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The study protocol was approved by Naval Health Research Center Institutional Review Board in compliance with all applicable Federal regulations governing the protection of human subjects. Research data were derived from an approved Naval Health Research Center, Institutional Review Board protocol numbers NHRC.2012.0006, NHRC.2014.0006, NHRC.2015.0013, and an “exempt” protocol.
EXECUTIVE SUMMARY

Background
Concomitant head injury and bodily pain is frequently observed in both civilian and military veteran populations.

Problem Statement
Although a growing body of literature quantifies these comorbidities in veteran populations, there is little available evidence in active duty military members.

Process
We evaluated associations between head injury and bodily pain in active duty military members in four independent cross-sectional studies, encompassing both combat and noncombat environments. We hypothesized that individuals endorsing head injury or a positive diagnosis of traumatic brain injury (TBI) would also experience greater bodily pain symptoms compared with those who did not. The main outcome measures for all studies were head injury or positive diagnosis of TBI.

Results
Across the four independent studies, the association between head injury and bodily pain was robust to numerous confounding influences, while behavioral health comorbidities consistently met criteria as mediators.

Conclusions
Bodily pain management is a key component in the medical care and rehabilitation of military personnel with head injuries.
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INTRODUCTION

Concomitant head injury and bodily pain is frequently observed in both civilian\textsuperscript{1} and military veteran populations.\textsuperscript{2} Although a growing body of literature quantifies these comorbidities in veteran populations,\textsuperscript{3-5} there is little available evidence in active duty military members. In one exception, Brickell et al\textsuperscript{6} showed that bodily pain symptoms increased substantially across three years after mild to moderate traumatic brain injury (TBI) in active duty service members. To our knowledge, there are no published studies of head injury within the combat environment. Therefore, there is a need to evaluate whether these associations are consistent across combat and noncombat settings using common metrics. Furthermore, numerous factors are believed to confound or mediate the association between head injury and bodily pain, such as extracranial (e.g., musculoskeletal) injuries,\textsuperscript{7} behavioral health comorbidities,\textsuperscript{8} and sleep disruption.\textsuperscript{9} A precise understanding of the connection between head injury and bodily pain can only be elucidated in studies that appreciate this inherent complexity.

We evaluated associations between head injury and bodily pain across four independent, cross-sectional studies of military members, encompassing both combat and noncombat environments. It was hypothesized that individuals endorsing head injury or a positive diagnosis of TBI would also experience greater bodily pain symptoms compared with those who did not.

METHODS

Study 1

Data source and subjects

As part of the Explosive Ordnance Disposal (EOD) Operational Health Surveillance System, 39 U.S. Navy EOD technicians (94.9% male; 23.1% age 25 to 29 years [n=9], 41.0% age 30 to 39
years [n=16], 35.9% age 40+ years [n= 14]) participated in this study. The research protocol (NHRC.2015.0013) was approved by the Naval Health Research Center Institutional Review Board.

**Measures**

*Head injury.* Participants reported if they had ever experienced a direct blow to the head, sustained any type of head injury, and/or received a medical diagnosis of TBI or concussion during their military career. Participants’ center of pressure movement was also measured using a portable balance tracking board (BTrackS, San Diego, CA). Center of pressure movement is an indirect measure of postural stability, which has been positively correlated to head injury/concussion in several populations (<30cm = normal, 30–49cm = high, ≥50cm = possible injury).10

*Bodily pain.* Participants were asked to report their average bodily pain on a scale of 0 to 10, with 10 as the highest level.

**Candidate covariates**

Candidate covariates for this study included sex, age, sleep disruption, fatigue, depressive symptoms, posttraumatic stress symptoms, extracranial injury, and pain medication use. Participants were asked to report the average number of hours of sleep they received per day and to rate their fatigue in the past week on a scale of 0 to 10, with 10 as the highest level. Depressive and posttraumatic stress symptoms were evaluated with the Patient Health Questionnaire (PHQ-8)11 (Cronbach’s $\alpha^{12} = .89$) and the Posttraumatic Stress Disorder (PTSD) Checklist for the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition13 (PCL-5; $\alpha=.90$), respectively. Participants were asked if they had ever sustained an injury to the upper extremities (i.e., shoulder, arm, elbow, hand, wrist), lower extremities (i.e., hip, leg, knee, ankle,
foot), or trunk (i.e., chest, back, abdomen, spine, pelvis); responses to these questions were then synthesized as a single measure of extracranial injury. Finally, participants indicated whether they were taking medications for chronic pain and, if so, which type of medication.

