

# Research Submission

## PTSD, Combat Injury, and Headache in Veterans Returning From Iraq/Afghanistan

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**Objective.**—To examine the relationship between posttraumatic stress disorder, combat injury, and headache in Operation Iraqi Freedom and Operation Enduring Freedom veterans at the VA San Diego Healthcare System.

**Background.**—Previous investigations suggest that a relationship between posttraumatic stress disorder and primary headache disorders exists and could be complicated by the contribution of physical injury, especially one that results in loss of consciousness. These associations have not been systematically examined in Operation Iraqi Freedom and Operation Enduring Freedom veterans.

**Methods.**—In this observational cross-sectional study, a battery of self-report, standardized questionnaires was completed by 308 newly registered veterans between March and October 2006. The Davidson Trauma Scale was used to determine the degree of posttraumatic stress disorder symptoms and combat-related physical injury was assessed by self-report. The presence of headache was based on a symptom checklist measure and self-reported doctor diagnoses. Logistic regression analysis was performed to predict presence of headache and determine odds ratios and 95% confidence intervals associated with demographic, military, in-theatre, and mental health characteristics.

**Results.**—About 40% of the veterans met the criteria for posttraumatic stress disorder; 40% self-reported current headache, 10% reported a physician diagnosis of migraine, 12% a physician diagnosis of tension-type headache, and 6% reported both types of headache. Results from the logistic regression model indicated that combat-related physical injury (odds ratio: 2.25; 95% confidence interval: 1.17-4.33) and posttraumatic stress disorder (odds ratio: 4.13; 95% confidence interval: 2.44-6.99) were independent predictors of self-reported headache. Additional analyses found that veterans with both tension and migraine headache had higher rates of posttraumatic stress disorder (chi-square [d.f. = 3] = 15.89;  $P = .001$ ) whereas veterans with migraine headache alone had higher rates of combat-related physical injury (chi-square [d.f. = 9] = 22.00;  $P = .009$ ).

**Conclusion.**—Posttraumatic stress disorder and combat-related physical injury were related to higher rates of self-reported headache in newly returning veterans. Our finding that posttraumatic stress disorder and injury during combat are differentially related to migraine and tension-type headache, point to a complex relationship between physical and psychological trauma and headache. These findings have implications for a comprehensive approach to interventions for headache and the physical and psychological sequelae of trauma.

**Key words:** headache, posttraumatic stress disorder, combat, physical injury, traumatic brain injury

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Accepted for publication June 25, 2009.

*Conflict of Interest:* None of the authors have any conflicts of interest to declare.

**Abbreviations:** ANOVA analysis of variance, AUDIT Alcohol Use Disorders Identification Test, CI confidence interval, DAST Drug Abuse Screening Test, DTS Davidson Trauma Scale, OEF Operation Enduring Freedom, OIF Operation Iraqi Freedom, OR odds ratio, PTSD posttraumatic stress disorder, TBI traumatic brain injury

(*Headache* 2009;49:1267-1276)

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## INTRODUCTION

Posttraumatic stress disorder (PTSD) is a psychiatric condition in which an overwhelming traumatic event results in intense fear, helplessness, horror, and avoidance of stimuli associated with the trauma.<sup>1</sup> Individuals with PTSD evidence widespread physiologic dysregulation in multiple systems including the hypothalamic-pituitary-adrenal axis and autonomic nervous system.<sup>2</sup> In addition, a large body of research has documented the negative impact of PTSD on physical health.<sup>3-5</sup> Limited research has shown that stress and headache may be linked through similar underlying mechanisms.<sup>6</sup> A biopsychosocial framework of primary headache disorders also suggests that psychological stress may mediate the onset and progression of headache disorder in addition to triggering and exacerbating individual attacks.<sup>6</sup>

However, only a few studies have focused on the relationship between headache and PTSD or PTSD symptoms. A study conducted in an orofacial pain center found that 1 out of every 6 patients diagnosed with migraine or tension-type headache endorsed symptoms consistent with PTSD;<sup>7</sup> 6.5% of migraine patients in another clinic met the criteria for PTSD.<sup>8</sup> Furthermore, a study examining PTSD symptoms in patients with episodic and chronic migraine headaches found that 43% of participants with chronic migraine vs 9.5% of participants with episodic migraine had symptoms suggestive of PTSD.<sup>9</sup> Finally, a recent study found that patients with chronic daily headache had significantly higher rates of PTSD than those with episodic migraine; major depression also played a role in that association.<sup>10</sup>

