

AD _____

Award Number: W81XWH-08-2-0105

TITLE: Deployment-Related Mild Traumatic Brain Injury (mTBI): Incidence Natural History and Predictors of Recovery in Soldiers Returning from OIF/OEF

PRINCIPAL INVESTIGATOR: Karen Schwab, Ph.D.

CONTRACTING ORGANIZATION: Henry M. Jackson Foundation for the
Advancement of Military Medicine
Rockville, MD 20852

REPORT DATE: May 2011

TYPE OF REPORT: Revised Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE 1 May 2011		2. REPORT TYPE Revised Annual		3. DATES COVERED 1 MAY 2010-30 APR 2011	
4. TITLE AND SUBTITLE Deployment-Related Mild Traumatic Brain Injury (mTBI): Incidence Natural History and Predictors of Recovery in Soldiers Returning from OIF/OEF				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-08-2-0105	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Karen Schwab, Ph.D. E-Mail: KAREN.SCHWAB@US.ARMY.MIL				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Henry M. Jackson Foundation for the Advancement of Military Medicine Rockville, MD 20852				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT NONE PROVIDED					
15. SUBJECT TERMS NONE PROVIDED					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	8	19b. TELEPHONE NUMBER (include area code)

Table of Contents

	Page
Introduction	1
Body	1-3
Key Research Accomplishments	3
Reportable Outcomes	3
Conclusion	4
References	4
Appendix	4
Supporting Data	4

Introduction

The overarching aim of this study is to describe the epidemiology, natural history, and prognostic predictors of mild traumatic brain injury (mTBI) in a well- defined cohort of 1,500 recently- deployed soldiers at Fort Carson and Fort Bragg. Mild traumatic brain injury is a frequent injury in theatre and there are substantial gaps in our understanding of the recovery patterns after this injury and whether currently used mTBI screening tools are and valid. This study is augmenting ongoing surveillance and clinical efforts at these locations by expanding the post-deployment assessment of traumatic brain injury (TBI) and TBI-related exposures; identifying pre-existing and deployment-related exposures and comorbid conditions that may influence the risk or prognosis of mTBI-related sequelae; determining the relationship of mTBI reported on screens with clinical interviews, and re-assessing this cohort at three, six, and twelve months after return from deployment with the aim of determining the persistence of post-deployment symptoms and the degree to which these symptoms impact on military or civilian employment, including fitness for military duty, functional status, and quality of life.

Body

The award was issued effective 1 May 2008. Regulatory reviews have been completed on the protocol for Fort Carson, and Fort Bragg has received local informal IRB approval. Second level review for Fort Bragg is expected in mid-summer. Fort Bragg will begin recruitment once final approval is received and the local IRB issues the start letter. The Fort Carson site has recruited a total of 452 subjects from three cohorts of soldiers returning from OIF/OEF. Six month follow-up rates are 57% for recruitment Group 1; and 46% for Group 2. Twelve month follow-ups have been completed for Group 1 (49%) and are in process for Group 2. The Qualitative Sub-study has recruited a total of 103 subjects over two recruitment cohorts, and has completed 6 and 12 month follow-ups on those subjects. Six and 12 month follow-up rates for the Qualitative Sub-study are 62% and 59% for Group 1; 27% and 43% for Group 2.

One research poster was presented, and one research presentation has been accepted in this time period (slides for presentation were not finalized during this annual report cycle). Dr. Scher presented a research poster based upon data from Group 1 recruitment at Fort Carson, "Headache Disorders in Recently Deployed Soldiers with and without Traumatic Brain Injury" to the 2011 Annual Meeting of the American Academy of Neurology in April 2011 (Appendix 1). Recent studies have reported that migraine-like and chronic daily headache are surprisingly common complaints in recently deployed soldiers. The analyses presented in the poster investigated the relationship of deployment mTBI to headache and headache type in recently deployed soldiers. Comparing soldiers

with deployment mTBI (n=174) and controls (n=202), Scher et al supported previous evidence and reported that most mTBI cases (91%) and controls (79%) reported headache in the past year. In addition, the researchers found that the character of headache differed for soldiers with and without mTBI. Soldiers with mTBI more often reported migraine, compared to controls who more often reported non-migraine headache or no headache ($p<.005$). And, soldiers with mTBI more often reported Chronic Daily Headache than controls (21% vs 7%, $p<.005$), as well as more often reported pain from headache/migraine in the previous three months (71% vs 51%, $p<.005$). Of those with migraine or possible migraine, mTBI was more often associated with aura (36% in soldiers with mTBI; 20% in soldier controls).

Dr. Scher is continuing her investigation of headache in soldiers recruited through the CDMRP award, both with detailed questionnaires and a sub-study focused on neurological evaluation of sample members with and without mTBI (CNRM award).

