Chronic Daily Headache in U.S. Soldiers After Concussion

Brett J. Theeler, MD; Frederick G. Flynn, DO; Jay C. Erickson, MD, PhD

Objective.—To determine the prevalence and characteristics of, and factors associated with, chronic daily headache (CDH) in U.S. soldiers after a deployment-related concussion.

Methods.—A cross-sectional, questionnaire-based study was conducted with a cohort of 978 U.S. soldiers who screened positive for a deployment-related concussion upon returning from Iraq or Afghanistan. All soldiers underwent a clinical evaluation at the Madigan Traumatic Brain Injury Program that included a history, physical examination, 13-item self-administered headache questionnaire, and a battery of cognitive and psychological assessments. Soldiers with CDH, defined as headaches occurring on 15 or more days per month for the previous 3 months, were compared to soldiers with episodic headaches occurring less than 15 days per month.

Results.—One hundred ninety-six of 978 soldiers (20%) with a history of deployment-related concussion met criteria for CDH and 761 (78%) had episodic headache. Soldiers with CDH had a median of 27 headache days per month, and 46/196 (23%) reported headaches occurring every day. One hundred seven out of 196 (55%) soldiers with CDH had onset of headaches within 1 week of head trauma and thereby met the time criterion for posttraumatic headache (PTHA) compared to 253/761 (33%) soldiers with episodic headache. Ninety-seven out of 196 (49%) soldiers with CDH used abortive medications to treat headache on 15 or more days per month for the previous 3 months. One hundred thirty out of 196 (66%) soldiers with CDH had headaches meeting criteria for migraine compared to 49% of soldiers with episodic headache. The number of concussions, blast exposures, and concussions with loss of consciousness was not significantly different between soldiers with and without CDH. Cognitive performance was also similar for soldiers with and without CDH. Soldiers with CDH had significantly higher average scores on the posttraumatic stress disorder (PTSD) checklist compared to soldiers with episodic headache. Forty-one percent of soldiers with CDH screened positive for PTSD compared to only 18% of soldiers with episodic headache.

Conclusions.—The prevalence of CDH in returning U.S. soldiers after a deployment-related concussion is 20%, or 4- to 5-fold higher than that seen in the general U.S. population. CDH following a concussion usually resembles chronic migraine and is associated with onset of headaches within the first week after concussion. The mechanism and number of concussions are not specifically associated with CDH as compared to episodic headache. In contrast, PTSD symptoms are strongly associated with CDH, suggesting that traumatic stress may be an important mediator of headache chronification. These findings justify future studies examining strategies to prevent and treat CDH in military service members following a concussive injury.

Key words: mild traumatic brain injury, concussion, posttraumatic headache, military
Over 160,000 U.S. military service members have been diagnosed with traumatic brain injury since 2000.1 Concussions occur in 15-23% of U.S. service members deployed in support of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).2-4 Headache is one of the most common symptoms after a concussion and may persist for months to years after injury. The prevalence of headaches in returning U.S. military service members who had a concussion while deployed to Iraq or Afghanistan ranges from 22% to 97%.2,3,5

Chronic daily headache (CDH), defined as 15 or more headache days per month, is one of the most disabling headache syndromes with a prevalence of 4-5% in the general population.6,7 A number of primary headache disorders may manifest as CDH. Chronic migraine is one of the most common and most disabling forms of CDH among primary headache disorders. Secondary headache disorders can also manifest as CDH. Head trauma has been suggested as an important risk factor in the development of chronic daily headache in civilians. It has been estimated that 15% of cases of CDH in the general population are attributable to head or neck trauma.8

Little is known about CDH in military populations. Given the association between head trauma and CDH in civilians, we hypothesized that CDH would be highly prevalent among service members who had a concussion while serving in Iraq or Afghanistan. We previously reported the prevalence, characteristics, and impact of headaches in a large cohort of returning U.S. soldiers who had a concussion while deployed to Iraq or Afghanistan.5 The aim of the current study was to determine the prevalence and characteristics of, and factors associated with, CDH in this same cohort of U.S. soldiers who had a deployment-related concussion.