Although physically injurious and traumatic events can lead to the development of both headache and PTSD, studies examining the relationship between these conditions have not explored the role of physical injury. For example, nearly 30% of patients who developed headache or experienced

marked exacerbation of an existing headache condition after a motor vehicle accident were found to have PTSD.<sup>11</sup> Additionally, victims of motor vehicle accidents who suffered a head injury during the accident and developed headache had significantly worse functioning on a number of measures than comparison groups with non-traumatic headache, motor vehicle accident victims without headache, or non-headache controls.<sup>12</sup>

The relationship between psychological and physical trauma is of particular relevance to the recent veteran population in the United States, for which previous studies have found high prevalence rates of PTSD, traumatic brain injury (TBI), and their co-occurrence. A recent study found that nearly 44% of Iraq war soldiers with TBI-related loss of consciousness, 27% of soldiers with TBI-related altered mental status, and 16% of soldiers with other physical injuries met criteria for PTSD.<sup>13</sup> Additional analyses that examined the relationship between PTSD, loss of consciousness, and measures of physical health indicated that PTSD and loss of consciousness were both strongly associated with reports of headache. This study, however, did not examine the potential contribution of combat injury without loss of consciousness to headache, nor did it examine the specific types of headache that might be associated with PTSD, TBI, or other injury. Two small studies found that returning US veterans with mild TBI from blast injuries had higher rates of headache as well as PTSD,<sup>14,15</sup> but these findings were primarily limited to veterans with documented neurocognitive deficits in 1 study and limited to veterans with physical injuries in the other study.

Taken together, previous investigations suggest that a relationship between PTSD and primary headache disorders exists and could be complicated by the contribution of physical injury, especially one that results in loss of consciousness or neurocognitive

deficits. To our knowledge, no study to date has comprehensively examined the association of PTSD, combat-related physical injury, TBI, and headache in veterans of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). Thus, our aim was to address these associations and to more specifically elucidate these relationships for migraine and tension-type headache. In these analyses, we address the following questions: (1) What are the self-reported prevalence rates of migraine and tension-type headache in OEF/OIF veterans? (2) Are PTSD and physical injury (ie, combat-related physical injury and TBI) independently associated with headache? And (3) Are the patterns of association different for migraine and tension-type headache?

## METHODS

**Study Population.**—This study was part of a larger cross-sectional evaluation of OEF/OIF veterans registering for care at the VA San Diego Healthcare System between March and October, 2006. During this time period, 442 veterans and reservists agreed to complete a battery of questionnaires at Member Services (initial registration). Of these, 44 (10%) did not take part in OEF or OIF. Of the remaining 398 OEF/OIF veterans, 308 (77%) had complete data and were included in the analyses. The study was approved by the University of California, San Diego Institutional Review Board, and by the VA San Diego Research and Development Committee. All authors had access to the data.

**Sources of Data.**—Veterans completed a packet of standardized questionnaires and rating scales to assess demographic, military, and in-theatre factors, mental health symptoms, and health-related diagnoses and symptoms.

**Demographic and Military Variables.**—The demographic and military questions included information on age, gender, race/ethnicity, rank, and branch of service.

**In-Theatre Variables.**—A series of dichotomous questions (ie, Yes or No answer choices) asked about: (1) experiencing an emotional trauma, including combat or non-combat experiences, (2) combat-related injury, and (3) a history of serious head injury including loss of consciousness. Information from the

latter 2 questions was used to classify veterans into 4 categories of physical injury: those who did not have any combat injury or history of serious head injury (non-injured), those with combat injury but no history of head injury, those with history of serious head injury only, and those with both types of injury. Veterans also completed the Combat Exposure Scale, a 7-item measure of wartime stressors experienced by combatants, that has good internal consistency (coefficient  $\alpha = 0.85$ ) and test-retest reliability ( $r = 0.97$ ).<sup>16</sup>