**Data analysis**

Data were analyzed using SPSS statistical software version 23.0. Descriptive analyses were conducted to summarize subject characteristics. To test each hypothesis, unadjusted differences between those participants with and without head injury were first evaluated with independent \( t \)-tests. Next, theoretically relevant variables were evaluated as potential covariates following standardized selection criteria. Specifically, a variable was selected as a covariate if it related to an independent variable (e.g., head injury) and the dependent variable of interest (e.g., pain; both \( P<.05 \)), thus qualifying as a potential confounder or mediator.\(^{14,15}\) Theoretically-supported candidate mediators were further evaluated following the principles of Baron and Kenny’s *causal steps approach*.\(^{16}\)

**Results**

One-fifth (21.6%; \( n=8 \)) of participants reported a direct blow to the head, 17.9% (\( n=7 \)) endorsed any type of head injury, and 15.4% (\( n=6 \)) reported receiving a medical diagnosis of TBI or concussion. One in 5 (20.5%; \( n=8 \)) registered high center of pressure scores (≥30). Pain ratings for this sample ranged from 0 to 6, and the mean (M) pain rating was 2.2 out of 10 (SD=1.5). EOD personnel endorsing a direct blow to the head (\( n=8 \)) reported greater bodily pain symptoms (3.9±1.6) compared with those who did not (\( n=31, 1.7±1.2 \)) (\( t(37) = -4.3, P<.001, d=1.7, \) large effect).\(^{17}\) Those endorsing any head injury (\( n=7 \)) reported greater bodily pain symptoms (4.3±1.3) compared with those who did not (\( n=32, 1.7±1.1 \)) (\( t(37) = -5.3, P<.001, d=2.8, \) large effect). Finally, those participants reporting a positive diagnosis of TBI (\( n=6 \)) endorsed greater
bodily pain symptoms (3.7±1.4) compared with those who did not (n=33, 1.9±1.4) ($t$(37) = −2.9, $P$=.007, $d$=1.3, large effect). In separate causal steps models, depressive and posttraumatic stress symptoms each met criteria as mediators of the association of positive TBI diagnosis with bodily pain. In all models, the observed associations between TBI and pain were not confounded by sex, age, extracranial injuries, sleep disruption, fatigue, or use of pain medication. No differences in bodily pain were observed between those whose center of pressure scores were ≥30 (n=8, 2.5±1.3) compared with those who scored <30 (n=31, 2.1±1.6) ($P$>.05).

**Study 2**

**Data source and subjects**

As part of the Sea, Air, and Land (SEAL) Sleep Study, subjects (N=68; age 33.0±7.1 years) were male active duty military members of the elite Navy SEAL community, assigned to Naval Special Warfare Group ONE located in San Diego, California. The research protocol (NHRC.2012.0006) was approved by the Naval Health Research Center Institutional Review Board.

**Measures**

*Head injury.* Participants reported if they had ever sustained any type of head injury or concussion (yes/no).

*Bodily pain.* Participants were asked to rate their bodily pain in the last four weeks on a scale of 1 to 10, with 10 as the highest level.

**Candidate covariates**

Candidate covariates for this study included age, sleep disruption, fatigue, depressive symptoms, posttraumatic stress symptoms, and bodily injury. Sleep efficiency was objectively derived by
actigraphy. Participants rated their typical daily fatigue during the past 4 weeks on a scale of 1 to 10, with 10 as the highest level. Depressive and posttraumatic stress symptoms were evaluated with the PHQ-8 ($\alpha=.93$) and the PTSD Checklist–Civilian Version ($\alpha=.79$), respectively. Participants also reported deployment-related bodily injuries.

**Data analysis**

An identical data analysis plan was followed as the one described in Study 1.

**Results**

Nearly two-thirds of SEALs (58.8%; $n=40$) reported a head injury. The mean pain rating for this sample was 3.7 out of 10 ($SD=2.1$), and pain ratings ranged from 1 to 9. The SEALs who endorsed head injury ($n=40, 4.2\pm2.2$) reported substantially greater bodily pain than those without head injury ($n=28, 2.9\pm1.6$) ($t(66) = −2.7, P=.01, d=.70$, medium effect). The association between head injury and pain was not confounded by age, fatigue, sleep disruption, depressive symptoms, PTSD symptoms, or bodily injury.

**Study 3**

**Data source and subjects**

As part of the Naval Unit Behavioral Health Needs Assessment Survey, 620 active duty Navy and Marine Corps personnel (85.6% male) participated in this study. One quarter (24.4%, $n=151$) were in a shore-based training status, 33.7% ($n=209$) were shipboard and deployed, while the remaining 41.9% ($n=260$) were shipboard in a non-deployed status. The majority of participants (41.1%, $n=253$) were age 17 to 24 years, while 32.8% ($n=202$) were age 25 to 29 years, 21.9% ($n=135$) were 30 to 39 years, and 4.2% ($n=26$) were 40+ years (3 participants [0.5%] had missing data). Participation was voluntary, and all subjects gave informed consent. The research protocol
(NHRC.2014.0006) was approved by the Naval Health Research Center Institutional Review Board, and all data were collected anonymously using unique identification codes.