METHODS
This study was approved by the Madigan Army Medical Center Institutional Review Board. A cross-sectional, questionnaire-based study was conducted with a cohort of 978 U.S. soldiers who screened positive for a deployment-related concussion upon returning from Iraq or Afghanistan. The details of the screening process and a description of the headaches in this same cohort have been previously reported.5 All soldiers underwent a clinical evaluation at the Madigan Traumatic Brain Injury Program that included a history, physical examination, 13-item self-administered headache questionnaire, and a battery of cognitive and psychological assessments as described previously. Information about head trauma was obtained by interviewing the soldier and reviewing theater medical records. The Madigan Redeployment Evaluation of Concussion (MREC) test, scored from 0 to 30 with below 25 defined as abnormal, was used to assess cognitive function. The MREC, which is similar to the Military Acute Concussion Evaluation (http://www.dvbic.org/images/pdfs/providers/MACE-Information-Paper-V3.aspx), is a neurocognitive screening instrument intended for evaluating soldiers with a deployment-related concussion after returning stateside. Posttraumatic stress disorder (PTSD) symptoms were assessed using the PTSD symptom checklist, military version (PCL). A global measure of acute traumatic brain injury (TBI) symptoms at the time of the injury was obtained using the 2-plus-10 questionnaire.5 The 2-plus-10 questionnaire consists of an initial 2-question followed by a 10-question screen if the soldier answers yes to either of the first 2 questions. This questionnaire is scored in a standardized manner from 0 to 39; the score from the 2-plus-10 questionnaire will herein be called the TBI Score.5 Data from soldiers with CDH, defined as headaches occurring 15 or more days per month for the previous 3 months, were compared to soldiers with episodic headaches who had less than 15 headache days per month.

Fisher’s exact test was used to test for differences in proportions, and unpaired t-test was used to test for differences in ordinal variables with a normal distribution. Correlation coefficients were calculated to test the relationship between individual variables where appropriate. P values less than .05 were considered significant.

RESULTS
Nine hundred fifty-seven of 978 soldiers with a deployment-related concussion reported headaches in the preceding 3 months. One hundred ninety-six soldiers (20%) reported 15 or more headache days per month for the previous 3 months and thereby met
criteria for CDH (Table 1). Soldiers with CDH had a median of 26.7 headache days per month, and the headache syndrome had been present for a median of 11.5 months. Forty-six (23%) of the soldiers with CDH reported headaches on 90 of the previous 90 days. One hundred seven (55%) soldiers with CDH had headaches that began within 1 week of head trauma and thereby met the time criterion for post-traumatic headache (PTHA). In comparison, 33% of episodic headaches had onset within 1 week of a concussion \( (P < .0001) \). Soldiers with CDH used abortive headache medications an average of 15.1 days per month compared to 3.3 days per month for soldiers with episodic headache \( (P < .0001) \). Ninety-seven (49%) soldiers with CDH used abortive headache medications on 15 or more days per month for the previous 3 months \( (P < .05) \).

Headache characteristics of CDH are summarized in Table 2. One hundred thirty (66%) soldiers with CDH had headaches meeting criteria for migraine compared to 49% of soldiers with episodic headache \( (P < .0001) \) (Table 2). CDHs were more likely than episodic headaches to be asymmetric \( (P < .0001) \), throbbing/pulsating \( (P < .05) \), worse with exertion \( (P < .01) \), disrupt normal activities \( (P < .0001) \), and accompanied by nausea \( (P < .0001) \) and photo or phonophobia \( (P < .0001) \).