**Mental Health Symptoms.**—A battery of commonly used and well-validated questionnaires assessed for mental health symptoms. The Alcohol Use Disorders Identification Test (AUDIT)<sup>17</sup> and Drug Abuse Screening Test (DAST)<sup>18</sup> were included to screen for drug and alcohol problems. Both the AUDIT and the DAST demonstrate strong sensitivity and specificity in identifying problematic alcohol and drug abuse, respectively.<sup>17,18</sup> Substance abuse was defined as a score of 5 or more on the AUDIT or a score of 2 or more on the DAST.<sup>17,18</sup> The Davidson Trauma Scale (DTS) was used to determine the degree of PTSD symptoms.<sup>19</sup> The DTS is an often-used measure of the frequency and severity of PTSD symptoms based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria.<sup>1</sup> This 17-item measure has good internal consistency ( $r = 0.99$ ) and test-retest reliability ( $r = 0.86$ ).<sup>19</sup> PTSD was defined as positive endorsement of trauma exposure and a DTS score of 40 or higher.<sup>19</sup> Finally, a 2-item depression screener asked about feeling down, depressed, or hopeless and little interest or pleasure in doing things for the last month. This depression screener has been used routinely in other studies published on VA populations as a general screen for depression.<sup>20</sup> The measure is psychometrically sound, useful for detecting depression in primary care settings, and has similar test characteristics to other case-finding instruments.<sup>21</sup> A positive depression screen was defined as endorsement of both depressed mood and anhedonia.

**Health-Related Diagnoses and Symptoms.**—Veterans also completed a 52-item checklist of medical symptoms, including headache, by indicating if the symptom was currently a problem. This

checklist was similar to those used in previous studies of health symptoms in veterans.<sup>22</sup> Another checklist asked veterans if they had been diagnosed with any medical conditions including migraine or tension-type headache. Self-reported headache as a symptom was used in the regression analyses to examine the association with PTSD and other factors, while physician-diagnosed migraine and tension-type headache were used in additional analyses to further explore the relationship between specific headache, PTSD, and combat injury.

**Statistical Analyses.**—Initial analyses (Pearson chi-square and 1-way analysis of variance [ANOVA]) were used to examine demographic and other differences between veterans with complete data and those who were excluded from the analyses due to missing data. Descriptive statistics were used to characterize the sample and assess the prevalence of mental health symptoms, self-reported headache, and physician-diagnosed migraine and tension-type headache. Pearson chi-square analyses with categorical variables and 1-way ANOVA for continuous variables were used to examine differences in demographic, military, mental health, and type of headache between veterans with and without self-reported headache. Effect size estimates also were calculated to examine the aforementioned factors using partial eta squared ( $\eta^2$ ) with a small effect defined as 0.01, medium as 0.06, and large as 0.14.

A logistic regression analysis was performed to predict the presence of self-reported headache and to determine odds ratios (OR) and 95% confidence intervals (CI). Variables could be conceptually grouped together into demographic, military, in-theatre, and mental health characteristics. Further, the groups of variables could be ordered logically based on previous research (eg, demographics and military characteristics before in-theatre and mental health characteristics). Thus, we used a combination of stepwise and hierarchical regression modeling. Covariates and factors were entered stepwise and hierarchically in 4 blocks. This strategy also controlled for potential correlations between variables included in different blocks (eg, rank and PTSD, or PTSD and physical injury). Block 1 consisted of demographic characteristics (gender, age, race). Block 2 consisted

of military characteristics (branch, rank). Rank was dichotomized as  $\leq$ E5 (lower rank enlisted, more likely to be in combat), and  $\geq$ E6 or officers (higher rank enlisted and officers, more likely to be in support roles). Block 3 consisted of in-theatre experiences (Combat Exposure Scale score, the 4-level physical injury variable). Block 4 consisted of mental health characteristics (substance abuse, depression, PTSD). Finally, Pearson chi-square tests were used to specifically examine the relationships between types of headache and key variables predictive of self-reported headache. Significant *P* value was set at .05. All analyses were conducted using SPSS v.15.0 (SPSS, Inc, Chicago, IL, USA).

## RESULTS

**Characteristics.**—Initial analyses indicated that other than race/ethnicity and type of headache (ie, migraine, tension-type, or both), the 308 OEF/OIF veterans who completed the assessment packet did not differ significantly from the 90 OEF/OIF veterans who were excluded from the analyses due to missing data. A larger proportion of veterans with incomplete data were African American (24% vs 14%; *P* = .04), and had both types of headache (11% vs 6%; *P* = .03), and fewer had tension-type headache (3% vs 12%; *P* = .03) than veterans with complete data.

The sample of 308 OEF/OIF veterans was composed primarily (88%) of young men (mean = 31.4 years; standard deviation = 8.2) who had held ranks  $\leq$ E5 (71%) and were mostly separated from the Navy (35%), Marines (35%), or Army (22%). About half of the veterans were white (46%), but consistent with the demographic makeup of the geographical area, there were substantial numbers of Hispanic (25%) and African American (14%) veterans.