**Measures**

*Head injury.* Participants reported if they had ever experienced a direct blow to the head, sustained any type of head injury, and received a medical diagnosis of TBI or concussion during their current assignment (yes/no).

*Bodily pain.* Participants were asked to report their average bodily pain on a scale of 0 to 10, with 10 as the highest level.

**Covariate selection**

Covariates for this study included age, gender, sleep disruption, fatigue, depressive symptoms, posttraumatic stress symptoms, and pain medication use. Participants were asked to report, on average, the number of hours of sleep they received per day and to rate their fatigue in the past week on a scale of 1 to 10, with 10 as the highest level. Depressive and posttraumatic stress symptoms were evaluated with the PHQ-9 ($\alpha=.95$) and the PCL-5$^{13}$ ($\alpha=.88$), respectively. Finally, participants indicated if they were currently taking medications for chronic pain and, if so, which type of medication.

**Data analysis**

An identical data analysis plan was followed as in Studies 1 and 2. Additionally, an exploratory analysis of variance (ANOVA) compared subgroups with exposure to head injury (i.e., direct blow or any head injury) but no TBI diagnosis (n=49); exposure to head injury with positive TBI diagnosis (n=9); and an unexposed subgroup (i.e., no direct blow, no head injury, and no TBI diagnosis; n=562) with respect to bodily pain.

**Results**
Prevalence of direct blow to the head, any head injury, and positive diagnosis of TBI or concussion during the current assignment were 6.9%, 6.9%, and 1.5%, respectively. Pain ratings ranged from 0 to 10 in this sample, and the mean pain rating was 2.3 (SD=2.0). Participants endorsing direct blow to the head during the current assignment (n=43) reported greater bodily pain symptoms (3.3±2.4) compared with those who did not (n=577, 2.2±2.0) (t(46) = −2.9, P=.006, d=.50, medium effect). In separate causal steps analyses, depressive and posttraumatic stress symptoms qualified as partial mediators of the association between direct blow to the head and pain symptoms. This observed association was not confounded by age, sex, or pain medication use, nor was it mediated by sleep disruption or fatigue. Those who reported any head injury during the current assignment (n=43) endorsed greater bodily pain symptoms (3.4±2.2) compared with those who did not (n=577, 2.2±2.0) (t(618) = −3.7, P<.001, d=.60, medium effect). In separate causal steps models, sleep disruption, fatigue, depressive symptoms, and posttraumatic stress symptoms qualified as partial mediators of the association between any head injury and pain symptoms. This observed association was not confounded by age, sex, or pain medication use. Finally, those participants reporting a positive diagnosis of TBI (n=9) during the current assignment endorsed greater bodily pain symptoms (3.6±3.1) compared with those who did not (n=611, 2.3±2.0) (d=.60, medium effect); however, this did not reach statistical significance (P=.06). Therefore, confounding and mediated effects were not explored. In the exploratory ANOVA, unexposed participants (n=562) reported less bodily pain (2.2±2.0) compared with exposed participants without (n=49, 3.2±2.0, P=.001) or with (n=9, 3.6±3.1, P=.043) TBI diagnosis (overall F=7.9, P<.001). The latter two groups did not differ from each other.
Study 4

Data source and subjects

The Behavioral Health Needs Assessment Survey evaluates a diverse population of U.S. Navy personnel deployed to combat zones in Iraq and Afghanistan from 2006 to 2014. The instrument was reviewed by the Naval Health Research Center Institutional Review Board and classified as “exempt” based on its primary surveillance mission and absence of identifiable information.

Measures

Head injury. Participants (N=1165) reported if they had sustained a blow/jolt to the head and/or sustained any head injury during the current deployment (yes/no).

Bodily pain. Participants reported if they had experienced any physical pain during the current deployment (yes/no).

Covariate selection

Candidate covariates included age, sex, sleep disruption, depressive symptoms (adapted from the PHQ-9 [α=.92] as done by Hoge et al21), and posttraumatic stress symptoms (PCL-C19; α=.93). Participants reported the average number of hours of sleep received per day during the current deployment.

Data analysis

In this study, the primary endpoint (bodily pain) was dichotomous. With this in mind, hypothesis tests were conducted using logistic regression models, and odds ratios were used as estimates of effect size.