Trauma characteristics are summarized in Table 3. The number of concussions, blast exposures per soldier, and concussions with loss of consciousness was not significantly different in soldiers with and without CDH. Soldiers with CDH reported more acute symptoms after concussion as manifested by higher TBI scores \( (P < .0001) \). One hundred eighty-

### Table 1.—Headache Features of Soldiers With Chronic Daily Headache

<table>
<thead>
<tr>
<th></th>
<th>Chronic Daily Headache</th>
<th>Episodic Headache</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, N (%)</td>
<td>196 (20)</td>
<td>761 (78)</td>
</tr>
<tr>
<td>Females</td>
<td>4 (2)</td>
<td>10 (1)</td>
</tr>
<tr>
<td>Median headache days/month</td>
<td>26.7</td>
<td>3.3</td>
</tr>
<tr>
<td>Median duration of headache syndrome (months)</td>
<td>11.5</td>
<td>10</td>
</tr>
<tr>
<td>** Soldiers with headache onset within 1 week of concussion, N (%)</td>
<td>107 (55)*</td>
<td>253 (33)</td>
</tr>
<tr>
<td>** Soldiers with headache onset within 1 month of concussion, N (%)</td>
<td>50 (26)**</td>
<td>143 (19)</td>
</tr>
<tr>
<td>** Soldiers with 15+ medication days/mo, N (%)</td>
<td>97 (49)*</td>
<td>16 (2)</td>
</tr>
</tbody>
</table>

\* \( P < .0001, ** P = .045. \)

### Table 2.—Headache Classification of Soldiers With CDH

<table>
<thead>
<tr>
<th></th>
<th>Chronic Daily Headache</th>
<th>Episodic Headache</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>196</td>
<td>761</td>
</tr>
<tr>
<td>Migraine, N (%)</td>
<td>130 (66)*</td>
<td>374 (49)</td>
</tr>
<tr>
<td>Possible migraine</td>
<td>55 (28)</td>
<td>265 (35)</td>
</tr>
<tr>
<td>Non-migraine</td>
<td>11 (6)*</td>
<td>122 (16)</td>
</tr>
<tr>
<td>Asymmetric</td>
<td>134 (68)*</td>
<td>377 (50)</td>
</tr>
<tr>
<td>Throbbing/pulsating</td>
<td>172 (88)**</td>
<td>609 (80)</td>
</tr>
<tr>
<td>Worse with physical exertion</td>
<td>130 (66)**</td>
<td>418 (55)</td>
</tr>
<tr>
<td>Disrupt normal activities</td>
<td>107 (55)*</td>
<td>290 (38)</td>
</tr>
<tr>
<td>Associated nausea</td>
<td>89 (45)*</td>
<td>234 (31)</td>
</tr>
<tr>
<td>Photophobia or phonophobia</td>
<td>151 (77)*</td>
<td>445 (58)</td>
</tr>
</tbody>
</table>

\* \( P < .0001, ** P = .0045, *** P = .013. \)
six (19%) soldiers reported blast as the only mechanism of head trauma without associated blunt impact (ie, blast-only), while 97 (10%) soldiers were diagnosed with a concussion without any exposure to a blast (ie, non-blast). A similar proportion of soldiers with CDH and episodic headache had blast-only and non-blast mechanisms of concussion (Table 3).

Cognitive function and PTSD symptoms are summarized in Table 4. Cognitive function, as measured by MREC scores, was similar for soldiers with and without CDH (Table 4). Soldiers with CDH had higher average scores on the PTSD checklist compared to soldiers with episodic headache (P < .0001). Forty-one percent of soldiers with CDH screened positive for PTSD, based on a PCL score of greater than 50, compared to only 18% of soldiers with episodic headache (P < .0001). In univariate analysis, PCL scores correlated with the number of blast exposures per soldier (P = .007).

**DISCUSSION**

This study examined CDH in a large cohort of returning U.S. Army soldiers who had a deployment-related concussion. We found that 20% of soldiers with a history of concussion had headaches manifesting as CDH. When one considers prevalence rates of CDH of 4-5% in the general population, the prevalence of CDH in soldiers after a deployment-related concussion is 4- to 5-fold higher. The high prevalence of CDH in soldiers after concussion is consistent with previous studies suggesting a role for mild head trauma in the development of CDH. In a U.S. population sample, 20% of males with CDH reported a preceding head or neck injury. We previously reported that one third of soldiers with a history of head or neck trauma referred to a military headache clinic had CDH.

