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Assessment of Plasma C-Reactive Protein as a Biomarker of PTSD Risk

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Abstract

Importance—Post-traumatic stress disorder (PTSD) has been associated in cross-sectional studies with peripheral inflammation. It is not known whether this observed association is due to

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PTSD predisposing to inflammation (as sometimes postulated) or to inflammation predisposing to PTSD.

Objective—To determine whether plasma concentration of the inflammatory marker, C-reactive protein (CRP), helps predict future PTSD symptoms.

Design and Setting—The Marine Resiliency Study (MRS), a prospective study of ~2,600 war zone-deployed Marines, during which PTSD symptomatology and various physiological and psychological parameters were determined pre-deployment and at approximately three and six months following a seven month deployment.

Participants—Subjects were recruited from four all-male infantry battalions imminently deploying to a war zone. Participation was requested of 2,978 subjects, of whom 2,610 (87.6%) consented and 2,555 (85.8%) were included in the current analysis. Post-deployment data on combat exposure were included from 2,215 subjects (86.7% of the 2,555 included subjects), and on PTSD symptomatology from 1,861 (72.8%) and 1,609 subjects (63.0%) at three and six months following deployment, respectively.

Main Outcome Measure(s)—PTSD symptoms three months after deployment, assessed by the Clinician Administered PTSD Scale (CAPS).

Results—We determined the effects of baseline plasma CRP concentration on post-deployment CAPS using Zero-inflated negative binomial regression (ZINBR), a procedure designed for distributions, such as CAPS in this study, which have an excess of zeros in addition to being positively skewed. Adjusting for baseline CAPS, trauma exposure, and other relevant covariates, we found baseline plasma CRP concentration to be a highly significant overall predictor of post-deployment CAPS scores (p=0.002): each 10-fold increment in CRP concentration was associated with an odds ratio of non-zero outcome (presence vs. absence of any PTSD symptoms) of 1.51 (95% CI, 1.15–1.97; p = 0.003) and a fold increase in outcome when non-zero (extent of symptoms when present) of 1.062 (95% CI, 0.99–1.14; p = 0.086).

Conclusions and Relevance—A marker of peripheral inflammation, plasma CRP, may be prospectively associated with PTSD symptom emergence, suggesting that inflammation may predispose to PTSD.

Introduction

Observational studies largely support an association of post-traumatic stress disorder (PTSD [1]) with increased peripheral inflammation (for a recent review of the overall evidence, see [2]). For instance, one large cross-sectional community-based study found that patients with PTSD had about twice the odds of those without this disorder of elevation in the inflammatory marker, C-reactive protein (CRP) [3]. Similarly, while some case-control studies have had negative or equivocal findings (e.g., [4,5]), in most such studies PTSD cohorts have had significantly greater plasma levels of CRP or IL-6, among other inflammatory markers, than did controls (e.g., [6–11]). This association is of prognostic significance because low grade inflammation is likely involved in the pathophysiology of the metabolic syndrome [12–14], a major cardiovascular risk factor [15,16]; and, indeed, PTSD has been found to be associated with this syndrome [17–24].

It is plausible that the observed association between PTSD and inflammation is due to PTSD-related stress hormone dysregulation leading to alterations in immune, and therefore inflammatory signaling (see, e.g., [7,25–27]). However, given the cross-sectional nature of the evidence at hand, it remains possible that rather than PTSD promoting inflammation, inflammation places individuals at heightened risk for developing PTSD in the setting of trauma – in other words, the direction of causality runs from inflammation to PTSD rather than from PTSD to inflammation.

Service members serving in the Iraq and Afghanistan conflicts endure substantial combat stress and consequent PTSD [28]. The Marine Resiliency Study (MRS) is a prospective field study of approximately 2,600 Marines and Sailors deployed to Iraq or Afghanistan, during which PTSD severity and various physiological and psychological parameters were determined pre- and post-deployment, affording an outstanding opportunity to investigate the causal relationship between inflammation and PTSD. In the current study, we have determined whether *baseline* peripheral inflammation, assessed by plasma CRP in the MRS, contributes to *post-deployment* PTSD symptomatology, assessed by scores on the Clinician Administered PTSD Scale (CAPS), adjusting for trauma exposure and other relevant covariates.