About 17.5% of the veterans reported only experiencing physical injury during combat, 4.2% reported only a history of serious head injury that included loss of consciousness, and 3.2% indicated experiencing both combat injury and a history of serious head injury. The mean Combat Exposure Scale score was in the moderate range (mean = 13.5; standard deviation = 10.5). Of all veterans, 39% screened positive for substance abuse, 46% screened positive for depression, and 40% met our criteria for

**Table 1.—Characteristics of OEF/OIF Veterans With and Without Self-Reported Current Headache**

Characteristics	Veterans with headache (n = 122)	Veterans without headache (n = 186)	P value
<i>Demographics</i>			
Age in years, mean (SD)	31.56 (8.0)	31.25 (8.3)	ns
Male (%)	86.9	88.7	ns
Race (%)			ns
White	49.2	44.1	
African American	15.6	12.4	
Hispanic	22.1	27.4	
Asian	11.5	14.0	
Other	1.6	2.2	
<i>Military</i>			
Branch (%)			ns
Army	21.3	22.6	
Marines	27.9	39.2	
National Guard	7.4	4.8	
Air Force	2.5	1.6	
Navy	41.0	31.7	
Rank (%)			ns
≤E5	73.8	69.9	
≥E6 and officers	26.2	30.1	
<i>In-Theatre</i>			
CES score, mean (SD)	14.84 (11.1)	12.60 (10.0)	ns
Physical injury (%)			.003
Combat-related injury	26.2	11.8	
Serious head injury	2.5	5.4	
Both combat and serious head injury	4.9	2.2	
<i>Mental health (%)</i>			
Substance abuse†	35.2	40.9	ns
Depression‡	59.8	37.1	<.001
PTSD§	59.0	26.9	<.001
<i>Type of headache (%)</i>			
Migraine	19.7	3.8	<.001
Tension-type	17.2	8.6	
Both migraine and tension-type	11.5	2.2	

†Substance abuse defined as a score of 5 or more on the AUDIT or a score of 2 or more on the DAST.

‡Depression defined as positive endorsement of both depressed mood and anhedonia in past month.

§PTSD defined as positive trauma and a score of 40 or higher on the Davidson Trauma Scale.

CES = Combat Exposure Scale; ns = not significant; OEF/OIF = Operation Enduring Freedom/Operation Iraqi Freedom; PTSD = posttraumatic stress disorder; SD = standard deviation.

PTSD. Additionally, 40% self-reported current headache, 10% reported a physician diagnosis of migraine, 12% a physician diagnosis of tension-type headache, and 6% reported both types of headache.

**Characteristics Among Veterans With and Without Headache.**—Table 1 presents information on the demographic, military, in-theatre, mental health, and headache characteristics of OEF/OIF veterans with and without self-reported current headache. The veterans did not differ on any of the demographic and

military characteristics, nor did they differ on mean Combat Exposure Scale score, or substance abuse. Effect sizes for these non-significant differences ranged from 0.003 to 0.073, suggesting small to medium effect estimates. Compared to veterans without self-reported headache, a significantly larger proportion of veterans with headache had experienced physical injury ( $P < .003$ ,  $\eta^2 = 0.116$ ) and screened positive for depression ( $P < .001$ ,  $\eta^2 = 0.223$ ) and PTSD ( $P < .001$ ,  $\eta^2 = 0.321$ ). As expected,



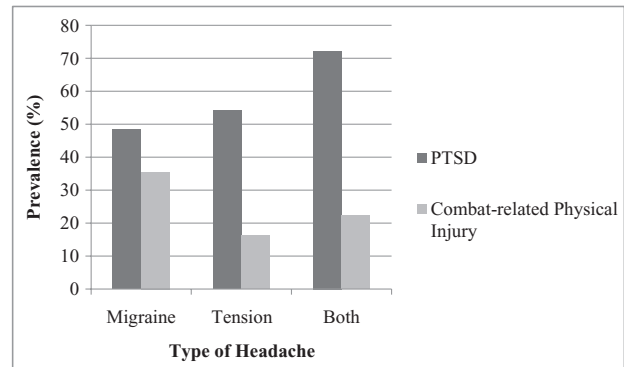
**Table 2.—Odds Ratios, 95% Confidence Intervals, and *P* Values for Predictors of Headache in the Final Regression Model**