Problems in accomplishing tasks: The approval process at Fort Bragg has been onerous with the identification of a replacement PI after the reassignment of the original PI to another Army Military Treatment Facility, and IRB requirements for the establishment of Memoranda of Understanding (MOA) for the links to military databases described in the protocol. The MOAs are in process and the IRB has agreed to review the data merges and related analyses once the MOAs are signed by the appropriate parties. As a result, the study at Fort Bragg was delayed for a period of approximately two years. We requested a one year no-cost extension from the USA Medical Research Acquisition Activity in order to accomplish maximum possible recruitment of the Fort Bragg sample [subsequently granted on 2 August 2011].

Task Reports:

Task 1: IRB approvals:

- Fort Carson has received all approvals (final on July 31, 2009)
- Fort Bragg awaiting final approval and start letter.

Task 2: Recruitment of Study Personnel

- Fort Carson: Completed
- Fort Bragg: Recruitment underway for Subject Recruiter/Research Assistant (to replace former incumbent); and for Study Interviewer. Headquarters: Data Manager/analyst recruitment underway.

Task 3-4: Study assessments and manuals completed and updated as needed.

Task 5: Training: Completed with current personnel; new personnel trained as required.

Tasks 6, 8, 9, 11: Recruitment, baseline evaluations, and follow-up interviews:

- Fort Carson: Has enrolled 451 subjects (out of projected 750), and continues to conduct follow-up interviews. Follow-up rate to date is 72% (3 mon); 52% (6 mon); 49% (12 mon)..; Qualitative sub study enrolled 103.
- Fort Bragg: Will begin enrollment once receive final approval and start letter.

Tasks 7 and 10: Interim Reports

- Poster presented at Neurology meetings in April 2011 describing initial findings regarding headache classification, experience of chronic daily headaches and prior diagnosis of migraine.
- Qualitative sub-study investigators will present selected findings in June 2011 Federal Interagency Conference on TBI at symposium, "Lifetime History of TBI – Implications for Current Functioning."
- Interim reports are in preparation to present findings from the Fort Carson cohort (interim reports will be finalized once the Fort Carson cohort recruitment is completed).

Tasks 12-14: Close out of data set and final report: Will be completed at end of the study.

Key Research Accomplishments:

- Deployment mTBI was found to be associated with migraine headaches
- Deployment mTBI was found to be associated with chronic daily headaches

Reportable Outcomes:

- Headache Disorders in Recently Deployed Soldiers with and without Traumatic Brain Injury: Poster presentation to the 2011 Annual Meeting of the American Academy of Neurology (April, 2011).
- Successful application and receipt of a Center for Neuroscience and Regenerative Medicine (CNRM) award to expand the study of Headache at the Fort Bragg CDMRP site. The application leveraged the CDMRP award and preliminary data on headache from the study.
- Presentation accepted on Lifetime History of TBI among Returning Service Members and Military Veterans (to be presented in June, 2011 at the 2011 Federal Interagency TBI Conference).

Conclusion:

After a substantial delay, Fort Bragg is close to initiating recruitment (as of the date of this annual report); Fort Carson has enrolled 451 subjects out of their target goal of 750 subjects. A one year no-cost extension will permit recruitment of all subjects for the baseline surveys and interviews at both sites. Fort Carson is projected to complete all follow-ups for the study, but even with the extension, Fort Bragg may not have sufficient time to complete all follow-ups on all recruited subjects. Both sites have implemented surge support plans in order to maximize recruitment of subjects during large redeployments in order to reach recruitment goals.

Preliminary analysis of headache data for the study (conducted on a sample size of 174 soldiers with mTBI, and 202 soldier controls) found more migraine and chronic daily headaches in returning soldiers with mTBI. Further, this initial study found that migraine headaches in returning soldiers with mTBI had different patterns of aura-like symptoms. These patterns will be further investigated in the study, as well as with neurological exams supported by separate CNRM funding. Headache is generally identified as the most common sequel of mTBI but its characterization and treatment are not well understood. Continued study can potentially improve future identification of headache patterns associated with mTBI and lead to better and more effective treatment approaches.

References:

A.I. Scher, A. Finkel, H. Terrio, L. Brenner, P. Feit, T. McFate, S. Lewis, K. Schwab, Headache Disorders in Recently Deployed Soldiers with and without Traumatic Brain Injury, Presentation to Annual Meeting of the American Academy of Neurology, April 2011.

Appendix:

Attachment 1: Poster presented April 2011 at the Annual Meeting of the American Academy of Neurology

Supporting Data

N/A at this time.



Headache Disorders in Recently Deployed Soldiers With and Without Traumatic Brain Injury



Ann I Scher, PhD¹, Alan Finkel, MD², Heidi Terrio, MD, MPH³, Lisa Brenner, PhD⁴,

Preethy Feit MS, MHS¹, Thomas McFate, PhD¹, Steven Lewis, MD², Karen Schwab, PhD⁵

¹Uniformed Services University, ²Womack Army Medical Center, ³Evans Army Community Hospital, ⁴VA Eastern Colorado Healthcare System, ⁵Defense Veterans Brain Injury Center

Introduction

Recent studies (Theeler 2008, 2010) suggest that migraine-like and chronic daily headache are surprisingly common complaints in recently deployed soldiers. The epidemiology, natural history, and phenotypic features of combat-related post-traumatic headache – as distinct from “normal” headache – are uncertain. We describe headache features and pain complaints in a group of recently deployed soldiers with and without mild traumatic brain injury (mTBI). Subjects are the first wave of participants in an ongoing longitudinal study.