Methods

Subjects

MRS is a prospective, longitudinal study of biological and neuropsychological modulators of combat stress-related PTSD in Marines [29]. Approval was received and has been maintained since August 2007 from the Institutional Review Boards of the University of California, San Diego, VA San Diego Research Service, and Naval Health Research Center. Subjects were recruited from four all-male infantry battalions that were imminently deploying to a war zone. Participation was requested of 2,978 subjects, of whom 2,610 (87.6%) provided written informed consent and were enrolled. Assessment of enrolled subjects began in July 2008 and continued through May 2012. Fifty-five of the enrollees were excluded from the current analysis because they did not deploy with their cohort or withdrew prior to completing the pre-deployment visit, so that the number of subjects included was 2,555. The demographics of these subjects are summarized in Table 1.

Data were collected approximately 1 month before a seven month-deployment (baseline; visit 0) and at 1 week, and 3 and 6 months following the deployment (visits 1, 2, & 3). Among the 2,555 included subjects, baseline plasma CRP concentrations were included from 2,484 subjects (97.2%) and baseline CAPS score from 2,533 (99.1%). For the other specific baseline variables utilized in the current statistical analyses (anthropometrics, psychometrics, and demographics; see below), individuals with included data ranged from 2,503 to 2,548 (98.0% to 99.7%). Data on combat exposure were obtained at visit 1 and were included from 2,215 subjects (86.7%); visit 2 CAPS scores from 1,861 subjects (72.8%); and visit 3 CAPS scores from 1,609 subjects (63.0%).

Measures

CAPS [30], a gold standard PTSD symptom scale, was the primary outcome measure for our analyses, since as a 136-point numerical scale it would be expected to yield greater discriminant power than the binary outcome of PTSD diagnosis. Trauma exposure occurring during combat was assessed with the Deployment Risk and Resilience Inventory Combat Experiences Scale (CES; http://www.ptsd.va.gov/), and exposure occurring in the aftermath of combat with the DRRI post-battle experience scale (PBE; http://www.ptsd.va.gov/). Baseline high-sensitive CRP plasma levels were measured using an enzyme-linked immunosorbent assay (ALPCO Diagnostics, Salem, NH). Measures for variables not included in the final regression model are described in the Supplementary Material (eMethods).

Statistical Methods

The association of our predictors of interest with CAPS was determined using zero-inflated negative binomial regression (ZINBR). Please see the Supplementary Material for a description of this method and the rationale for its choice. Potential confounders were selected for inclusion in regression modeling on the basis of their univariate association, at a lenient significance threshold ($p<0.2$), with both the outcome (post-deployment CAPS) and the predictor of interest (plasma CRP concentration) (determined by ANOVA, linear regression, or ZINBR as appropriate). The values for plasma CRP concentrations were skewed and were therefore log-transformed prior to analyses. Ordinal and binomial logistic regression were used to determine the effects of the same predictors as in the final ZINBR model (Table 2) on the categorical outcomes at visit 2 of full PTSD (as defined in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition [DSM-IV]) [31], partial PTSD [32–34], or no PTSD. Statistical analyses were performed with either SPSS v20.0 (IBM, Armonk, NY) or (in the case of ZINBR) with the R statistical package (http://cran.r-project.org/). All *p* values reported are two-tailed.

Results

Choice of Outcomes and Model Covariates

Baseline and post-deployment values of subjects for the variables included in the statistical models are listed in Table 1, along with selected additional characteristics. PTSD symptomatology, assessed by CAPS scores (see Methods), increased significantly between the baseline and three month post-deployment visits used for our analysis (visits 0 and 2), and then trended back towards baseline in line with findings in a recent systematic review [35]. Of note, in contrast to CAPS, subjects' scores on the anxiety and depression scales, BAI and BDI (see eMethods for description of these metrics), dropped markedly after completion of deployment (Table 1), potentially reflecting the relief experienced by service personnel upon return from combat. Thus, the observed post-deployment increases in PTSD symptomatology were not attributable to broad psychopathology or general psychological distress.