Predictors	Odds ratio	95% confidence interval	<i>P</i> value
<i>Physical injury</i>			
Combat-related injury	2.25	1.17-4.33	.015
Serious head injury	0.37	0.09-1.48	ns
Both combat and serious head injury	1.43	0.37-5.53	ns
No injury		Reference	
<i>PTSD</i>			
Yes	4.13	2.44-6.99	<.001
No		Reference	
<i>Substance abuse</i>			
Yes	0.54	0.32-0.92	.024
No		Reference	

ns = not significant; PTSD = posttraumatic stress disorder.

veterans with self-reported headache had significantly more physician diagnoses of migraine, tension-type, or both types of headache ( $P < .001$ ;  $\eta^2 = 0.337$ ,  $\eta^2 = 0.229$ , and  $\eta^2 = 0.374$ , respectively). Veterans who reported current headache but were not diagnosed by a physician (about 12%) did not differ from veterans with both current headache symptoms and physician diagnoses on any of the study variables.

**Predictors of Headache.**—The stepwise hierarchical logistic regression model predicting self-reported headache from demographic, military, in-theatre, and mental health characteristics was significant and fit the data well (chi-square [d.f. = 5] = 45.36; -2 log likelihood = 368.22;  $P < .001$ ). Table 2 presents the OR, 95% CI, and *P* values associated with the predictors that remained significant in the final model. Physical injury, PTSD, and substance abuse were significant and independent predictors of self-reported headache. Veterans with combat-related physical injury only were 2.25 times more likely ( $P = .015$ ) while those with PTSD were 4 times more likely ( $P < .001$ ) to report headache than veterans without either combat injury or PTSD. Those who screened positive for substance abuse were half as likely to report headache compared with those without substance abuse ( $P = .02$ ).



**Figure.—Prevalence of posttraumatic stress disorder (PTSD) and combat injury by type of headache.**

**PTSD, Combat Injury, and Types of Headache.**—Additional analyses examined the relationship between PTSD, physical injury, and type of headache. The Figure presents the rates of PTSD and combat-related physical injury – the 2 key predictors of self-reported headache – for veterans with physician diagnoses of migraine or tension-type headache, or both. Veterans with both types of headache had higher rates of PTSD (chi-square [d.f. = 3] = 15.89;  $P = .001$ ,  $\eta^2 = 0.211$ ) whereas veterans with only migraine headache had higher rates of combat-related physical injury (chi-square [d.f. = 9] = 22.00;  $P = .009$ ,  $\eta^2 = 0.170$ ).

## DISCUSSION

We found that the self-reported rates of migraine and tension-type headache in the overall sample of OEF/OIF veterans and reservists were similar to those reported in a number of large-scale epidemiological studies.<sup>23-26</sup> The prevalence of self-reported headache also was consistent with an estimated rate of 36% (95% CI = 33-39%) in combat veterans,<sup>27</sup> and in line with the prevalence of migraine headache in a recent study of OIF veterans.<sup>28</sup> Several factors were independently related to the self-report of current headache. While veterans who screened positive for substance abuse were less likely to report headache, veterans with PTSD and those who reported combat-related physical injury were substantially more likely to report headache. Additionally, PTSD was associated with both migraine and tension-type headache while combat-related physical injury was primarily related to migraine headache.

To our knowledge, this is the largest study to examine the prevalence of migraine and tension-type headache in OEF/OIF veterans and reservists and to investigate the relationship between PTSD and combat-related physical injury to these primary headaches. We found that PTSD is a key predictor of headache and is associated with both migraine and tension-type headache. The mechanisms underlying this relationship are likely to be multifactorial and complex. There is some evidence that psychological stress is a central contributor to primary headache due to chronic activation of the hypothalamic-pituitary-adrenal axis and other physiological systems of the stress response.<sup>6</sup> Alternately, at least 1 study has found that those with PTSD after a motor vehicle accident were more likely to have a prior history of headache than those without PTSD,<sup>11</sup> pointing to the interactive nature of the stress and headache relationship. Others have proposed a model of shared vulnerability, where genetic, familial, physiological, or psychological factors predispose individuals to develop both PTSD and a pain condition in response to traumatic events.<sup>29</sup> We have found, for example, that familial factors (ie, genetic and environmental factors that are shared within families) partly contribute to the relationship between PTSD symptoms and migraine headache and may predispose individuals to developing both conditions.<sup>30</sup> Finally, there are physiological, cognitive, affective, and behavioral factors associated with both PTSD and headache that serve to mutually maintain these conditions.<sup>29,31</sup> Regardless of the underlying mechanism, our findings underscore the need to assess for PTSD and headache co-occurrence and to provide adequate treatment for the symptoms of both disorders.