Head trauma can trigger new headaches and/or can exacerbate preexisting primary headaches. When new headaches...
headaches develop within 1 week after head trauma, they are classified as posttraumatic headaches according to ICHD-2. Compared to episodic headache, we found that CDH was significantly associated with headache onset within a week of the concussive event. Soldiers with CDH were 1.7-fold more likely to have headaches meeting ICHD-2 criteria for PTHA compared to soldiers with episodic headaches. This finding further supports trauma as a triggering event in the development of CDH. Given the increased propensity of posttraumatic headaches to manifest as CDH, interventions administered early after injury that prevent headache chronification may be beneficial. It may be more effective to prevent the development of CDH early after injury than to treat established CDH.

Migraine was the headache phenotype in 66% of soldiers with CDH in our study, with an additional 28% having multiple features of migraine. Migraine headaches were significantly more common in soldiers with CDH compared to those with episodic headache. In a headache clinic-based population, migraine was the headache phenotype in over 90% of soldiers with posttraumatic headache, over half of whom had CDH. In comparison, the prevalence of chronic migraine is 2% in the general U.S. population and 4% in Army soldiers post-deployment. These findings support a strong association between concussion and chronic migraine in U.S. service members. Chronic migraine should be regarded as the predominant headache syndrome among soldiers with posttraumatic CDH.

Topiramate and botulinum toxin are the only treatments that have been shown to be effective for chronic migraine in the general population. It remains to be determined if these treatments are also effective for posttraumatic chronic migraine. In an uncontrolled observational study, topiramate was associated with headache improvement in soldiers with chronic PTHA, many of whom had posttraumatic chronic migraine. Identifying effective therapies for posttraumatic chronic migraine is an important goal of future research.

Exposure to an explosive blast was the mechanism of concussive injury in over 80% of soldiers in our study, similar to findings reported by other studies of service members deployed to Iraq or Afghanistan. The potential mechanisms of blast-induced neurotrauma are complex and may include primary effects from the blast wave, secondary effects caused by fragments or debris, tertiary effects of rapid acceleration and deceleration, flash burns, and effects of inhalation of toxic gases. We found no differences in blast exposures between soldiers with CDH compared to those with episodic headaches. Likewise, in a clinic-based population, headache frequency was found to be similar between soldiers with blast-related concussion and non-blast causes of concussion. Wilk et al recently reported that blast mechanism was associated with persistence of headaches and tinnitus at 3 to 6 months in soldiers with concussion and loss of consciousness. The available information suggests that while blast injury increases the likelihood of developing chronic headaches that persist beyond 3 months after injury, it does not appear to affect the frequency of headaches as compared to other mechanisms of concussion.

An important question is whether the severity of head trauma or repetitive head injuries increases the risk of CDH. Couch et al found an association between multiple head and neck traumas and CDH in the general population. We did not find significant differences in the total number of concussions or the number of concussions resulting in loss of consciousness between soldiers with CDH and episodic headaches. Soldiers with CDH did report more symptoms immediately after the concussion, as measured by the TBI score, suggesting that they may have experienced a more acutely symptomatic injury and perhaps, by extension, a potentially more severe concussion. This is a tenuous assertion that requires validation by prospective studies because of the high likelihood of recall bias.