We included baseline CAPS scores (hereafter, termed CAPS0) as a covariate in all statistical analyses of the outcome of visit 2 CAPS (hereafter, CAPS2) so as to adjust for any

differences between subjects in CAPS2 that were attributable to pre-existing differences in CAPS0; this also adjusted for any effects of baseline PTSD symptomatology on the subsequent trajectory of the disorder. In addition to CAPS0, CES and PBE scores (determined at visit 1 immediately following deployment) were also included as covariates in regression models to adjust for differences between subjects in traumatic exposure during and after combat, respectively (please see *Methods* for details). Moreover, since the four MRS battalions differed from one another in their war zone experiences and in the timing of their training regimen relative to the period of data collection, cohort assignment of each subject was set as a factor in regression analysis. Multiple other potential confounders were evaluated, including several previously associated with both PTSD and peripheral inflammation (baseline depression, anxiety, and alcohol and tobacco use [36–52]) and various anthropometric and demographic variables (listed in Table 1); however, none met criteria for inclusion in the regression models.

Zero-Inflated Negative Binomial Regression of Post-Deployment CAPS

In accordance with the analyses described above, our ZINBR model (please see *Methods*) of CAPS2 comprised plasma CRP concentration, baseline CAPS, cohort assignment, and CES and PBE scores. CRP was a highly significant overall predictor of CAPS2 in this model ($p = 0.002$ by likelihood-ratio test), as were each of the other predictors (Table 2). (CRP was also a highly significant predictor in the analogous linear regression model with the same covariates [with a similar p value; $p = 0.002$]; however, as noted in the Supplementary Material, ZINBR is significantly superior to linear regression when modeling the outcome of CAPS.) We assessed all two-way interactions with CRP; none were statistically significant. Of note, based on analysis of the scores on CAPS subscales, the greatest effect of CRP appeared to be in the domain of hyper-arousal (subscale D of CAPS; overall $p = 0.0004$), with less of an effect on numbing (subscale CN; $p = 0.032$), and lesser effects still on re-experiencing (subscale B; $p = 0.277$) and avoidance (subscale CA; $p = 0.571$)

In the zero component of the ZINBR model, CRP was a positive predictor of CAPS2: each one unit increment in $\log_{10}$ plasma CRP concentration (i.e., each 10-fold increase in CRP concentration) was associated with a fold change in the approximate odds of obtaining a CAPS2 score greater than zero (hereafter referred to as odds ratio of non-zero CAPS2) of 1.507 (95% confidence interval: 1.153–1.969; $p = 0.003$) (Table 2). Stated in the context of the range of CRP concentrations in our study population, a one standard deviation increase in $\log_{10}$ CRP (corresponding to a 3.57-fold increase in CRP concentration) was associated with an odds ratio (OR) of 1.254 (1.082–1.454; Figure 1A). By comparison, one standard deviation increases in other measures were associated with ORs of 4.149 (3.060–5.626; $p < 0.001$); 1.388 (1.055–1.826; $p = 0.019$), and 1.428 (1.131–1.802; $p = 0.003$) in the case of CAPS0, CES, and PBE, respectively. Consistent with the findings obtained with CRP treated as a continuous predictor, categorization of CRP revealed a trend toward greater OR of non-zero outcome with increasing CRP category (though, there was, as expected, a loss of statistical power) (Figure 1C).

Likewise, CRP was a positive predictor of CAPS2 scores in the count component of the ZINBR model (which approximately predicts the extent of the outcome when it is non-zero;

please see *Methods*): each 10-fold increase in CRP concentration was associated with a 1.062-fold increase in CAPS2. However, this effect was statistically significant only at the trend level (95% confidence interval: 0.991–1.138; $p = 0.086$ [two-tailed]) (Table 2). Accounting for the ranges in values of the predictors, a one standard deviation increase in $\log_{10}$ CRP was associated with 1.034-fold change (0.995–1.074) in CAPS2, while one standard deviation increases were associated with fold changes of 1.362 (1.310–1.416; $p < 0.001$), 1.110 (1.046–1.177; $p = 0.001$), and 1.203 (1.131–1.280; $p < 0.001$), in the cases of CAPS0, CES, and PBE, respectively (Figure 1B).