Unlike the previous investigation by Hoge and colleagues that found an association between head injury with loss of consciousness and headache in Iraq soldiers,<sup>13</sup> we found that combat-related physical injury but not a history of head injury increased the likelihood of headache in this veteran sample. Although the demographic and other characteristics of our sample were comparable to those in the aforementioned study<sup>13</sup> and other nationally representative studies,<sup>32</sup> the difference in findings could be related to the timing of head injury or comorbidity of

head and other physical injury. For example, in the Hoge et al study, veterans who suffered a head injury with loss of consciousness during combat also may have experienced other physical injuries. Our findings are more consistent with those of Theeler and colleagues, who found an increased prevalence of headache in veterans with mild TBI and physical injuries.<sup>15</sup> Together, these findings suggest that the associations observed for TBI and headache in previous studies may be due to the contribution of combat-related physical injury rather than the specific effects of head injury. Mechanistic studies of the association between PTSD, combat-related physical injury, TBI, and headache are needed to further examine these complex relationships and shed light on the physiological and psychological factors that increase the risk of developing these conditions.

The apparent protective effects of substance abuse are noteworthy. There is some evidence that veterans may use alcohol and drugs to self-medicate for pain and other symptoms.<sup>27</sup> It is possible that self-medication with drugs or alcohol may lead to minimization of symptoms and subsequent underdiagnosis and under-treatment of headache disorders.

Our findings support the need for a multidisciplinary approach to the assessment and treatment of both psychological and physical symptoms in OEF/OIF veterans. The assessment of trauma-related factors in patients with physical injury, TBI, or headache, and likewise, the assessment of headache and other pain symptoms in patients with PTSD are likely to facilitate treatment. Additionally, early detection and treatment in primary care settings may help to reduce barriers to care and lessen morbidity.<sup>33,34</sup> More research is needed to determine optimal treatment of OEF/OIF veterans with co-occurring symptoms.

The principal limitation of this study is that results were based on self-reported data and could have been affected by recall bias. Use of self-reported physician diagnoses also excludes individuals whose symptoms have not been formally diagnosed. Although the rates of primary headache and other variables were consistent with what has been reported previously and support the validity of our findings, the gold standard for the diagnosis of migraine or tension-type headache is the application

of the International Headache Society's classification criteria (ICHD-2) with a physician evaluation. Thus, findings from this study should be replicated using a comprehensive assessment of PTSD, combat-related physical injury, TBI, and headache. A second limitation is the lack of information on veterans' history of headache prior to deployment to OEF/OIF. Therefore, we must reiterate that our findings are based on cross-sectional data and do not imply that PTSD causes headache or preexisting history of headache predisposes one to the development of PTSD. Another limitation stems from the lack of a randomly selected OEF/OIF sample. This point is underscored by differences in the types of headache reported by veterans who completed the assessment packet and those who did not. Additionally, we found that OEF/OIF veterans who did not complete the survey were more likely to be African American than veterans who were included in the analyses. Several studies have documented similar racial differences in enrollment or completion of research studies.<sup>35-37</sup> Thus, our findings may only be relevant to non-African American veterans seeking care at a VA medical center.

## CONCLUSION

In conclusion, we found that PTSD and combat-related physical injury were independent predictors of headache in OEF/OIF veterans and were differentially related to migraine and tension-type headache. Future studies should replicate these findings with a more comprehensive assessment of PTSD, combat-related physical injury, TBI, and headache. In addition, the mechanisms underlying these associations should be examined. Veterans could benefit from an interdisciplinary assessment and treatment approach that includes psychosocial and medical components.

*Acknowledgments:* Dr. Afari is supported in part by the National Institute of Health (R01AR051524 and U01DK082325). Dr. Baker is supported in part by Department of Defense and VA research grants (Merit, HSR&D, and Cooperative Studies). Dr. Moeller-Bertram is supported in part by a grant from the Foundation for Anesthesia Education and Research. Drs. Afari, Heppner, Moeller-Bertram, and Baker are supported in part by the VA Center of Excellence for Stress and Mental Health. We

appreciate the efforts and support of Mr. Michael Kilmer of the Social Work Service, and Mr. Glenn White and his staff at Member Services of the VA San Diego Healthcare System. Portions of this study were presented at the VA Mental Health Conference in July, 2008 and the 24th annual meeting of the International Society for Traumatic Stress Studies in November, 2008.

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#### (a) Conception and Design

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