Methods

Sampling Frame: Our sampling frame consists of soldiers undergoing routine post-deployment health assessments at Fort Carson, CO. These soldiers had recently returned from deployment in Iraq or Afghanistan and had not been medically evacuated. We recruited a random sample of screen-positive mTBI cases and screen-negative controls based on their answers on a self-administered screen for mTBI. Screen-positive mTBI was defined as reporting a deployment-related injury (fragment, bullet, vehicular, fall, explosion, etc) that was associated with alteration of mental status (e.g. being dazed or confused, not remembering the injury, loss of consciousness, etc).

Study Sample: We report on the first wave of participants in this ongoing study, consisting of 376 soldiers (>95% male, 174 mTBI cases and 202 controls).

Headache Assessment: The headache interview consists of a detailed 31-item self-administered questionnaire consistent with ICHD-II diagnostic criteria. We classified headaches as: migraine with or without aura, probable migraine, and non-migraine headache. We defined chronic daily headache (CDH) as headache of any type on 15 or more days per month, further divided into continuous vs. non-continuous headache.

Aura-like symptoms were screened as follows:

“Some people have changes in their vision before or during their headaches. Have you ever seen things like spots, stars, lines, flashing lights, zigzag lines, or loss of vision with your headaches?”
 “Have you ever had a feeling of numbness or tingling in any part of your body or face with your headaches?”

Typical Aura: Screens positive for visual or sensory aura, had at least two attacks lifetime, aura has gradual onset, aura lasts 15 to 60 minutes. All others screening positive for visual or sensory aura were defined as *atypical aura*.

Other Pain: We report on the (3-month) prevalence of other pain conditions, as assessed with the Chronic Pain Grade (adapted from Von Korff et al, Pain 1992).

Table 1: Results from Self-Administered Headache Questionnaire

	Mild TBI Cases (n=174)	Controls (n=202)	Cases vs. Controls
HEADACHE CLASSIFICATION			
No headache	9%	21%	P<0.005
Non-migraine headache	39%	46%	
Probable migraine	24%	20%	
Migraine	29%	12%	
	100%	100%	
AURA CLASSIFICATION			
No aura	64%	79%	P<0.005
Atypical aura	21%	13%	
Typical aura	15%	7%	
	100%	100%	
CDH CLASSIFICATION			
No CDH	79%	93%	P<0.005
Headache >= 15 days/month	13%	6%	
Continuous Headache	9%	1%	
	100%	100%	
Ever diagnosed with migraine?	17%	32%	P<0.05
*of those with migraine or probable migraine			

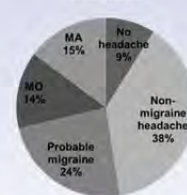
Table 2: Chronic Pain Grade

	Mild TBI Cases (n=174)	Controls (n=202)	Cases vs. Controls
<i>In the last three months, did you have back pain, neck pain, etc (ordered by frequency)</i>			
Headache/migraine	71%	51%	P<0.005
Back	66%	51%	P<0.005
Joint	61%	49%	P<0.05
Neck	51%	34%	P<0.005
Stomach	35%	16%	P<0.005
Facial	17%	12%	
Chest	16%	12%	
Other	6%	8%	
<i>Which pain bothered you the most in the past three months (ordered by frequency)</i>			
Back	34%	34%	P=NS
Headache/migraine	28%	21%	
Joint	23%	26%	
Neck	7%	5%	
Other	3%	6%	
Stomach	1%	5%	
Chest	1%	1%	
Facial	1%	1%	

Results

Most mTBI cases (91%) and controls (79%) reported headache in the past year. Migraine was prevalent in 29% of cases vs. 12% of controls. Typical migraine aura (see methods) was reported in 15% of cases vs. 7% of controls – or in roughly half of migraineurs. Chronic daily headache (15+ days per month but not continuous) was prevalent in 13% of mTBI cases vs. 6% of controls. Continuous CDH was prevalent in an additional 9% of mTBI cases and in 1% of controls. Other pain complaints were common – particularly back, joint, and neck pain. Although headache/migraine was the most commonly reported type of pain in mTBI subjects, back pain was reported to be most bothersome over the last three months.

mTBI Cases



Controls



MO = Migraine without aura; MA = Typical migraine aura
 Non-migraine headache = does not meet criteria for MO, MA, or probable migraine
 No headache = no headache last year

Discussion

Consistent with prior reports, migraine and very frequent headache were highly prevalent in this cohort of recently deployed soldiers, even in the absence of recent head injury. Further exploration of aura-like symptoms and continuous headache as possible diagnostic markers of headache related to mild TBI is warranted. Recruitment and 3-month, 6-month, and 1-year follow-up interviews are ongoing.

Sponsorship

Congressionally Directed Medical Research Programs and the Center for Neuroscience and Regenerative Medicine

UNIFORMED SERVICES UNIVERSITY
 of the Health Sciences