Logistic Regression of Post-Deployment PTSD

In addition to analysis of the continuous outcome of visit 2 CAPS, we performed logistic regression of the categorical outcome of PTSD (DSM-IV definition [31]) at visit 2, using the same covariates as in the ZINBR model. CRP was a significant predictor in this analysis as well, albeit not to as great a degree as in the ZINBR model: each 10-fold increment in CRP concentration was associated with an OR of PTSD of 1.501 (1.017 – 2.215; $p = 0.041$). Taking into account the ranges of predictor values, a one standard deviation increase in $\log_{10}$ CRP was associated with an OR of PTSD of 1.252, while, by comparison, one standard deviation increases in CAPS0, CES, and PBE were associated with ORs of 2.303, 1.431, and 1.351 for respectively (Table 3 and Figure 2A). Conversely, adjusted baseline CRP values for subjects with and without PTSD at visit 2 were 0.998 and 0.755 mg/l, respectively (adjusted for the same covariates as the logistic regression model) (Figure 2B). CRP was similarly a significant predictor in ordinal logistic regression of the diagnostic categories of PTSD, partial PTSD [32–34], or neither ($p = 0.029$; please see eResults and eFigure 1).

We also performed sub-group analyses excluding subjects at various thresholds of the model variables – plasma CRP, baseline CAPS, CES, and PBE. CRP effects in these subsets were generally similar to those obtained when considering all subjects, indicating that the effects are not being “driven” by subjects at the extremes of baseline PTSD symptomatology, plasma CRP, or combat exposure (please see eResults and eFigure 2). Moreover, CRP was not significantly associated with baseline CAPS or PTSD diagnosis (p = 0.518 and 0.217, respectively), indicating that CRP is not a mediator or proxy for the effects of one of these other predictors on CAPS2.

Comment

We report here a significant effect of baseline CRP on post-deployment PTSD symptom emergence in Marine and Navy combatants, suggesting that levels of this inflammatory marker may be prospectively associated with resilience versus risk for PTSD. CRP predominantly influenced the likelihood of subjects endorsing the presence vs. absence of PTSD symptoms rather than the extent of symptoms when present (as indicated by its greater statistical significant in the zero model of the ZINBR compared with the count and logistic regression models), and had a greater effect on the hyper-arousal and numbing symptom clusters than on the other clusters. Conceivably, high CRP levels mark a state of vulnerability to developing these symptoms of PTSD, while the influences of other factors prevail in determining the severity of symptoms once they are manifested.

It is sometimes postulated that the observed association between PTSD and peripheral inflammation owes to the former disorder predisposing to the latter, plausibly due to PTSD-induced dysregulation of the stress axis resulting in disinhibition of pro-inflammatory pathways (see, e.g., [7,25–27]). Our data raise the converse possibility – that individuals with lesser inflammation may be relatively resilient and those with greater inflammation relatively vulnerable to developing PTSD symptoms. In other words, a characteristic conventionally considered to be 'physiological' rather than 'psychological' may significantly influence the tendency to develop PTSD. However, the possibility that higher CRP levels at baseline resulted from preceding trauma cannot be excluded, This supposition is also supported by the recent finding that the risk for PTSD following medical illness during military deployment is comparable to that following physical injury [53,54].

The underlying mechanism may involve the actions of inflammatory cytokines, which in addition to their well-characterized adverse effects on metabolic and therefore cardiovascular health [12–14] also have adverse effects on mental health [55–57]. In particular, depression, has long been known to be associated with increased peripheral inflammation [36,46–50] (with some recent studies suggesting that baseline inflammation may predict subsequent depression [37,38]) and, notably, inflammatory cytokines are known to elicit symptoms of depression [58–63] (reviewed in [2,56,57,64]). Furthermore, peripheral inflammation has been associated with impairments in memory and executive function [65–69]. Significantly, inflammatory cytokines have been demonstrated to suppress hippocampal neurogenesis in animals [70] and have been associated with low hippocampal volume in humans [71], a neuroanatomical trait that might mark vulnerability to PTSD – in studies of identical twins discordant for combat trauma exposure, twin pairs in which the combat-exposed member developed PTSD had smaller hippocampi than the other twin pairs [72,73].