Psychological trauma and posttraumatic stress may be significant mediators of headache chronicity after head trauma. In support of this, we found that soldiers with CDH had more symptoms of PTSD and were more than twice as likely to screen positive for PTSD compared to soldiers with episodic headaches. Indeed, 41% of soldiers with CDH had a positive screen for PTSD. Additionally, PCL scores were significantly correlated to the number of headache days and blast exposures. Studies in civilian and military populations have demonstrated an association
between PTSD and an increased frequency of headache.\textsuperscript{19,20} Bryan et al, using regression modeling, found a statistically significant association between PTSD symptoms and headache severity in veterans of the wars in Iraq and Afghanistan.\textsuperscript{21}

The extent to which symptoms of the post-concussive syndrome after mild head injury can be attributed to PTSD or depression in returning U.S. service members remains a topic of significant debate.\textsuperscript{22,23} In a pivotal study by Hoge et al, after controlling for PTSD and depression, headache was the only symptom significantly associated with mild concussion in 2525 U.S. Army infantry soldiers screened 3-4 months after return from a 1 year deployment to Iraq.\textsuperscript{2} Thus, while posttraumatic stress may magnify the frequency and severity of headaches, it does not appear to be the proximate cause of headaches in this population. The observed high prevalence of PTSD in our study cohort, particularly among soldiers with CDH, reinforces the importance of screening soldiers and veterans for PTSD and, when positive, referring them for behavioral health evaluation and treatment.

Another important factor that can contribute to headache chronicification is overuse of acute analgesic medications resulting in medication overuse headache (MOH). Medication overuse has been implicated in transforming episodic migraine to chronic migraine.\textsuperscript{24} Medication overuse is defined as use of abortive headache medication on 15 or more days per month for 3 or more months.\textsuperscript{10} Nearly half (49\%) of soldiers with CDH in our study met criteria for possible MOH. The majority, 80\% or more, of soldiers in this cohort used nonsteroidal anti-inflammatory agents and acetaminophen as abortive headache medications.\textsuperscript{5} We may have underestimated possible MOH in the proportion of soldiers using prescription medications such as triptans or narcotics (less than 10\% of soldiers in this cohort\textsuperscript{5}) or combination analgesics such as acetaminophen-aspirin-caffeine (6\% of soldiers in this cohort\textsuperscript{5}) given the lower threshold of medication days per month associated with MOH with use of these medications. A diagnosis of definite MOH requires resolution of headaches following cessation of the overused analgesics medication(s). Thus, it is not possible to determine precisely the proportion of subjects in our study who had definite MOH. Avoiding medication overuse in the first place and identifying and addressing MOH when it develops are strategies that may decrease the development of CDH in soldiers following a concussion.

This study has many limitations related to the questionnaire-based, cross-sectional design. Headache frequency was retrospectively reported by soldiers and was not prospectively recorded in a headache log. It is possible that recall errors in reporting headache frequency resulted in misclassification of some soldiers with regard to having CDH or episodic headache. Likewise, reporting of blast exposures and acute symptoms of concussion that may have occurred many months ago are subject to recall error. Screening for preexisting headaches was not performed, potentially contributing to misattribution and making an analysis of incident headaches vs worsening of previous headache syndromes impossible. While all soldiers met screening criteria for a deployment-related concussion, concussion severity was not determined, thereby limiting any conclusions regarding concussion severity and headache chronicity drawn from this study. Theater records were used to validate some of these events but were not available in all cases. Soldiers in the study were evaluated at a TBI clinic, and this type of setting may have inclined them to over-report symptoms. Finally, this study may not be representative of all U.S. service-members with a deployment-related concussion as it was conducted at a single U.S. Army installation over a 6-month period.

CONCLUSIONS

The prevalence of CDH in U.S. soldiers after a deployment-related concussion is 20\%, or 4- to 5-fold higher than that seen in the general population. CDH in soldiers with concussion usually has multiple features of migraine and frequently resembles chronic migraine. Onset of headaches within 1 week of a concussion is associated with the development of CDH as compared to episodic headache. Overuse of headache abortive medications, raising the possibility of MOH, occurs in half of soldiers with CDH. Blast exposure and multiple concussions are common in this population, but these factors are not specifically associated
with CDH as compared to episodic headache. PTSD symptoms are strongly associated with CDH suggesting that traumatic stress may be a significant mediator of headache chronicity. These findings justify future studies examining strategies to prevent and treat CDH in military service members.

REFERENCES


