physical conditions.

During the last 4 weeks, how much have you been bothered by any of the following problems?	Not Bothered	Bothered a Little	Bothered a Lot	
Stomach pain	☐	☐	☐	
Back pain	☐	☐	☐	
Pain in your arms, legs, or joints (knees, hips, etc.)	☐	☐	☐	
Pain or problems during sexual intercourse	☐	☐	☐	
Headaches	☐	☐	☐	
Chest pain	☐	☐	☐	
Dizziness	☐	☐	☐	
Fainting spells	☐	☐	☐	
Feeling your heart pound or race	☐	☐	☐	
Shortness of breath	☐	☐	☐	
Constipation, loose bowels, or diarrhea	☐	☐	☐	
Nausea, gas, or indigestion	☐	☐	☐	
Women only: Menstrual cramps or other problems with your periods	☐	☐	☐	
Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several Days	More than half the days	Nearly every day
Trouble falling or staying asleep or sleeping too much	☐	☐	☐	☐
Feeling tired or having little energy	☐	☐	☐	☐

Figure 1.

Figure 2.