Nevertheless, the causal relationships between psychiatric disorders and inflammation are likely to be complex. For instance, in one recent large, prospective, population-based study, cumulative episodes of depression predicted subsequent CRP levels [74], although this effect was attenuated after controlling for BMI and smoking, suggesting that it might be attributable in part to depression-related lifestyle changes rather than directly to the neurophysiology of depression. Importantly with respect to PTSD, much work in animal models supports the conclusion that chronic stress induces immunological changes that culminate in a pro-inflammatory phenotype (see, e.g., [75–77]). Thus, inflammation may both contribute to PTSD and be a consequence of the stressors that led to the disorder.

Strengths of our study include its size, prospective design, and adjustment for multiple potential confounders. Moreover, owing to the youth of the study participants (mean age, 22.8 years) and their relative physical fitness (given the requirements for combat deployment), it is unlikely for chronic physical illness to have confounded the observed effects of baseline CRP on post-deployment PTSD symptomatology. However, certain limitations merit discussion. First, the relative fitness of our cohort also limits the generalizability of our findings, as does the absence of females. In addition, whereas CRP concentrations fluctuate substantially in response to transient inflammatory states (such as minor infections; [78]), values in our subjects were determined only once and thus may be

relatively “noisy”. Moreover, use of anti-inflammatory medications, which might also have contributed to variability in CRP levels, was not ascertained in our study. However, it should be noted that such variability would generally be expected to bias towards the null hypothesis.

Finally, with regard to missing data, as noted in the *Methods*, 27.2% of subjects did not have determination of CAPS2. However, CRP values did not differ significantly between subjects for whom CAPS2 scores were present vs. absent; and, conversely, CAPS2 was not significantly different when comparing subjects for whom CRP values were present vs. absent (not shown). Moreover, we have found the “effect size” of CRP on visit 2 CAPS or PTSD diagnosis (the CRP-associated odds ratio or fold change) to be generally similar across subsets of subjects having markedly different mean values for the various covariates in our regression models (please see eResults). This suggests that even if the subjects with missing data were considerably different from the other subjects with regard to CES, PBE, or baseline CAPS scores, the CRP effect sizes that we observed are likely to be similar to those that would have been obtained had their data not been missing. Taken together, these results suggest that missing data might not have appreciably biased our findings concerning CRP effects on PTSD symptomatology.