Results
Prevalence of a blow/jolt to the head and any head injury during the current deployment were 3.7% (n=43) and 4.6% (n=54), respectively. Nearly 1 in 5 participants (18.2%, n=212) reported any physical pain during the current deployment. Those who endorsed any injury to the head during the current deployment were 3.9 times as likely to report any bodily pain (overall model \( \chi^2=7.8, P<.01; \) Nagelkerke R\(^2\)=.01, Hosmer-Lemeshow \( \chi^2=.00, P>.05; \) Wald \( \chi^2=5.2, P=.02 \)). In separate causal steps analyses, depressive and posttraumatic stress symptoms qualified as mediators of the association between head injury and bodily pain symptoms. The observed association was not confounded by age or sex, nor was it mediated by sleep disruption or fatigue. Similar unadjusted associations of a blow/jolt to the head with bodily pain was observed, but the model did not reach statistical significance (\( P=.07 \)). Therefore, confounding and mediated effects were not explored.

**DISCUSSION**

Reliable associations were observed between head injury and bodily pain across four independent studies of military personnel. This is consistent with recent observations of veteran populations,\(^3,4\) as well as a smaller knowledge base regarding active duty military members.\(^6\) Our exploratory analyses further suggested that it may be exposure to head injuries per se, rather than TBI diagnosis, that increases bodily pain. Altogether, the current study uniquely contributes to the literature by demonstrating stable and substantial associations between head injury and bodily pain in diverse military populations, across both combat and noncombat environments, using essentially common metrics.

A direct association between head injury and bodily pain is biologically plausible. For instance, Kim et al\(^22\) found that injury of the spinothalamocortical tract (which mediates sense of
touch, pain, and temperature) predicts centralized pain in patients with mild TBI. A second plausible mechanism concerns the periaqueductal gray (PAG). This structure encircles the cerebral aqueduct at the tegmentum of the midbrain, which is believed to be vulnerable to head injury. The PAG is a main descending pain inhibitory system, and PAG injury has been linked to heightened centralized pain. Recently, Jang et al not only identified PAG injury in patients with centralized pain following TBI compared with healthy controls, but also correlated the magnitude of injury to the degree of reported pain symptoms.

The association of head injury and bodily pain was consistently, though not always (see Study 3), mediated by depressive and posttraumatic stress symptoms. This finding could further implicate the PAG, inasmuch as it also modulates fear, anxiety, and depression. It is plausible then, that head injuries may selectively damage the PAG, which not only alters fear and emotional processing, but also elevates bodily pain. This is further supported in the broader literature by consistent observations of the polytrauma triad expression (i.e., the coexistence of head injury, posttraumatic stress symptoms, and bodily pain). This is also aligned with the depression–pain syndrome model, which describes comorbidity of depressive symptoms with bodily pain, their reciprocal influences, as well as the crossover effects of pain and antidepressant medication. Patients with multiple pain symptoms are 3 to 5 times more likely to be depressed than patients without pain, and the presence of pain symptoms doubles the risk for comorbid depression. The PAG, then, may represent a common biological mechanism underlying these associations.

**Study limitations**

Although we achieved ample commonality of metrics across the four studies, subtle differences in methodology and measurement render a comparison across these studies imperfect.
Additionally, we were able to evaluate confounding influences of extracranial injury in only 2 of the 4 studies. These limitations are counterbalanced by the fact that we produced the same overall finding across four different military populations, despite slight variations in metrics, both with and without extracranial injury as a candidate covariate, and while controlling for other theoretically-important confounds (e.g., posttraumatic stress symptoms).

CONCLUSIONS

Reliable associations were observed between head injury and bodily pain across four independent studies. Collectively, these studies demonstrate substantial effect sizes, robustness to confounding influences, and replicability across diverse military populations and a broad spectrum of military environments. Therefore, bodily pain management should be a key component in the medical care and rehabilitation of military personnel with head injuries.
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**Head Injury and Bodily Pain in Military Personnel: Robust Evidence in Combat and Noncombat Environments**

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**14. ABSTRACT**
Background: Concomitant head injury and bodily pain is frequently observed in both civilian and military veteran populations. Problem Statement: Although a growing body of literature quantifies these comorbidities in veteran populations, there is little available evidence in active duty military members.

Process: We evaluated associations between head injury and bodily pain in active duty military members in four independent cross-sectional studies, encompassing both combat and noncombat environments. We hypothesized that individuals endorsing head injury or a positive diagnosis of traumatic brain injury (TBI) would also experience greater bodily pain symptoms compared with those who did not. The main outcome measures for all studies were head injury or positive diagnosis of TBI.

Results: Across the four independent studies, the association between head injury and bodily pain was robust to numerous confounding influences, while behavioral health comorbidities consistently met criteria as mediators.

Conclusions: Bodily pain management is a key component in the medical care and rehabilitation of military personnel with head injuries.

**15. SUBJECT TERMS**
Head injuries; Pain; Military; Sleep; Fatigue

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