Our results, if validated by future studies, could have important clinical implications. If peripheral inflammation contributes to the development of PTSD, interventions to decrease inflammation, such as dietary or life-style modifications [79–81], might ameliorate the severity of this disorder. At minimum, our findings are consistent with the old adage: *mens sana in corpore sano*, a healthy mind in a healthy body.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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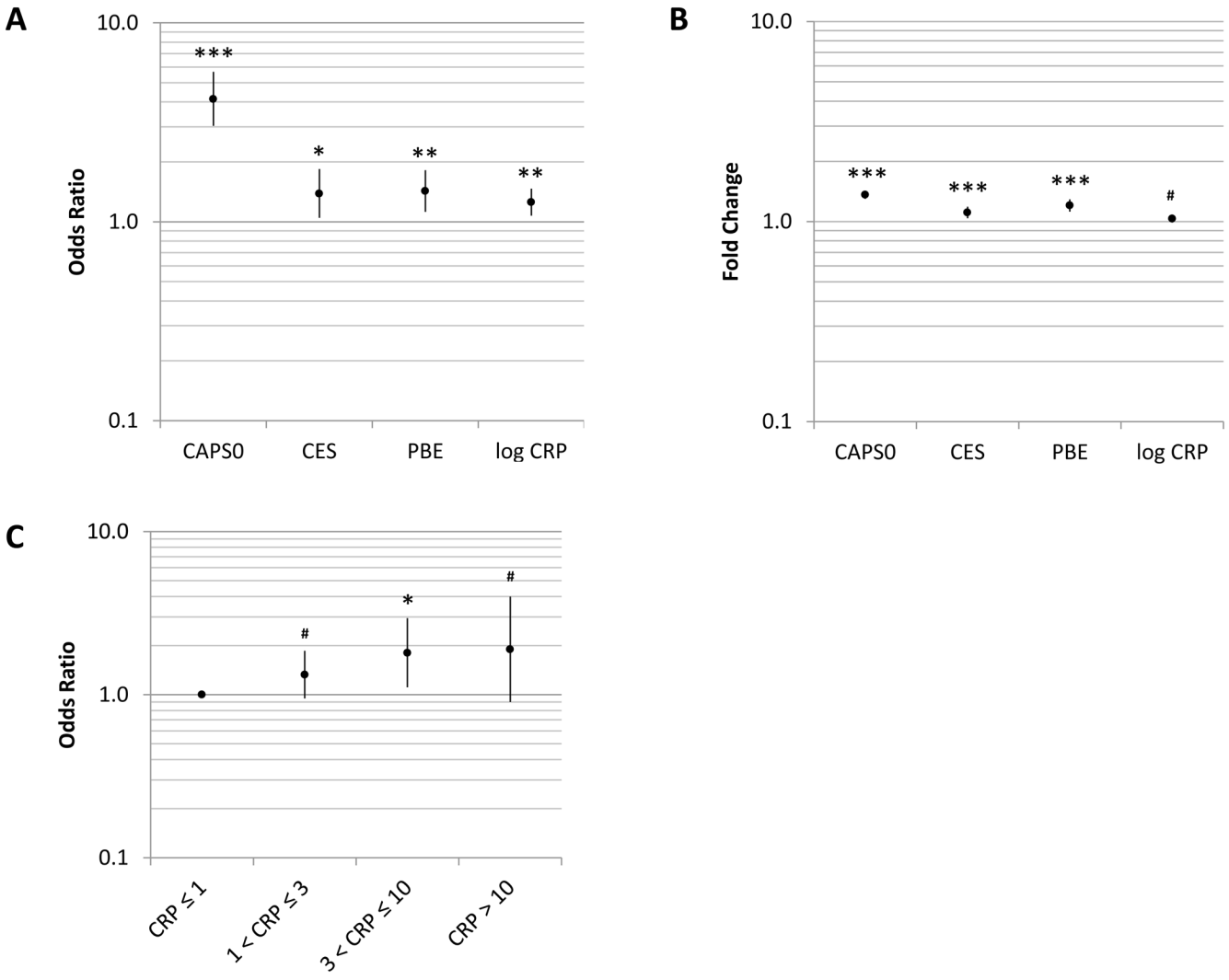

Figure 1.

A, Adjusted odds ratios of a non-zero Clinician Administered PTSD Scale score at visit 2 (CAPS2) associated with one standard deviation increases in the indicated variables. *B,* Adjusted fold changes in CAPS2 associated with one standard deviation increases in the indicated variables. Data in A and B are from the zero inflated negative binomial regression (ZINBR) model summarized in Table 2. *C*, Odds ratios of non-zero CAPS2 by baseline plasma C-reactive protein concentration category (≤1 [reference category], 1–3, 3–10, and >10 mg/l), as determined by ZINBR and adjusted for the same covariates as the model in Table 2. CAPS0, Clinician Administered PTSD Scale at visit 0 (baseline); CES, Combat Exposure Scale; PBE, post-battle experience; CRP, baseline plasma C-reactive protein concentration. Error bars delineate 95% CIs; ***, p<0.001; **, p<0.01, *, p<0.05, #, p<0.1 (all values two-tailed). Please refer to the text for details.

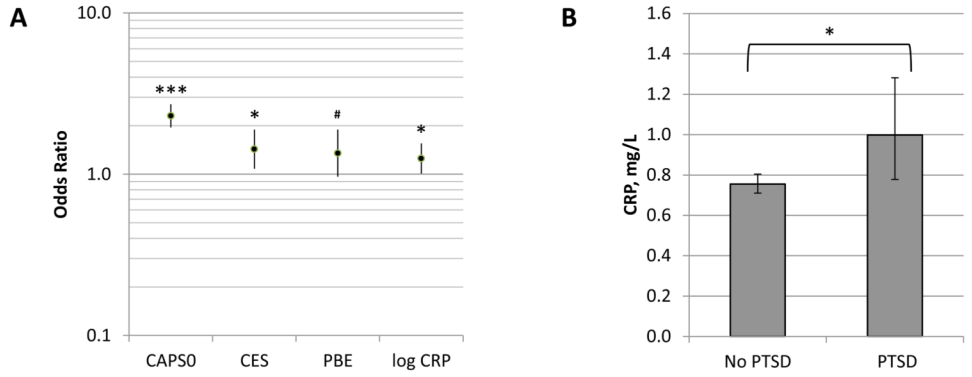

Figure 2.

A, Adjusted odds ratios of PTSD at visit 2 associated with one standard deviation increases in the indicated variables. Data are from the binomial logistic regression model summarized in Table 3. *B,* Baseline plasma C-reactive protein concentration of subjects without or with PTSD at visit 2, adjusted for the same covariates as the logistic regression model in Table 3. CAPS0, Clinician Administered PTSD Scale at visit 0 (baseline); CES, Combat Exposure Scale; PBE, post-battle experience; CRP, baseline plasma C-reactive protein concentration. Error bars delineate 95% CIs; ***, $p<0.001$; *, $p<0.05$, #, $p<0.1$ (all values two-tailed). Please refer to the text for details.

Table 1

Selected baseline and post-deployment characteristics of study subjects. CRP, C-reactive protein; BMI, body mass index; AUDIT-C, Alcohol Use Disorders Identification Test–consumption; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CAPS, Clinician Administered PTSD Scale; CES, Combat Exposure Scale; PBE, post-battle experience; visit 0, baseline; visit 2, three months post-deployment; visit 3, six months post-deployment. See Methods for definition of variables and for additional details concerning subjects' demographics and military characteristics.

	N	Min.	Max.	Mean or Percentage[a]	Median	Std. Deviation
Demographics						
Age	2548	18	48	22.78	21.83	3.51
Ethnicity[a]	2540					
Non-Hispanic				76.5%		
Hispanic				23.2%		
Race[a]	2503					
European-American				82.7%		
African-American				4.7%		
Asian-American				2.7%		
American Indian				1.4%		
Pacific Islanders				1.5%		
Mixed				5.0%		
Educational Level[a]	2538					
High School Graduate				64.3%		
College				32.3%		
Post-Graduate				0.5%		
Marital Status[a]						
Never Married				61.1%		
Married				34.8%		
Divorced or Separated				3.5%		
Military Characteristics						
Service Length, months	2538	0	324	36.29	26.00	24.45
Previously Deployed	2541	--	--	51.3%	--	--
Enlisted	2540			97.4%		
Plasma CRP, mg/l	2484	0.03	28.53	1.93	0.79	3.31

	N	Min.	Max.	Mean or Percentage[a]	Median	Std. Deviation
Waist circumference, inches	2533	25.75	48.63	33.62	33.25	3.00
BMI	2533	18.83	41.41	27.60	27.42	3.24
Mean arterial blood pressure, mm Hg	2527	64.67	148.33	90.38	90.00	7.98
AUDIT-C	2527	0	12	5.06	5.00	3.61
BAI, visit 0	2519	0	53	6.79	4.00	7.85
BAI, visit 2	1850	0	57	4.79	2.00	7.36
BAI, visit 3	1609	0	63	4.22	1.00	7.26
BDI, visit 0	2526	0	51	6.59	4.00	7.67
BDI, visit 2	1854	0	54	5.05	2.00	6.80
BDI, visit 3	1612	0	46	4.79	2.00	6.82
CAPS, visit 0	2533	0	101	14.89	10.00	15.37
CAPS, visit 2	1861	0	120	17.40	12.00	18.01
CAPS, visit 3	1617	0	107	15.41	10.00	17.39
PTSD, visit 0	2533			4.7%		
PTSD, visit 2	1861			6.3%		
PTSD, visit 3	1617			5.1%		
CES	2189	0	64	13.57	9.00	11.39
PBE	2204	0	15	5.65	4.00	4.79

[a] A small proportion of subjects did not provide data on these demographic traits so that the percentages do not add up to 100%.

Table 2

Zero-inflated negative binomial regression (ZINBR) model of post-deployment (visit 2) Clinician Administered PTSD Scale score. The number of subjects in this model was 1719. OR, odds ratio; CI, confidence interval; CAPS0, Clinician Administered PTSD Scale score at visit 0 (baseline); CES, Combat Exposure Scale score; PBE, post-battle experience score; CRP, baseline plasma C-reactive protein concentration.

	Zero model			Count model			
Variable	**OR[a,b]**	**95% CI**	***P* value**	**Fold change[c,d]**	**95% CI**	***P* value**	**Overall *P* value[e]**
Intercept[b,d]	1.254	0.765 – 2.054	0.369	10.569	9.288 – 12.026	0.000	
Cohort 1	1.922	1.077 – 3.429	0.027	1.031	0.895 – 1.186	0.676	0.000
Cohort 2	0.569	0.359 – 0.902	0.016	0.943	0.833 – 1.068	0.354	0.000
Cohort 3	0.632	0.413 – 0.968	0.035	0.778	0.699 – 0.865	0.000	0.000
Cohort 4	0[f]						
CAPS0	1.097	1.075 – 1.119	0.000	1.020	1.018 – 1.023	0.000	0.000
CES	1.029	1.005 – 1.054	0.019	1.009	1.004 – 1.014	0.001	0.000
PBE	1.077	1.026 – 1.131	0.003	1.039	1.026 – 1.053	0.000	0.000
log CRP	1.507	1.153 – 1.969	0.003	1.062	0.991 – 1.138	0.086	0.002

[a] Ratio of approximate odds of non-zero outcome (computed by exponentiating the corresponding coefficient in the regression model and adjusted for the variables listed in the table).

[b] Value for the intercept indicates approximate odds of non-zero outcome at baseline (cohort equals 4 and all other parameters have zero values).

[c] Approximate fold change in outcome, in the event of a non-zero outcome (computed by exponentiating the corresponding coefficient in the regression model and adjusted for the variables listed in the table).

[d] Value for the intercept indicates approximate outcome, in the event of a non-zero outcome, at baseline (cohort equals 4 and all other parameters have zero values).

[e] By the likelihood ratio test

[f] This parameter is set to zero because it is redundant.

Table 3

Binomial logistic regression of post-deployment (visit 2) PTSD diagnosis. The number of subjects in this model was 1719. OR, odds ratio; CI, confidence interval; CAPS0, visit 0 (baseline) Clinician Administered PTSD Scale score; CES, Combat Exposure Scale score; PBE, post-battle experience score; CRP, baseline plasma C-reactive protein concentration.

Variable	OR[a,b]	95% CI	*P* value
Intercept[b]	0.009	0.004 – 0.020	<0.001
Cohort 1	0.999	0.407 – 2.452	0.999
Cohort 2	1.130	0.539 – 2.366	0.747
Cohort 3	0.809	0.449 – 1.457	0.480
Cohort 4	0[c]		
CAPS0	1.056	1.044 – 1.067	<0.001
CES	1.032	1.007 – 1.058	0.012
PBE	1.065	0.993 – 1.142	0.079
log CRP	1.501	1.017 – 2.215	0.041

[a] Odds ratio of PTSD (computed by exponentiating the corresponding coefficient in the regression model and adjusted for the variables listed in the table).

[b] Value for intercept indicates the odds of PTSD at baseline (cohort equals 4 and all other parameters have zero values).

[c] This parameter is set to zero because it is redundant.